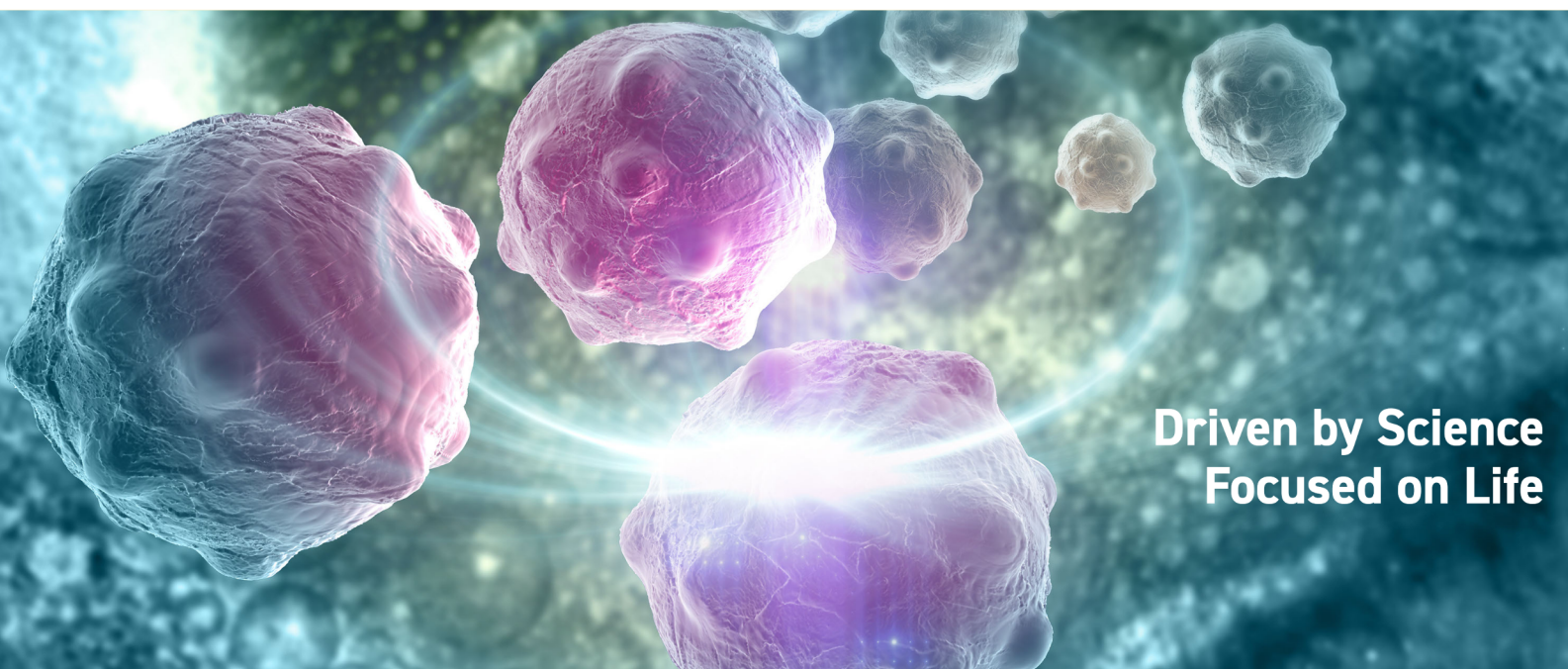
Nuvation Bio

2021 Annual Report



Dear Fellow Stakeholders,

The last two years of the Covid pandemic have illustrated for much of the world, the powerful ability of strong science focused on important unmet medical needs to shape our world and change individual patient destinies. At Nuvation Bio, these are our guiding principles as evidenced by our tag line "Driven By Science and Focused On Life". Our mission is to identify and develop solutions for some of the world's most difficult-to-treat cancers and to bring them to patients as quickly as is humanly possible.

After founding and serving as CEO of Medivation from 2003 until our acquisition by Pfizer in 2016, I was privileged to be able to continue and expand upon the mission we started at Medivation by founding Nuvation Bio in April 2018. Medivation went public via a SPAC merger in December 2004, going on to become one of the most successful SPACs in biotech history. Nuvation Bio was also fortunate to go public via a SPAC merger in February 2021, raising an additional $644 million after a $275 million Series A financing. With our robust pipeline and balance sheet, we feel well-positioned to carry out our mission above.

In 2021, the Nuvation Bio team made significant progress in the clinic for our lead product candidate NUV-422, a cyclin-dependent kinase (CDK) 2/4/6 inhibitor. NUV-422 received IND clearance as well as FDA Fast Track Designation for the treatment of high-grade gliomas, including glioblastoma multiforme, Orphan Drug Designation for the treatment of malignant gliomas, and clearance of two additional IND applications for the treatment of advanced breast cancer and prostate cancer. Throughout 2021, multiple dozens of patients were dosed with NUV-422 in our first-in-human Phase 1 dose escalation study. In 2021, Nuvation Bio's BD2-selective bromodomain and extra-terminal (BET) inhibitor NUV-868 also completed IND-enabling studies and received IND clearance for the treatment of advanced solid tumors. Furthermore, significant progress was made in multiple other preclinical programs, especially the drug-drug conjugate (DDC) platform, where many difficult challenges intrinsic to this extremely complex chemistry were successfully solved.

Additionally in 2021, in spite of the pandemic and a global talent crunch, we succeeded in hiring an elite workforce which we chose to base in both New York City and San Francisco because we concluded that it was more important to have the best talent rather than all employees under one roof. Having offices in the two cities also provided greater flexibility in our evolved remote/in-office hybrid structure that enabled us to recruit and retain top talent. We also adapted to changes in outsourcing trends necessitated by the pandemic to exploit the increased potential efficiency of using multiple remote contract research organizations to reshape our preclinical basic biology and chemistry as well as manufacturing efforts to achieve even higher productivity per unit FTE costs than the previous year and further diversify our risk, perhaps a silver lining to the Covid cloud.

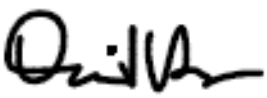
We are well-positioned to build upon this momentum in 2022 and expect to achieve additional milestones across our broad pipeline of novel oncology therapeutic candidates for difficult-to-treat cancers. We look forward to sharing important development updates this year, which we hope will include:

- NUV-422: Completing the Phase 1 dose escalation portion of our ongoing monotherapy Phase 1/2 study of NUV-422 in high grade gliomas, HR+/HER2- advanced breast cancer (aBC) and metastatic castration-resistant prostate cancer (mCRPC), announcing our Recommended Phase 2 Dose and presenting data from our Phase 1 study publicly for the first time. We also plan to initiate a Phase 1b/2 trial for NUV-422 in patients with HR+/HER2- aBC, either alone or in combination with

fulvestrant, and a Phase 1b/2 study for NUV-422 in patients with mCRPC in combination with enzalutamide.

- NUV-868: Initiating a Phase 1 monotherapy dose escalation study of NUV-868 for the treatment of advanced solid tumors.
- Pre-clinical programs: Announcing next milestones for the DDC, Wee1 and A2A programs.

These last two years have been difficult ones. The grueling pandemic, the recent extreme stock market volatility, especially in the healthcare sector, and the many ramifications of the recent Russia-Ukraine conflict have caused profound disruptions in many aspects of our lives. Volodymyr Zelensky has shown the world that great focus and fortitude, strong conviction in doing what's right and having a lot of ammunition can allow even a small nation to accomplish things that were largely unimaginable. Nuvation Bio is also a small group, at currently only 65 employees. But our team of stalwart and expert professionals is absolutely focused on and dedicated to fighting and winning our war with cancer and with a lot of ammunition on our balance sheet (thanks to all of you as our financial supporters), we believe that we are extremely well-positioned to make advancements that many might have considered difficult if not unimaginable. Thanks to all of you for your support and we look forward to keeping you apprised of our further developments.



David Hung, M.D.

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2021

OR

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

FOR THE TRANSITION PERIOD FROM _____ TO _____

Commission File Number 001-39351

NUVATION BIO INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**85-0862255**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
1500 Broadway, Suite 1401 New York, New York	**10036**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (332) 208-6102

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Class A Common Stock, Par Value $0.0001 Per Share	**NUVB**	**New York Stock Exchange**
Warrants to Purchase Class A Common Stock	**NUVB.WS**	**New York Stock Exchange**

Securities registered pursuant to section 12(g) of the Act: None

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ NO ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES ☒ NO ☐

Indicate by check mark whether the Registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer", "accelerated filer", "smaller reporting company", and "emerging growth company" in Rule 12b-2 of the Exchange Act:

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☒
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The aggregate market value of the voting common stock, par value $0.0001 per share, held by non-affiliates of the registrant computed by reference to the closing sales price for the registrant's common stock on June 30, 2021, as reported on the New York Stock Exchange was approximately $1,340,000,971.

In determining the market value of the voting stock held by any non-affiliates, shares of common stock of the registrant beneficially owned by directors and officers have been excluded. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 18, 2022, the registrant had 218,059,125 shares of Class A common stock and 1,000,000 shares of Class B common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

Certain portions of the registrant's definitive proxy statement relating to the Company's Annual Meeting of Stockholders, to be filed with the Securities and Exchange Commission within 120 days of the registrant's fiscal year ended December 31, 2021, are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated.

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CAUTIONARY INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K for the year ended December 31, 2021, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which are subject to the "safe harbor" created by those sections, concerning our business, operations, and financial performance and condition as well as our plans, objectives, and expectations for business operations and financial performance and condition. Any statements contained herein that are not of historical facts may be deemed to be forward-looking statements. You can identify these statements by words such as "anticipate," "assume," "believe," "could," "estimate," "expect," "intend," "may," "plan," "should," "will," "would," and other similar expressions that are predictions of or indicate future events and future trends. These forward-looking statements are based on current expectations, estimates, forecasts, and projections about our business and the industry in which we operate and management's beliefs and assumptions and are not guarantees of future performance or development and involve known and unknown risks, uncertainties, and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this Annual Report on Form 10-K may turn out to be inaccurate. Factors that could materially affect our business operations and financial performance and condition include, but are not limited to, those risks and uncertainties described herein under "Item 1A—Risk Factors." You are urged to consider these factors carefully in evaluating the forward-looking statements and are cautioned not to place undue reliance on the forward-looking statements. The forward-looking statements are based on information available to us as of the filing date of this Annual Report on Form 10-K. Unless required by law, we do not intend to publicly update or revise any forward-looking statements to reflect new information or future events or otherwise. You should, however, review the factors and risks we describe in the reports we will file from time to time with the Securities and Exchange Commission, or the SEC, after the date of this Annual Report on Form 10-K.

SUMMARY RISK FACTORS

Below is a summary of material factors that make an investment in our securities speculative or risky. Importantly, this summary does not address all of the risks and uncertainties that we face. Additional discussion of the risks and uncertainties summarized in this risk factor summary, as well as other risks and uncertainties that we face, can be found under the section titled "*Risk Factors*" in Item 1A of this Annual Report on Form 10-K. The below summary is qualified in its entirety by that more complete discussion of such risks and uncertainties. You should consider carefully the risks and uncertainties described in the section titled *"Risk Factors*" as part of your evaluation of an investment in our securities:

- We have a limited operating history and have incurred significant losses since inception and anticipate that we may continue to incur losses for the foreseeable future, and may never achieve or maintain profitability.
- We will need substantial funding to pursue our business objectives. If we are unable to raise capital when needed or on favorable terms, we could be forced to delay, reduce or terminate our product development, other operations or commercialization efforts. Additionally, raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish proprietary rights.
- If we do not obtain regulatory approval for and successfully commercialize our product candidates in one or more indications or we experience significant delays in doing so, we may never generate any revenue or become profitable.
- Our approach to the discovery and development of product candidates based on our Drug-Drug Conjugate platform is unproven and is based on novel technology, and we do not know whether we will be able to develop any products of commercial value, or if competing technological approaches will limit the commercial value of our product candidates or render our platform obsolete.
- Clinical trials are very expensive, time-consuming and difficult to design and implement, and involve uncertain outcomes. Furthermore, results of earlier preclinical studies and clinical trials may not be predictive of results of future preclinical studies or clinical trials.
- We may encounter substantial delays in our preclinical studies or clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

- If any of our product candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, its ability to market the drug could be compromised.
- We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or at the commercial stage, and our product liability insurance may not cover all damages from such claims.
- We have never commercialized a product candidate and we may lack the necessary expertise, personnel and resources to successfully commercialize any of our products that receive regulatory approval on our own or together with collaborators.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- Even if we obtain regulatory approval for our product candidates, they will remain subject to ongoing regulatory oversight.
- We rely on third parties to perform the chemistry work associated with our drug discovery and preclinical activities and to conduct our preclinical studies and future clinical trials, and our business could be substantially harmed if these third parties cease performing services or perform in an unsatisfactory manner.
- We do not have our own manufacturing capabilities and will rely on third parties to produce clinical and commercial supplies of NUV-422 and our other current and future product candidates.
- If we are not able to establish collaborations, we may have to alter some of our future development and commercialization plans. If we are not able to establish further collaborations, we may have to alter some of our future development and commercialization plans.
- Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors and customers will be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, health information privacy and security laws and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.
- If we are unable to obtain, maintain, protect and enforce sufficient patent and other intellectual property rights for our product candidates and technology, or if the scope of patent and other intellectual property rights obtained is not sufficiently broad, we may not be able to compete effectively in our market.
- Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.
- We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful, and issued patents covering our technology and product candidates could be found invalid or unenforceable if challenged.
- Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could negatively impact the success of our business.
- Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.
- Our business, operations and clinical development plans and timelines and supply chain could be adversely affected by the effects of health epidemics, including the ongoing COVID-19 pandemic, on the manufacturing, clinical trial and other business activities performed by us or by third parties with whom we conduct business, including our CMOs, CROs, shippers and others.
- Our future success depends on our ability to retain Dr. Hung and our other key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

- The dual-class structure of our common stock has the effect of concentrating voting power with our Chief Executive Officer, which limits other stockholders' ability to influence the outcome of important transactions, including a change in control.

PART I

Item 1. Business.

Business Combination of Panacea Acquisition Corp. and Nuvation Bio Inc.

On February 10, 2021, (the "Closing Date"), Nuvation Bio Inc., a Delaware corporation ("Legacy Nuvation Bio"), Panacea Acquisition Corp. ("Panacea"), and Panacea Merger Subsidiary Corp, a Delaware corporation and a direct, wholly owned subsidiary of Panacea ("Merger Sub") consummated the transactions contemplated by an Agreement and Plan of Merger among them dated October 20, 2020 ("Merger Agreement").

Pursuant to the terms of the Merger Agreement, a business combination of Panacea and Legacy Nuvation Bio was effected through the merger of Merger Sub with and into Legacy Nuvation Bio, with Legacy Nuvation Bio surviving as a wholly owned subsidiary of Panacea (the "Merger"). On the Closing Date, Legacy Nuvation Bio changed its name to Nuvation Bio Operating Company Inc. and Panacea changed its name to Nuvation Bio Inc. (the "Company" or "Nuvation Bio").

In connection with the closing of the Merger, our Class A common stock and warrants to purchase shares of our Class A common stock began trading on The New York Stock Exchange under the symbols "NUVB" and "NUVB.WS," respectively, on February 11, 2021. The disclosure in Items 1 and 1A of this report gives effect to the Merger and includes the operations of Legacy Nuvation Bio prior to the Merger.

Business Overview

Nuvation Bio is a clinical-stage biopharmaceutical company developing differentiated and innovative therapeutic candidates focused on treating patients with the most difficult-to-treat cancers, for which conventional therapies have failed. We are advancing up to six wholly owned compounds that have resulted from our drug discovery and development programs, which include NUV-422 a cyclin-dependent kinase ("CDK") inhibitor, NUV-868 a bromodomain and extra-terminal ("BET") inhibitor, NUV-569 a Wee1 inhibitor, an A2A adenosine receptor inhibitor program, and a drug-drug conjugate ("DDC") platform.

We were founded in 2018 by our chief executive officer, David Hung, M.D., who founded Medivation, Inc. and led its successful development of oncology drugs Xtandi® and talazoparib (now marketed as Talzenna®), leading to its $14.3 billion sale to Pfizer Inc. ("Pfizer") in 2016.

We leverage our team's extensive expertise in medicinal chemistry, preclinical discovery, manufacturing, drug development and commercialization to bring forward novel small molecules that improve the activity and overcome the liabilities of currently marketed drugs to address major unmet needs in oncology.

The foundations of our approach include:

- ***The pursuit of validated targets***: We identify and pursue oncology targets validated by strong clinical or preclinical data that provide a high degree of confidence in generating clinically meaningful benefit. We focus on targets where there has been some progress by others in generating clinical candidates or FDA-approved drugs, and we then attempt to design novel therapeutic candidates to overcome the encountered safety liabilities or limitations in efficacy. As an example, in preclinical studies, our lead product candidate, NUV-422, has demonstrated improvements in potency and selectivity of the CDK target class to reduce off-target toxic effects and to overcome specific drug-resistance mechanisms and improve anti-tumor activity.
- ***Innovative medicinal chemistry expertise***. We use our medicinal chemistry proficiency to generate differentiated therapeutic candidates, focused on improving their safety, anti-tumor activity and pharmacologic profiles over other standard of care ("SOC") therapies. We also use innovative medicinal chemistry approaches to generate novel classes of molecules such as our DDCs.

- ***Human capital management***: We believe our employees are our greatest assets, and we recognize that attracting, motivating and retaining talent at all levels is vital to our continued success. We are building a culture that fosters a productive, professional and inclusive work environment, where our employees can thrive, have fun, and be inspired to perform their best work.

The following table summarizes our product candidate pipeline:

Program	Product Candidate	Potential Indication(s)		Current Stage				Anticipated Milestones
				Preclinical	Phase 1	Phase 2	Phase 3	
CDK 2/4/6	NUV-422	Glioblastoma	Recurrent GB					Phase 1 Dose Escalation Data by Year- End 2022; Phase 2 Initiation by Year- End 2022
		Breast Cancer	2L + aBC Monotherapy					Phase 2 Initiation by Year- End 2022
			2L+ aBC Brain Metastases					Phase 2 Initiation by Year- End 2022
			2L/3L aBC + Fulvestrant					Phase 1b Initiation Mid-2022
		Prostate Cancer	mCRPC Monotherapy					Phase 2 Initiation by Year- End 2022
			mCRPC + Enzalutamide					Phase 1b Initiation Mid-2022
BET	NUV-868	Advanced Solid Tumors						Phase 1 Initiation Mid-2022
WEE1	NUV-569	Advanced Solid Tumors						IND Submission by Year- End 2022
Adenosine Antagonist	A2A	Advanced Solid Tumors with Immuno-Oncology						Clinical Candidate Selection by Year- End 2022
Drug-Drug Conjugate (DDC) Platform	DDC	Solid Tumors						Clinical Candidate Selection by Year- End 2022

2L: Second Line; A2A: A2A Adenosine Receptor Inhibitor; aBC: Advanced Breast Cancer; BET: Bromodomain and Extra-Terminal Motif Proteins; CDK: Cyclin-Dependent Kinase; GB: Glioblastoma; mCRPC: Metastatic Castration Resistant Prostate Cancer; NUV: Nuvation Bio

Our lead product candidate, NUV-422, is a selective small molecule inhibitor of CDK 2, 4 and 6. Relative to currently approved CDK4/6 inhibitors, NUV-422 also targets CDK2, a cell cycle checkpoint altered in multiple tumor types including high-grade gliomas, breast cancer and prostate cancer. NUV-422 has been designed to limit CDK1 inhibition, a potential cause of toxicity, and has shown favorable blood-brain barrier penetration in preclinical studies. We believe that a CDK2/4/6 inhibitor that limits CDK1 inhibition can bring greater benefit to a broader patient population. In October 2020, the U.S. Food and Drug Administration ("FDA") cleared our first investigational new drug ("IND") application for NUV-422 to treat high-grade gliomas and we initiated a Phase 1/2 clinical trial for this indication in December 2020. In December 2021, the FDA cleared two additional INDs for NUV-422 for the treatment of advanced breast cancer ("aBC") and for the treatment of prostate cancer, respectively. Additional trials and trial expansion are planned for NUV-422 in 2022. The FDA granted Orphan Drug Designation to NUV-422 for the treatment of malignant gliomas and Fast Track Designation for the treatment of high-grade gliomas.

Our second product candidate is NUV-868, a BD2-selective oral small molecule BET inhibitor. NUV-868 inhibits the protein BRD4, a key member of the BET family that epigenetically regulates a number of important proteins that control tumor growth and differentiation, including oncogenes such as c-myc. Notably, BET proteins have critical biological functions and are found to be altered in many human cancers (Bechter and Schoffski, 2020). We have designed NUV-868 to potentially reduce the therapeutic limiting toxicities of BRD4 inhibitors currently in development by optimizing BD2 versus BD1 selectivity. NUV-868 is almost 1,500 times more selective for BD2 than BD1. Non-selective BD1/2-inhibitors in development have been associated with tolerability issues, potentially due to BD1 inhibition, especially in the gastrointestinal ("GI") tract and bone marrow (Faivre et al 2020). NUV-868 in combination with androgen receptor-directed therapies may help to overcome resistance in prostate cancer. In addition, NUV-868 in combination with PARP inhibitors may have synergistic activity to increase efficacy across multiple solid tumors. In January 2022, the FDA cleared an IND for NUV-868 for the treatment of advanced solid tumors, and we intend to initiate a Phase 1 trial for this indication in mid-2022.

We are also developing several other therapeutic candidates, including NUV-569. NUV-569 is a differentiated oral small molecule selective inhibitor of Wee1 kinase, an important regulator of DNA damage repair. Wee1 inhibitors increase the efficacy of DNA-damaging therapies by forcing cancers to replicate before they can repair their damaged DNA. Inhibition of this kinase can cause a tumor cell to divide before it has finished repairing its DNA, causing catastrophic DNA damage and programmed cell death. NUV-569 is designed to limit off-target effects by improving its kinase selectivity, which may improve tolerability including reduction of bone marrow and GI toxicity. Because Wee1 inhibitors synergize with DNA-damaging therapies like radiation and certain types of chemotherapy to increase

anti-tumor activity, Wee1 inhibitors like NUV-569 may have wide applicability in treating many different types of cancer. We intend to submit an IND for NUV-569 by the end of 2022 and initiate Phase 1 trials in patients with advanced solid tumors following IND clearance. We are also continuing to evaluate additional Wee1 inhibitors for the potential to increase efficacy and further widen the therapeutic window.

Our adenosine receptor inhibitors are designed to have high affinity for the A_{2A} adenosine receptor, which plays multiple critical roles in human physiology and pathophysiology including anti-cancer immunity. Accumulation of adenosine in the tumor microenvironment may be a critical factor in limiting the activity of currently available immuno-oncology drugs, including anti-PD(L)1 drugs and anti-cancer chimeric antigen receptor T cells. Thus, targeting the adenosine receptor may overcome this blockade, leading to improved anti-cancer activity in tumors which are resistant to immuno-oncology drugs and adoptive T cell therapies. We intend to nominate a clinical development candidate by the end of 2022.

Our DDC platform is a novel therapeutic approach within the drug-conjugate class of anti-cancer therapies with parallels to Antibody-Drug Conjugates ("ADCs"). ADCs have been effective treatments in oncology, with ten drugs approved by the FDA and an estimated $11.0 billion in worldwide sales expected in 2023. We believe our DDC candidates could expand the therapeutic potential for the drug-conjugate class due to inherently differentiated properties versus ADCs, including a simpler manufacturing process, the potential to cross the cell membrane and recognize intracellular targets, and the potential for oral or intravenous ("IV") dosing. We are designing DDCs to selectively deliver potent anti-cancer therapeutics to cancer cells to exert greater toxicity against these target tumor cells than against healthy non-target tissues. Utilizing this platform, we are able to conjugate tissue-selective targeted small molecules with anti-tumor agents to create unique therapeutic candidates. We have accomplished this by synthetically fusing a proven anti-cancer small molecule drug to a second small molecule that selectively binds distinct receptors that are preferentially expressed in cancer cells. These tissue-specific receptors create a "sink" that not only may concentrate the targeted drug in cancer cells but may also magnify the effects of the drug in those cells, while preventing similar effects in cells that do not express the targeted receptor. We believe this would allow our DDC candidates to limit some of the adverse effects commonly seen with many cancer drugs, such as bone marrow suppression and GI toxicity. Because this program at its core fuses the active sites of two or more small molecules to each other to generate a new small molecule with improved activity and targeted specificity, they are called DDCs. We intend to nominate a DDC clinical development candidate by year end 2022.

Strategy

We strive to deliver meaningful benefit to patients with serious unmet medical needs in oncology by developing novel and differentiated therapies. The core elements of our strategy include:

- ***Rapidly advance the development of our lead product candidate, NUV-422, a CDK2/4/6 inhibitor, toward regulatory approval for the treatment of various cancers.*** We have advanced NUV-422 through preclinical studies that have informed a robust clinical development plan. We plan to explore NUV-422 both as a monotherapy and in combination with SOC agents. In December 2020, we began a monotherapy Phase 1/2 study (Protocol NUV-422-02) for NUV-422 in high-grade gliomas and later amended the protocol in the second quarter of 2021 to include hormone receptor-positive/human epidermal growth factor receptor-2-negative locally advanced or metastatic breast cancer (HR+ HER2- aBC) and metastatic castration-resistant prostate cancer ("mCRPC"). This Phase 1/2 study (NUV-422-02) includes expansion cohorts in glioblastoma, HR+ Her2- aBC with and without active brain metastases and mCRPC that will begin in 2022. NUV-422-02 also includes a pre-surgical sub-study in patients with recurrent glioblastoma to evaluate NUV-422 concentrations and pharmacodynamic effects in brain tumor tissue. In addition, in 2022, we plan to initiate a Phase 1b/2 combination study with fulvestrant in patients with HR+ HER2- aBC who have received prior hormonal therapy combined with an approved CDK 4/6 inhibitor, as well as a Phase 1b/2 combination study with enzalutamide in patients with mCRPC who have received prior treatment with abiraterone acetate. We are evaluating other potential indications and clinical studies for NUV-422.
- ***Advance our deep oncology pipeline of novel and differentiated therapeutic candidates developed against clinically validated targets.*** We design our product candidates to have optimized properties including their ability to limit specific adverse effects of competitive compounds and/or to enhance their anti-tumor potential by targeting additional drivers of tumor resistance. Overall, in addition to the three INDs already submitted and cleared for NUV-422 and the initial IND cleared for NUV-868, we

anticipate submitting multiple IND applications to the FDA over the next six years to expand and move our programs forward. We plan to advance NUV-868, a BD2-selective oral small molecule BET inhibitor, into the clinic by mid-2022 and to submit an IND for NUV-569, a differentiated oral small molecule selective inhibitor of Wee1 kinase, by year end 2022.

- ***Advance candidates from our DDC platform to expand our oncology-focused pipeline.*** We are developing a pipeline of new chemical entities that leverage the tissue-specific targeting capabilities of small molecule nuclear hormone receptor binders, including androgen and estrogen receptor binders, fused to warheads that include PARP inhibitors and known chemotherapeutic agents. We intend to nominate a DDC clinical development candidate by year end 2022.
- ***Continue to leverage our deep insights in medicinal chemistry to pursue innovative clinical candidates.*** We have established medicinal chemistry expertise that have enabled us to rapidly pursue our current pipeline and platform. We intend to leverage these capabilities to pursue both new and validated targets in patients with serious unmet medical needs.
- ***Evaluate strategic opportunities to accelerate development timelines and maximize value of our product candidate pipeline.*** We currently own the exclusive worldwide development and commercial rights to each of our product candidates. We intend to evaluate collaborations that could maximize the value of our product candidate pipeline, either through the evaluation of our product candidates in combination with compounds owned by third parties or through geographic collaborations outside of the U.S. that allow us to leverage the existing infrastructure of other companies.
- ***Build a fully integrated global oncology company.*** We intend to continue building a fully integrated research, development and commercialization focused company. Our team's track record of success underscores their proven expertise in discovering, developing and delivering innovative medicines to patients. If our therapeutic candidates are approved, we intend to establish a focused commercial infrastructure and selectively expand our global commercial capabilities.

Programs

Overview of NUV-422: CDK2/4/6 Inhibitor Program

Our lead product candidate, NUV-422, is a potent and selective small molecule inhibitor targeting CDK2, CDK4 and CDK6. These are members of the CDK family of proteins that play a critical role in the regulation of tumor growth. Inhibition of cell cycle kinases CDK4 and CDK6 results in significant therapeutic effect in patients with HR+ HER2- aBC, and these results have led to the approvals of three CDK4/6 inhibitors, palbociclib, ribociclib and abemaciclib. Although these advancements have greatly expanded the treatment options for breast cancer patients, insensitivity to CDK4/6 inhibition has been found in some patients with primary or acquired resistance. As a result, therapeutic resistance and disease progression continue to limit the efficacy and duration of clinical benefit of these therapies. One known mechanism by which some breast cancer patients become resistant to currently approved CDK inhibitors is through CDK2 signaling, which allows cancer cells to bypass CDK4/6 inhibition. Beyond breast cancer, CDK2 activation is known to drive tumorigenesis in multiple solid tumors including brain cancer and prostate cancer, and increased CDK2 activity is associated with lower overall patient survival and recurrence. NUV-422 selectively inhibits CDK4/6, similar to the approved CDK4/6 inhibitors, but also potently inhibits CDK2. Since its initial discovery in our chemistry program, we have advanced NUV-422 through preclinical studies and have initiated clinical studies in multiple advanced solid tumors, including recurrent/refractory glioblastoma, HR+ HER2- aBC with and without active brain metastases, and mCRPC. We are exploring NUV-422 as both a monotherapy and in combination with SOC agents. We began a monotherapy Phase 1/2 study (Protocol NUV-422-02) in December 2020 in high-grade gliomas and later amended the protocol in the second quarter of 2021 to include HR+ HER2- aBC and mCRPC. We are continuing to enroll patients in the monotherapy Phase 1 dose escalation portion of the study and data from this portion of the study is expected to be shared in the second half of 2022. The FDA granted Orphan Drug Designation to NUV-422 for the treatment of malignant gliomas and Fast Track Designation for the treatment of high-grade gliomas.

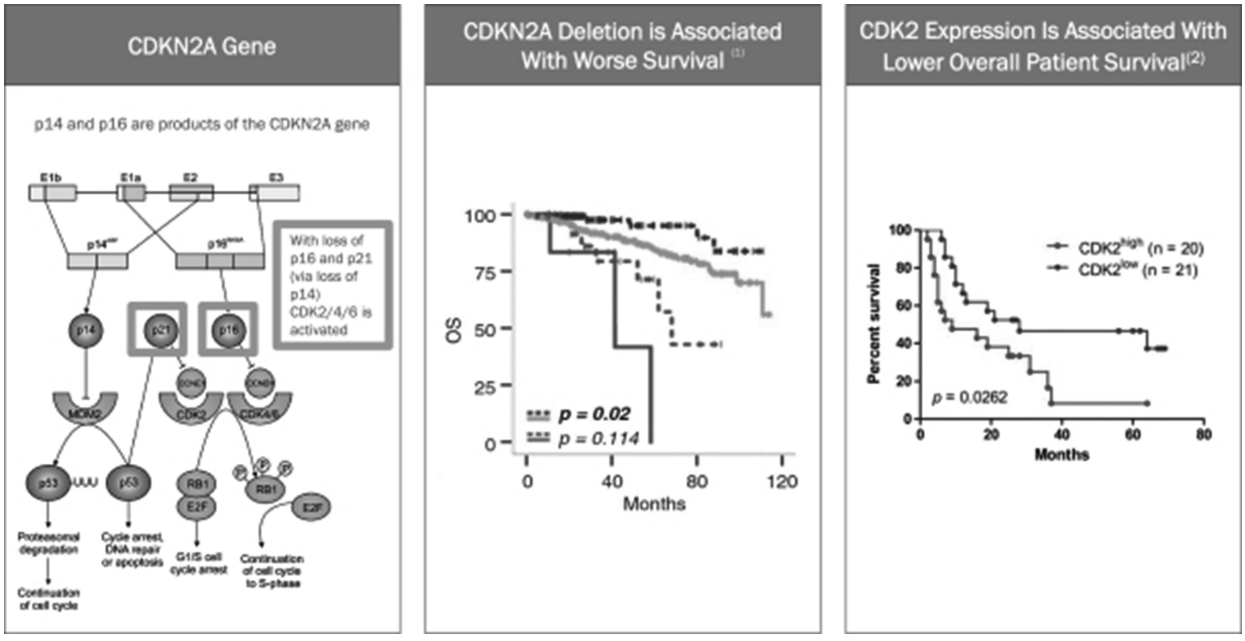
CDK2 as a novel mechanism of resistance to standard therapies and an oncogenic driver in multiple cancers

The CDK family of proteins regulates cell cycle progression and transcriptional regulation. Recent advances in treatments using CDK inhibitors have focused on inhibition of CDK4 and CDK6, but preclinical studies and clinical

trials suggest CDK2 may play an important role as a driver of tumor cell growth and an underlying mechanism of both primary and acquired resistance to CDK4/6 inhibitors. CDK2 is an essential regulator of cell division and multiple events within the cell cycle, including centrosome duplication, DNA synthesis and G1-to-S-phase transition. CDK2 can bind both cyclin E and cyclin A, which play roles in the cell cycle. Cyclin D typically binds CDK4/6 and is thus a target of CDK4/6 inhibitors, but in the absence of CDK4/6, cyclin D can activate CDK2, which subsequently drives cell cycle progression.

We believe that CDK2 plays a key role in patients who either do not respond to current therapies or develop primary or secondary resistance to ongoing treatment. We and others have shown that CDK2 function can drive multiple cancers, including in gliomas, breast cancer and prostate cancer. CDK2 expression is elevated in multiple patient tumor tissues, and increased CDK2 expression correlates with a worse survival outcome (Tadasse, et al 2020, Wang et al 2016). It was also recently shown that nearly 70% of high-grade glioma patients carry a homozygous deletion of *CDKN2A*, which encodes for p14 and p16, which are tumor suppressors that inhibit CDK4/6 directly and CDK2 through p21 (Reinhardt, et al 2018, Verhaak, et al 2010). These results, some of which are depicted in the diagram and graphs below, suggest that targeting CDK2, in addition to CDK4/6 in these cancers may lead to a blockade of an important aberrant mechanism of tumor growth and resistance to therapy leading to an improvement of clinical outcomes.

CDKN2A-DELETION DRIVES PRIMARY HIGH-GRADE GLIOMAS

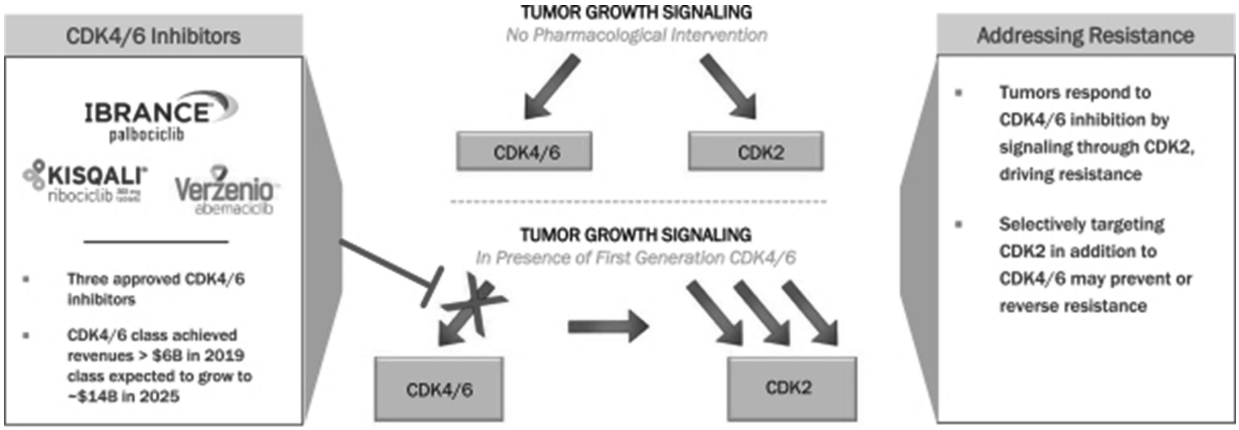


(1) Appay et al., 2020

(2) Wang et al., 2016

In addition to primary resistance and *de novo* tumorigenesis, there are preclinical and clinical data suggesting that CDK2 may be involved in acquired resistance to cancer therapy. Metastatic breast cancer patients enrolled in the PALOMA-3 study who did not benefit from palbociclib therapy demonstrated overexpression of c-myc and cyclin E1 (Turner et al 2018). Since c-myc acts upstream to activate CDK2 and cyclin E1 binds CDK2 to drive the cell cycle, these results suggest CDK2 may be responsible for tumor resistance to palbociclib treatment. Taken together, these preclinical and clinical data demonstrate that CDK2 plays a unique role in promoting tumor growth in multiple types of cancer and that targeting CDK2 in addition to CDK4/6 may help patients overcome the CDK2-mediated resistance to approved therapies, including palbociclib and other CDK4/6 inhibitors.

CDK2 DRIVES RESISTANCE TO CDK4/6 INHIBITORS



Limitations of Other CDK Inhibitors

While CDK4/6 inhibitors demonstrated significant clinical benefit in patients with hormone-receptor-positive breast cancer including an improvement in overall survival, emerging preclinical and clinical evidence suggests that targeting CDK2 in addition to CDK4/6 may provide further benefit to cancer patients whose tumors may be driven by CDK2. These may include breast cancer that does not benefit from treatment with approved CDK4/6 inhibitors and other cancers wherein CDK2 dysregulation may contribute to tumor growth and worse clinical outcomes. It has been reported that of the three CDK4/6 inhibitors approved by the FDA for the treatment of patients with hormone receptor-positive breast cancer (ribociclib, palbociclib, abemaciclib), only abemaciclib demonstrated some anti-CDK2 activity, albeit extremely weak activity, in the hundreds of nanomolar half-maximal inhibitory concentration ("IC50") range (Chen, et al, 2016). The IC50 is a measure of how much of a particular drug or other substance (inhibitor) is required for 50% inhibition of a specific biological or biochemical function, and IC50 values in the hundreds of nanomolar range are considered a sign of relatively weak inhibition. As evidenced by the recently reported divergent outcomes in the breast cancer adjuvant trials of palbociclib (PALLAS and PENELOPE-B studies) and abemaciclib (MonarchE study), patients who received treatment with abemaciclib experienced significant improvement in invasive disease-free survival and distant relapse-free survival (Johnston, et al, 2020), while no such effect was reported for patients in palbociclib trials (Mayer, et al 2020). Moreover, only abemaciclib received approval by the FDA as monotherapy for metastatic breast cancer patients, while ribociclib and palbociclib are only approved in combination with hormonal therapy, suggesting a potential benefit of even weak CDK2 inhibition in addition to CDK4/6 inhibition.

We and others have shown that it is critical to target CDK2, CDK4 and CDK6, while limiting CDK1 inhibition, which is a ubiquitously expressed CDK, the inhibition of which is known to cause severe toxicities in animal models and in patients. Dinaciclib is a potent inhibitor of CDK1 in addition to CDK2 with IC50 for both in the low nanomolar range, indicating strong inhibition. When tested as a once weekly intravenous infusion in a clinical trial (Nemunaitis, et al 2013), despite early signs of anti-tumor activity, 60% of patients experienced grade 3-4 adverse events, including nausea, vomiting, liver enzyme elevation, hyperbilirubinemia and hematological adverse events (neutropenia, anemia). Consequently, clinical development of dinaciclib has been discontinued.

To our knowledge, there is one clinical-stage CDK2/4/6 inhibitor:

- PF-06873600 (Pfizer) is a CDK2/4/6 inhibitor in a Phase 2 clinical trial being evaluated as a monotherapy and in combination with fulvestrant. While PF-06873600 inhibits CDK2/4/6, it also strongly inhibits CDK1 with an IC50 in the single-digit nanomolar range, which could result in a poor therapeutic index. We believe that limiting CDK1 inhibition is critical to developing a safe and efficacious next-generation CDK inhibitor drug.

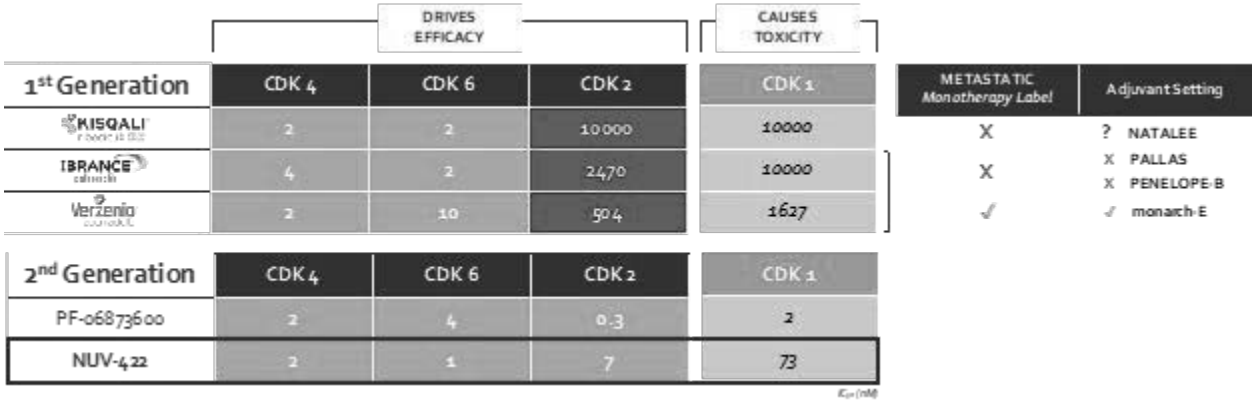
In addition to a CDK2/4/6 inhibitor, Pfizer is also developing a CDK2-selective inhibitor (PF-07104091) which is being combined with palbociclib (CDK4/6 inhibitor) in HR+HER2- aBC validating the approach of inhibiting CDK2 in addition to CDK4 and CDK6.

NUV-422 Differentiation

NUV-422 is a next-generation CDK inhibitor discovered in our chemistry program, which potently inhibits CDK2, CDK4 and CDK6, while limiting CDK1 inhibition as shown in the table below. NUV-422 is approximately equal to approved drugs ribociclib, palbociclib and abemaciclib in its ability to inhibit CDK4 and CDK6, but it additionally inhibits CDK2, like PF-06873600. But importantly, unlike PF-06873600, NUV-422 does not potently inhibit CDK1, demonstrating at least a 10-fold lower IC50 for CDK1 than CDK2, but even greater than that for CDK4/6. We believe this positions NUV-422 as a promising next-generation CDK inhibitor with superior CDK2/4/6 vs CDK1 selectivity. In preclinical studies, we have shown that NUV-422 exhibits good drug-like properties, with oral bioavailability, suitable pharmacokinetic and drug metabolism profiles, and a nonclinical safety profile consistent with the class of CDK4/6 inhibitors, as well as a scalable manufacturing process. We have shown that NUV-422 demonstrates strong anti-proliferative activity across multiple human cancer cells.

NUV-422: POTENT INHIBITOR OF CDK2/4/6

IC50 Values: Lower value indicates stronger inhibition



Our Current Opportunities for NUV-422

Overview of Recurrent or Refractory High-Grade Gliomas

Cancer is the second leading cause of mortality in the U.S. and accounts for nearly one in four deaths. Primary tumors of the central nervous system ("CNS") remain among the most difficult to treat, with a 5-year overall survival of approximately 35%. Gliomas represent 75% of malignant primary brain tumors and glioblastoma multiforme ("GBM") accounts for over half of all gliomas. Compared to other areas of oncology, relatively few advances have been made in the treatment of brain cancers. Temozolomide ("TMZ") is commonly used in front-line settings in combination with radiation, and it was first approved more than fifteen years ago in 2005. Bevacizumab approval soon followed in 2009 for recurrent GBM, but its use remains controversial due to conflicting clinical trial results. Consequently our initial proposed indication, recurrent or refractory high-grade gliomas, remains a significant unmet medical need with the first *de facto* option for recurrent GBM patients being clinical trials. Based on the preclinical data we have generated and clinical data others have generated, including patient biopsy, genetic sequencing and survival data, there is a strong biological rationale for targeting CDK2 in gliomas, including GBM. Coupled with preclinical data demonstrating preferential accumulation of NUV-422 in the brain without evidence of CNS toxicity, we believe that NUV-422 has the potential to bring significant clinical benefit to high-grade glioma patients.

Clinical Rationale for Targeting CDK2/4/6 in Gliomas

There is evidence suggesting CDK inhibition may be a promising therapeutic strategy in gliomas due to the role of CDKN2A deletion and CDK2 overexpression. Loss of CDKN2A occurs in majority of GBM (Brennan et al 2013). CDKN2A deletion and CDK2 overexpression are associated with worse survival in primary high-grade gliomas

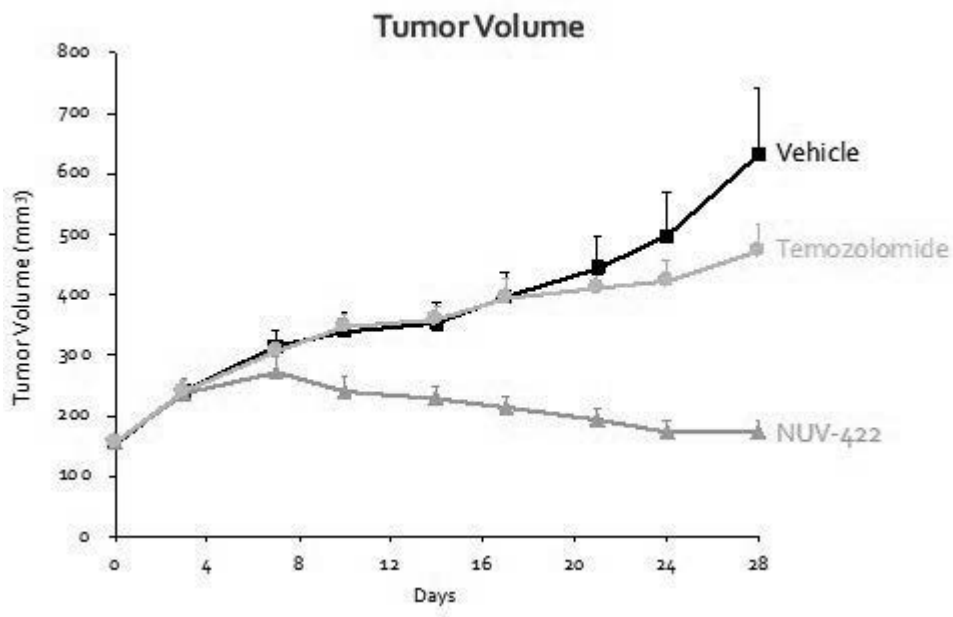
(Appay et al., 2020, Wang et al., 2016). Abemaciclib (a potent inhibitor of CDK4/6 and weak inhibitor of CDK2) demonstrated an improvement of PFS in ND GBM patients in Phase 2 (Wen et al, 2021).

Preclinical Data

The *in vitro* anti-proliferative activity of NUV-422 was evaluated in six glioma cell lines, five of which have known CDKN2A deletions. Treatment with NUV-422 resulted in dose-dependent growth inhibition of all six glioma cell lines, with mean absolute IC50 values in the nanomolar range.

The *in vivo* antitumor activity of NUV-422 and TMZ was evaluated in a cell line-derived xenograft model, which harbors a CDKN2A deletion, implanted subcutaneously in the flank of immunocompromised mice. NUV-422 was administered orally once daily ("QD") at 30 mg/kg. NUV-422 treatment resulted in reduced tumor volume ($p < 0.0001$) of tumors compared to the vehicle-treated group. In contrast, SOC TMZ had no significant effect on tumor growth compared to the vehicle-treated group. These results are illustrated in the following chart.

NUV-422 INHIBITS TUMOR GROWTH BETTER THAN SOC TMZ IN GLIOBLASTOMA XENOGRAFT MODEL



Following a single 30 mg/kg and 100 mg/kg oral dose of NUV-422 in rats, the brain-to-plasma concentration ratios at six hours post-dose ranged from 11 to 12. These data, set forth in the following table, demonstrate high blood-brain barrier ("BBB") penetration of NUV-422.

HIGH CONCENTRATIONS OF NUV-422 IN THE BRAIN

NUV-422 Concentration Six Hours Post Dose (Rat)

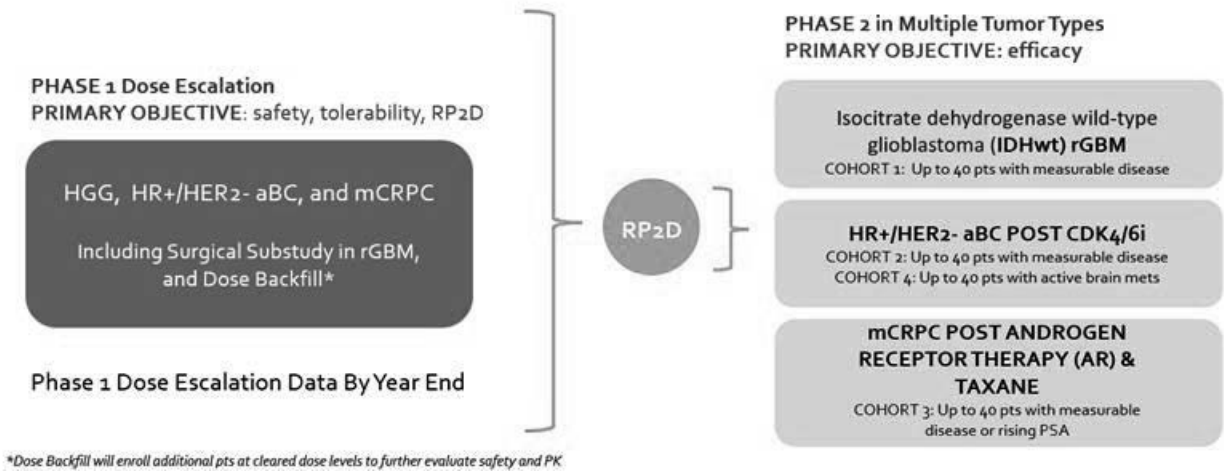
Dose (mg/kg)	Brain Conc (nM)	Plasma Conc (nM)	Brain / Plasma Ratio
30	4096	375	11
100	5827	506	12

Clinical Development Plan for NUV-422 in Brain Tumors

We have successfully completed IND-enabling studies of NUV-422, our lead product candidate. The molecule has favorable pharmacological properties with a wide therapeutic index and has demonstrated a consistent nonclinical safety profile supportive of advancement into clinical trials. Most importantly, based on preclinical data, NUV-422 is unique among CDK inhibitors in that it is much more brain-penetrant and maintains a longer half-life in the brain than in the plasma, approximately 12 times the exposure in the brain compared to the plasma. We believe these characteristics will allow NUV-422 to more potently engage the intended targets in brain tumors compared to other CDK inhibitors that have been tested in brain tumors to date.

In October 2020, the FDA accepted our first IND application for NUV-422 for the treatment of patients with high-grade gliomas, including GBM. In December 2020, we began a monotherapy Phase 1/2 study (Protocol NUV-422-02) in high-grade gliomas and later amended the protocol in the second quarter of 2021 to include HR+ HER2- aBC (with and without brain metastases) and mCRPC. We are continuing to enroll patients in the monotherapy Phase 1 dose escalation portion of the study and data from this portion of the study is expected to be shared in the second half of 2022. After the determination of the recommended Phase 2 dose, the Phase 2 portion will enroll recurrent GBM,HR+ HER2- aBC, and mCRPC patients. This study is designed to evaluate safety and efficacy of NUV-422 as a monotherapy in these advanced solid tumors. This trial design is depicted below.

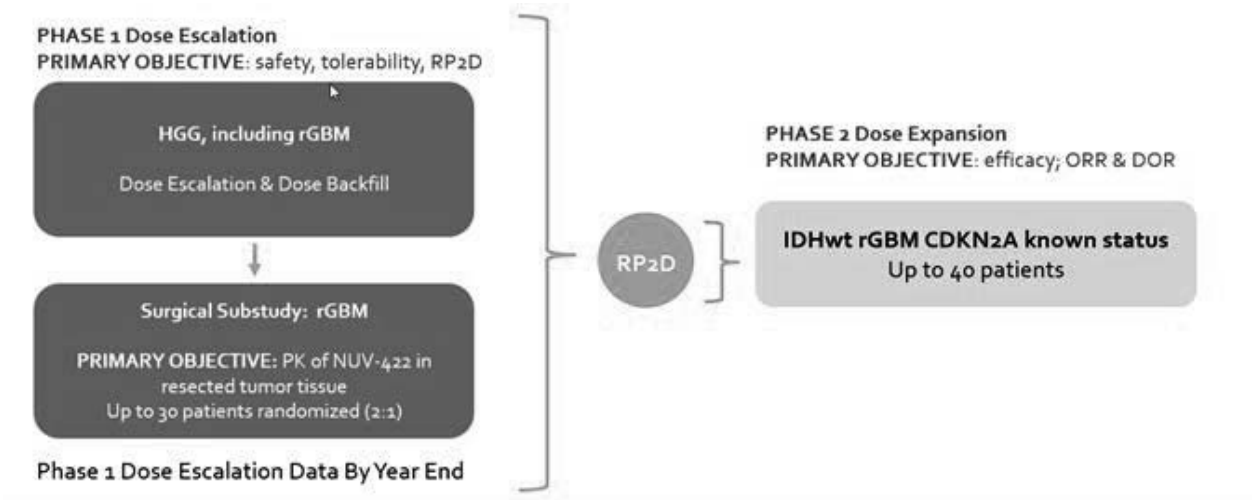
NUV-422-02: Seamless Phase 1/2 Trial Design



As part of the Phase 1 portion of the NUV-422-02 study, a surgical sub-study will be initiated to characterize the pharmacokinetics of NUV-422 in resected tumor tissue. In this sub-study, thirty patients with recurrent IDH-WT GBM requiring surgery per standard of care will be enrolled. Twenty patients will be randomized to receive NUV-422 for approximately 8 to 21 days before surgery. Ten patients will be randomized to receive no drug before surgery and can proceed to surgery per Investigator discretion. After recovery (14 – 21 days post-surgery), all 30 patients in this surgical cohort will have the option to receive NUV-422, if deemed appropriate by the Investigator.

After the determination of the recommended Phase 2 dose, the Phase 2 portion will enroll up to 40 patients with recurrent IDH-WT GBM with known CDKN2A/B/C status into Cohort 1. For these recurrent GBM patients, radiographic tumor assessments will be performed based on RANO criteria [Wen et al, 2010] to determine the primary objective of overall response rate (ORR) and duration of response (DOR).

NUV-422-02 rGBM Monotherapy Phase 1/2



The FDA granted Orphan Drug Designation to NUV-422 for the treatment of malignant gliomas and Fast Track Designation for the treatment of high-grade gliomas.

Overview of Metastatic Breast Cancer

Breast cancer is the most frequent malignancy in women worldwide, and the second most common cancer worldwide, with an estimated 1.8 million new diagnoses per year. In the U.S., breast cancer has the highest prevalence among all cancers. The Surveillance, Epidemiology, and End Results ("SEER") Program at National Cancer Institute estimates that in 2020, there will be 276,000 new cases of breast cancer in the U.S. alone, and more than 40,000 deaths. Treatment options for breast cancer depend on many factors, including the stage of cancer. Breast cancer is a heterogeneous disease which is grouped into several clinical subtypes based on the expression of three proteins: ER, progesterone receptor ("PR") and HER2. Both ER and PR are hormone receptors, and tumors that express either of these receptors are referred to as hormone receptor-positive. The ACS estimates that approximately 75-80% of all breast cancers express estrogen receptor ("ER+") highlighting the central role of ER signaling in driving a large majority of breast cancer. Although early-stage non-metastatic disease is curable in approximately 70-80% of patients, advanced breast cancer with distant organ metastases is considered incurable with currently available therapies (Harbeck, et al 2019). Advanced breast cancer comprises inoperable locally advanced breast cancer, which has not spread to distant organs, and metastatic (stage IV) breast cancer; common sites of spread are bone, lungs, liver and brain. Currently, it is a treatable but virtually incurable disease, with metastases to distant sites, including the brain, being the cause of death in almost all patients, and a median overall survival of two to three years. Patients with metastatic breast cancer receive treatments that aim to relieve their symptoms and to prolong quality-adjusted life expectancy.

For patients with advanced ER+ breast cancer, endocrine therapy has been the backbone of treatment with a focus on developing a new generation of selective ER modulators ("SERMs"), aromatase inhibitors ("AIs") and selective ER degraders ("SERDs") due to emerging resistance to approved drugs. This resistance to endocrine treatment is due to multiple mechanisms, including changes in ER signaling and activation of other molecular pathways, such as CDK, mammalian target of rapamycin ("mTOR"), phosphoinositide 3-kinase ("PI3K"), mitogen-activated protein kinase ("MAPK") and others (McAndrew & Finn, 2020). Recently, several agents targeting these mechanisms have been approved by the FDA: mTOR inhibitor (everolimus [2012]), followed by the approval of 3 CDK4/6 inhibitors (palbociclib [2015], ribociclib [2018] and abemaciclib [2018]), and more recently the PI3K inhibitor alpelisib for a subgroup of patients with PI3K alterations (2019). For a select group of patients with homologous recombination-deficient ("HR-D") breast cancer, talazoparib, an oral PARP inhibitor, was approved by the FDA in 2018. All three approved CDK4/6 inhibitors—palbociclib, abemaciclib and ribociclib—are used in the metastatic setting. While patients with HR+ HER2- advanced breast cancer derive significant clinical benefit with first line treatment with a CDK4/6 inhibitor in combination with hormonal therapy, the majority eventually experience progression of their disease.

In 2019, worldwide sales for endocrine and targeted therapies treating ER+ breast cancer patients totaled $9.6 billion, with CDK4/6 inhibitors accounting for more than $6.0 billion. Given the incidence rate and cost of treatment, by 2027 the market size for adjuvant therapy, first line treatments and second line treatments in ER+ breast cancer could total $25 billion, $8 billion and $4 billion, respectively, with CDK4/6 inhibitors expected to account for approximately $14.0 billion.

Clinical Rationale for Targeting CDK2/4/6 in Breast Cancer Patients with Brain Metastases and Other Tumors.

It is estimated that at least 15% and as high as 50% of breast cancer patients will develop brain metastases during the course of their disease (Leone et al 2019). Patients with breast cancer brain metastasis (BCBM) have a poor prognosis with short overall survival and low quality of life. The prevalence of BCBM is increasing as treatment of primary cancers and imaging techniques improve. In addition, the brain is a "sanctuary site" for breast cancer cells treated with drugs that have poor penetration into the CNS. Thus, although a multitude of systemic treatment options exist for extracranial breast metastases, brain metastases continue to pose treatment challenges in clinical practice. For ER+ mBC patients, though recent Phase 3 trials demonstrated a PFS and even an overall survival benefit for CDK4/6 inhibitors in the first or second-line setting, there is limited evidence to inform their CNS-specific activity (Nguyen, et al 2019). Many studies included patients with stable and treated brain metastases or excluded patients with brain metastasis altogether, thus, the potential utility of CDK4/6 inhibitors for the prevention of CNS metastases remains unknown. A study of abemaciclib in BCBM patients demonstrated a slightly over 24% intracranial clinical benefit rate with 5% intracranial response rate (Tolaney et al 2020). While brain exposure was favorable in some of the patients, the overall low response rate in and outside the brain demonstrated that inhibition of CDK4/6 alone may not be enough for substantial control of the disease in this patient population. In addition, analyses of breast cancer metastases identified CDKN2A/p16 as a gene potentially associated with development of brain metastases. Patients with a higher p16 score had higher risk of brain metastases and worse overall survival (Furet, et al., 2017). Thus, targeting CDK2 in addition to CDK4/6 may present an important therapeutic strategy in ER+ mBC. In addition, up to 50% of patients with advanced HER2+ breast cancer who develop brain metastases, and a combination strategy of CDK2/4/6 inhibition with HER2-targeted therapy may warrant further investigation.

Overall, brain metastases develop in nearly 30% of patients with solid tumors. Cancers of the lung, breast and skin (melanoma) most frequently develop brain metastases and account for 67–80% of patients. Brain metastases from solid extracranial tumors represent an unmet need of increasing relevance as their incidence is rising considerably and is now estimated to be approximately 10 times higher than for primary malignant brain tumors. Thus, we may opt to study the effect of NUV-422 on brain metastases in patients whose primary tumor location is other than breast (e.g., lung, skin, and/or gastrointestinal tract).

Clinical Rationale for Targeting CDK2/4/6 in ER+ mBC

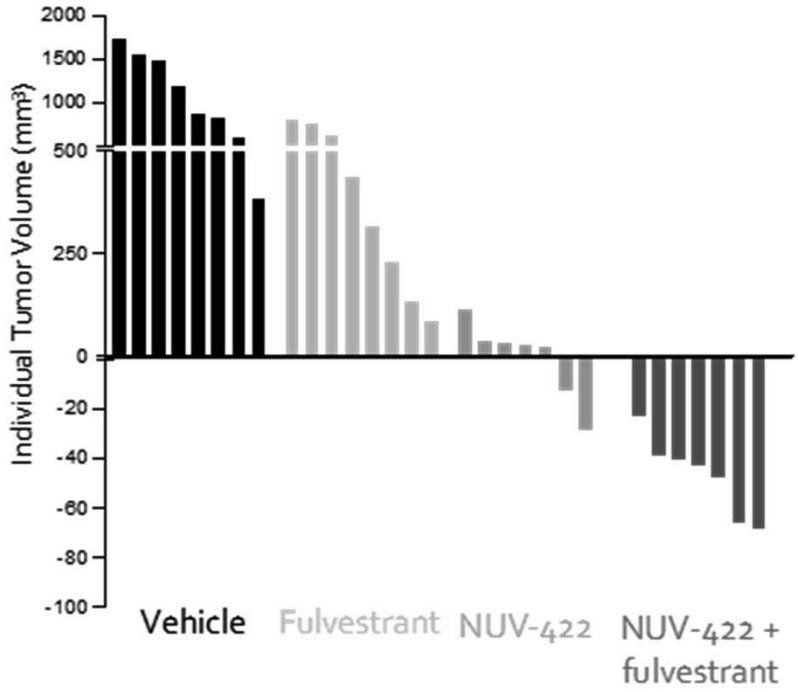
It was recently reported in the PALOMA-3 trial of ER+ mBC patients that cyclin E1 overexpression is a potential resistance mechanism to palbociclib (Turner, et al 2019). The efficacy of palbociclib plus fulvestrant was approximately halved in patients with high cyclin E1 expression compared to patients with low cyclin E1 expression (median PFS of 7.6 vs 14.1 months, respectively). Since Cyclin E is a known binding partner to CDK2 leading to cell cycle progression, these results reinforce that CDK2 is a key bypass kinase of CDK4/6 inhibition that may be responsible for driving resistance to palbociclib.

Preclinical Data

The activity of NUV-422 as a single agent and in combination with approved and investigational SERDs was explored in several clinically relevant breast cancer models.

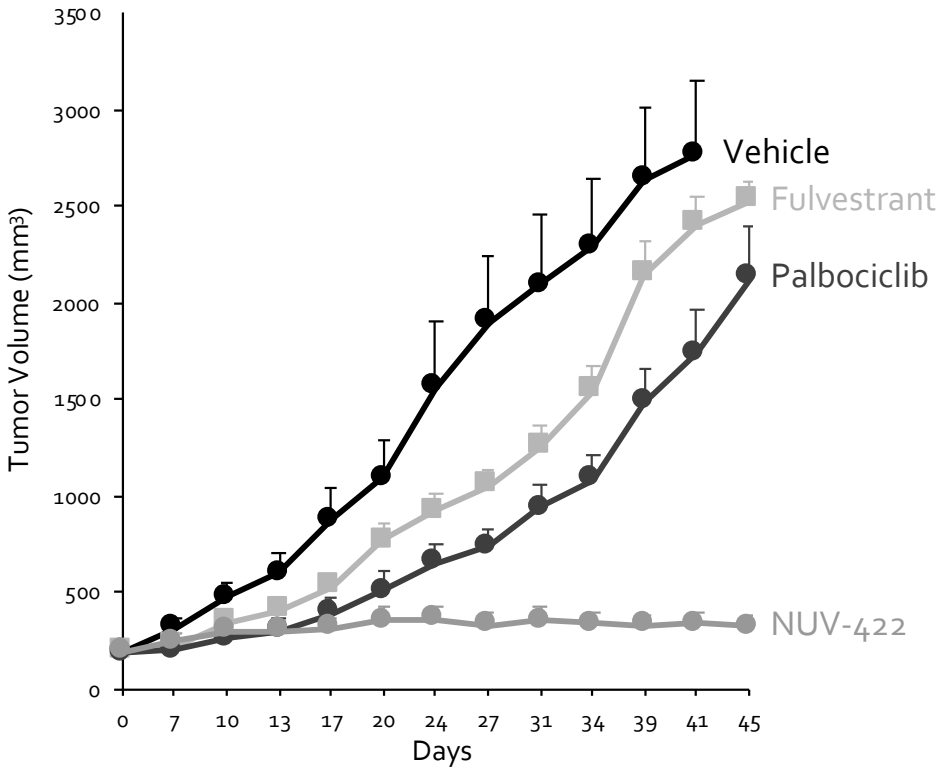
- In a cell line derived xenograft model, the *in vivo* antitumor activity of NUV-422 alone and in combination with fulvestrant (Faslodex), an approved SERD, was evaluated. NUV-422 was administered orally QD at 30 mg/kg. NUV-422 treatment resulted in several tumor regressions compared to the vehicle-treated group. While fulvestrant alone had a significant effect on tumor volume, the combination of NUV-422 and fulvestrant results in several deep regressions in tumor volume. These results are illustrated in the figure below.

NUV-422 IS SUPERIOR TO FULVESTRANT IN XENOGRAFT MODEL OF ER+ METASTATIC BREAST CANCER



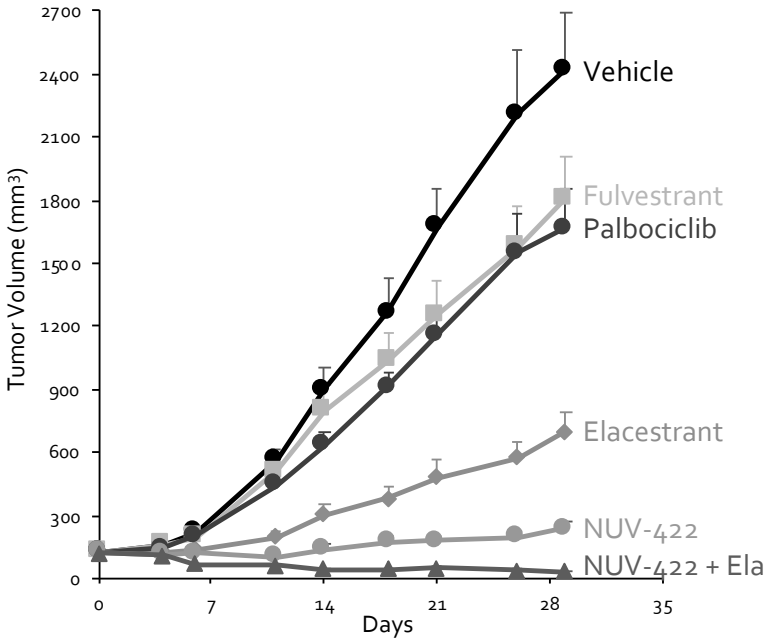
- In a patient-derived xenograft model that harbored an ESR1 mutation and that was derived from a patient previously treated with a combination of letrozole and palbociclib, NUV-422 (30 mg/kg QD) treatment resulted in reduced tumor volume ($p<0.0001$) compared to the vehicle-treated group. Additionally, NUV-422 resulted in significantly reduced tumor volume when compared to comparator standard-of-care agents fulvestrant ($p <0.0001$) and palbociclib ($p=0.0004$). These results are illustrated in the figure below.

NUV-422 INHIBITS GROWTH OF AN ESR1 MUTANT BREAST CANCER MODEL DERIVED FROM A PATIENT THAT RECEIVED PRIOR CDK THERAPY



- The *in vivo* antitumor activity of NUV-422 alone and in combination with elacestrant, an investigational oral SERD, was evaluated in an ESR1 mutant patient-derived xenograft model. NUV-422 was administered orally QD at 30 mg/kg. NUV-422 treatment resulted in reduced tumor volume ($p<0.0001$) compared to the vehicle-treated group. Additionally, NUV-422 resulted in significantly reduced tumor volume when compared to comparator standard-of-care agents fulvestrant ($p<0.0001$) and palbociclib ($p<0.0001$). Lastly, NUV-422 in combination with elacestrant resulted in deep tumor regressions. These results are illustrated in the figure below.

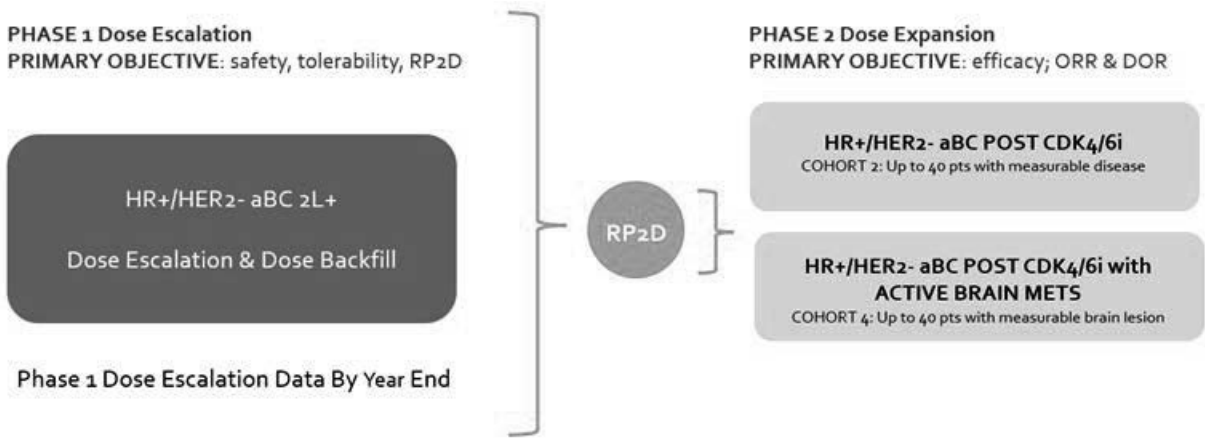
NUV-422 IN COMBINATION WITH AN INVESTIGATIONAL ORAL SERD, ELACESTRANT, CAUSES DEEP REGRESSIONS IN AN ESR1 MUTANT PATIENT-DERIVED XENOGRAFT MODEL



Development Plan for NUV-422 in aBC

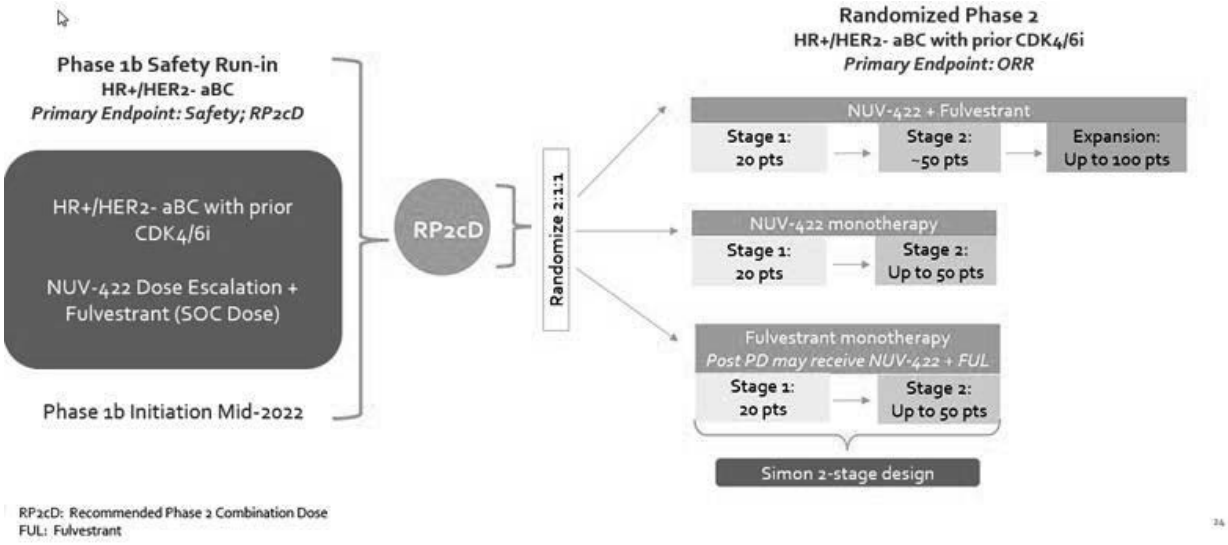
For metastatic or advanced breast cancer, we are exploring NUV-422 as both a monotherapy and in combination with SOC agent, fulvestrant. We began a monotherapy Phase 1/2 study (Protocol NUV-422-02) in December 2020 in high-grade gliomas and later amended the protocol in the second quarter of 2021 to include HR+ HER2- aBC. We are continuing to enroll patients in the monotherapy Phase 1 dose escalation portion of the study and data from this portion of the study. After the determination of the recommended Phase 2 dose, the Phase 2 portion will enroll recurrent HR+ HER2- aBC with and without active brain metastases. Up to 40 patients will be enrolled into each of these aBC cohorts. Eligible patients must have received at least 1 but not more than 4 prior lines of systemic therapy for aBC including at least 1 prior line of hormonal therapy in combination with an approved CDK4/6 inhibitor. The primary objective is ORR and DOR based on radiographic tumor assessments performed per RECIST 1.1 criteria for both cohorts. For the aBC active brain metastases cohort, efficacy will be determined by radiographic tumor assessments performed by RANO-BM criteria [Lin et al, 2015], which will be used to derive intracranial ORR and DOR.

NUV-422-02 2L+ aBC Monotherapy Phase 1/2



In December 2021, the FDA cleared an IND for NUV-422 for the treatment of HR+ HER2- aBC. In 2022, we plan to initiate a Phase 1b/2 study in patients with HR+ HER2- aBC who have received prior hormonal therapy combined with an approved CDK 4/6 inhibitor. This study will begin with a Phase 1b dose escalation portion designed to evaluate safety and tolerability of the NUV-422 plus fulvestrant combination and to determine a recommended Phase 2 combination dose of NUV-422. The Phase 2 portion is a randomized, non-comparative study designed to evaluate the safety and efficacy of NUV-422 in combination with fulvestrant relative to NUV-422 monotherapy and fulvestrant monotherapy. Up to 200 patients may be enrolled into the Phase 2 portion across three arms. The primary endpoint for Phase 2 portion is ORR based on radiographic tumor assessments performed per RECIST 1.1 criteria.

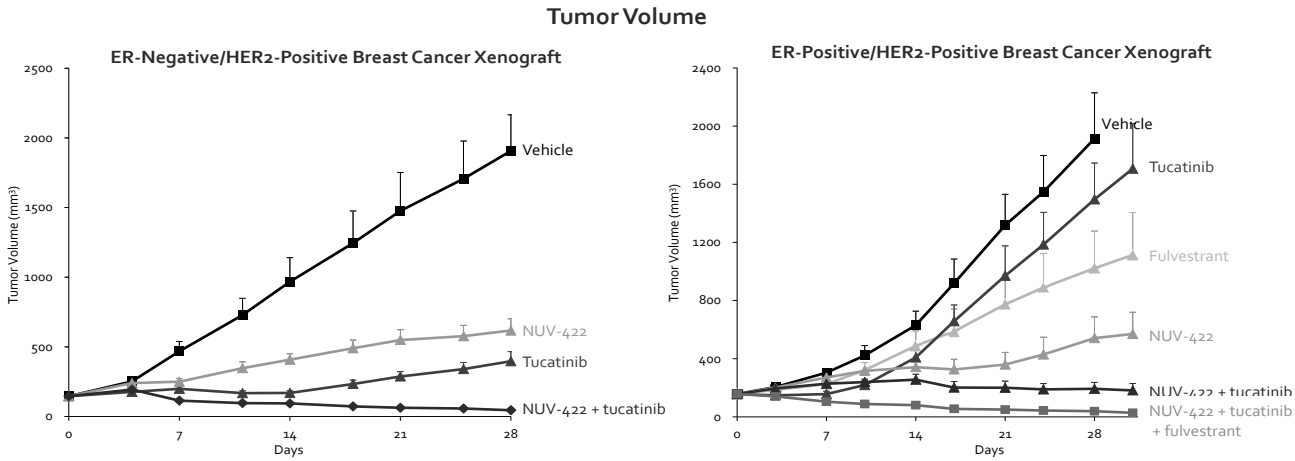
NUV-422-03 Phase 1b/2 HR+ HER2- aBC study NUV-422 In Combination with Fulvestrant



Additional Preclinical data suggests broad potential for NUV-422 in endocrine-independent breast cancer.

The in vivo antitumor activity of NUV-422 was evaluated in an ER+ and an ER- model of Her2+ breast cancer. NUV-422 inhibited tumor growth in both models as a single agent and in combination with Tucatinib (Tukysa). Additionally, in the ER+ HER2+ model, the triple combination of NUV-422, tucatinib, and fulvestrant caused tumor regressions. The results are illustrated in the figure below.

NUV-422, AS A SINGLE AGENT, AND IN COMBINATION WITH SOC AGENTS, TUCATINIB AND FULVESTRANT, CAUSES REGRESSION OF HER2+ BREAST CANCER XENOGRAFTS



Prostate Cancer Overview

Prostate cancer is reported as the second and third leading cause of cancer death for men in the U.S. and in Europe, respectively. SEER cancer statistics estimated that approximately 175,000 men in the U.S. and 450,000 men in the EU5 would be diagnosed with prostate cancer in 2020, potentially resulting in a $15 billion market opportunity given the costs of treatment.

For early stage prostate cancer, the SOC is a radical prostatectomy, the removal of the prostate via surgery, or radiation therapy. While potentially curative, prostatectomy and/or radiation can result in serious side effects, including urinary and fecal incontinence and erectile dysfunction, as a result of damage to surrounding vital structures, blood vessels and nerves. Given the invasive nature of the procedure, prostatectomy surgery also brings the risk of complications with anesthesia, bleeding and infection.

mCRPC is the most advanced form of the disease, and there are approximately 35,000 to 45,000 new incidences of mCRPC each year. Men with mCRPC have a poor prognosis and a predicted survival rate of fewer than two years from the initial time of progression.

Current SOC for men with castration-resistant prostate cancer provides that patients should initially receive a combination of androgen deprivation therapy ("ADT") and either abiraterone, which works by decreasing androgen levels, or enzalutamide, which works by blocking androgen binding to AR. If the disease progresses despite these second-generation hormonal therapies, chemotherapy is considered the next treatment option. Treatment with chemotherapy is generally postponed for as long as possible due to its effect on patient's quality of life and the potential for severe side effects including neuropathies, nausea, diarrhea, decreased mental capacity and increased risk of infections.

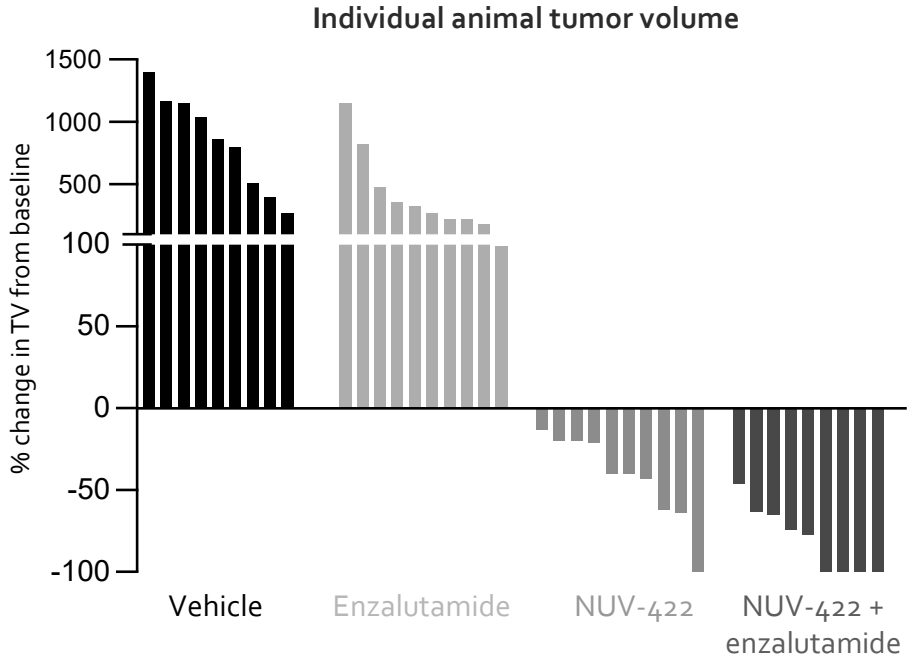
Clinical Rationale for Targeting CDK2/4/6 in mCRPC.

The role of CDK2 as a crucial factor in development of metastases in patients with prostate cancer has been supported by an extensive analysis of patient gene sequencing data and clinical outcomes (Yin, et al 2018). This analysis identified CDK2 and CDKN2C as one of the most important genes in transcriptional dysregulation in prostate cancer when expression of CDK2 was significantly associated with recurrence of prostate cancer ($p = 0.00793$). The importance of CDK2 in cancer growth is further supported by knockout experiments suggesting that CDK2 is critical to the cell invasion. While a clinical trial of abemaciclib plus abiraterone in later line prostate cancer (CYCLONE 2) is ongoing and an additional study may be initiated soon in earlier line prostate cancer (CYCLONE 3). A randomized study of palbociclib with ADT in metastatic hormone-sensitive prostate cancer (mHSPC) patients demonstrated that addition of this CDK4/6 inhibitor to ADT did not improve prostate specific antigen endpoints or PFS in this population (Palmbos, et al 2021). Thus, targeting CDK2 in combination with hormonal therapy may be able to address an important unmet medical need in mCRPC patients who progress on current SOC therapy.

Preclinical Data

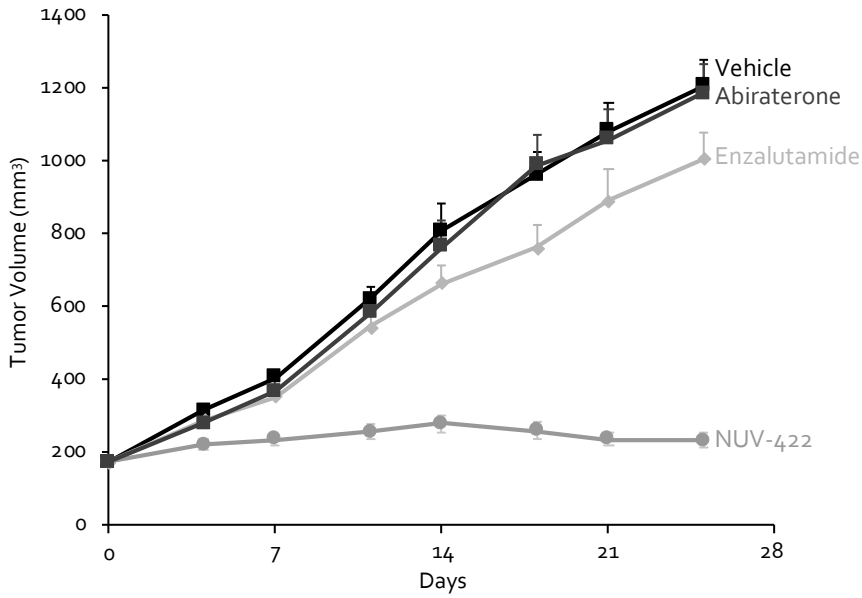
The in vivo antitumor activity of NUV-422 alone and in combination with enzalutamide (Xtandi), an approved prostate cancer drug, was evaluated in a patient-derived xenograft model, implanted subcutaneously in the flank of immunocompromised mice. NUV-422 was administered orally QD at 30 mg/kg. Treatment with NUV-422 alone resulted in reduced tumor volume compared to the vehicle-treated group. As illustrated in the figure below, while enzalutamide alone had very little effect on reducing tumor volume, the combination of NUV-422 and enzalutamide resulted in an enhanced antitumor effect, where all treated animals had marked tumor regression and half of the animals had complete tumor regression.

DEEP TUMOR REDUCTIONS OBSERVED IN ENZALUTAMIDE-RESISTANT PATIENT-DERIVED XENOGRAFT PROSTATE MODEL



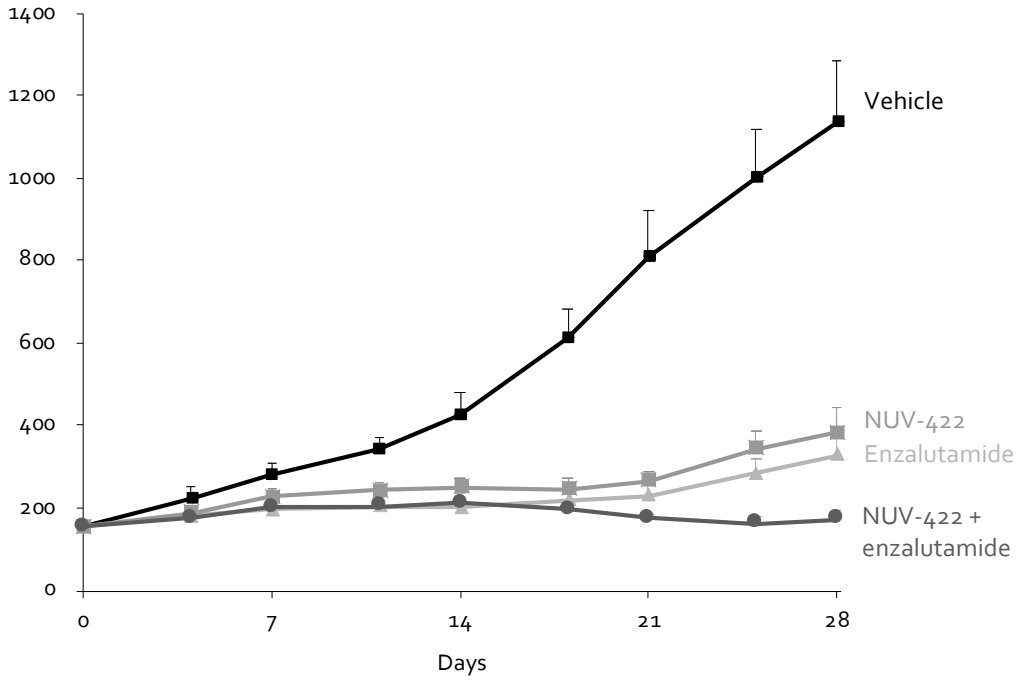
The in vivo antitumor activity of NUV-422 was evaluated in an androgen receptor variant, ARv-7, harboring cell line-derived prostate xenograft model, implanted subcutaneously in the flank of immunocompromised mice. NUV-422 was administered orally QD at 30 mg/kg. Treatment with NUV-422 alone resulted in reduced tumor volume ($p<0.001$) when compared to the vehicle-treated group, as well as approved SOC groups, enzalutamide ($p<0.001$) or abiraterone ($p<0.001$). Abiraterone or enzalutamide did not cause significant growth inhibition in this model. The results are illustrated in the figure below.

NUV-422 EXHIBITS ANTI-TUMOR ACTIVITY IN AN ARV-7 PROSTATE CANCER MODEL RESISTANT TO ANTI-ANDROGEN THERAPIES



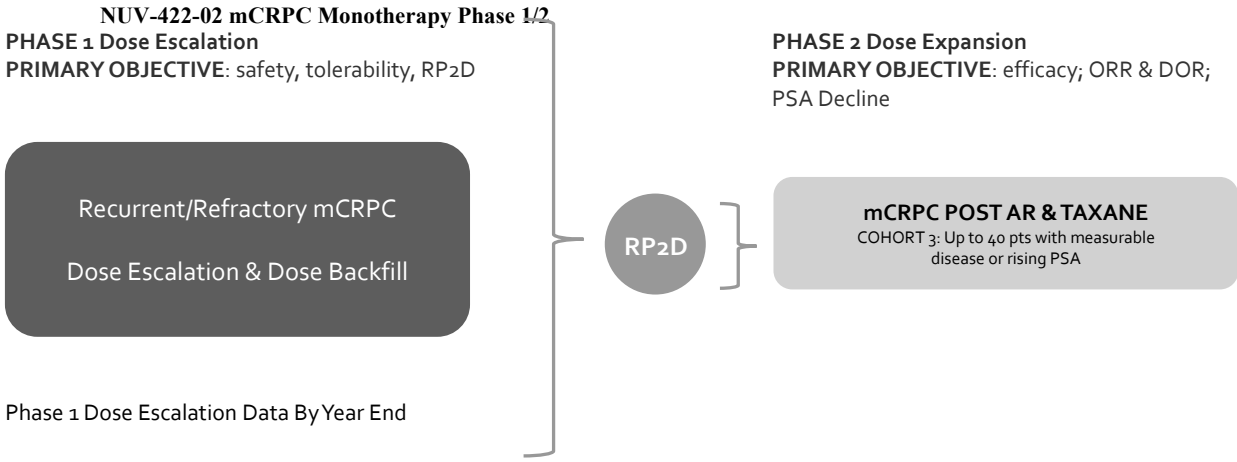
The in vivo antitumor activity of NUV-422 alone and in combination with enzalutamide, an approved prostate cancer drug, was evaluated in an androgen-sensitive cell line-derived xenograft model, implanted subcutaneously in the flank of immunocompromised mice. NUV-422 was administered orally QD at 30 mg/kg. As shown in the figure below, treatment with NUV-422 alone, and in combination with enzalutamide, resulted in significantly reduced tumor volume ($p<0.001$) compared to the vehicle-treated group. NUV-422 in combination with enzalutamide resulted in further growth inhibition when compared to the single agent groups.

NUV-422 IN COMBINATION WITH ENZALUTAMIDE CAUSES SIGNIFICANT TUMOR GROWTH INHIBITION IN ANDROGEN-SENSITIVE PROSTATE CANCER XENOGRAFT



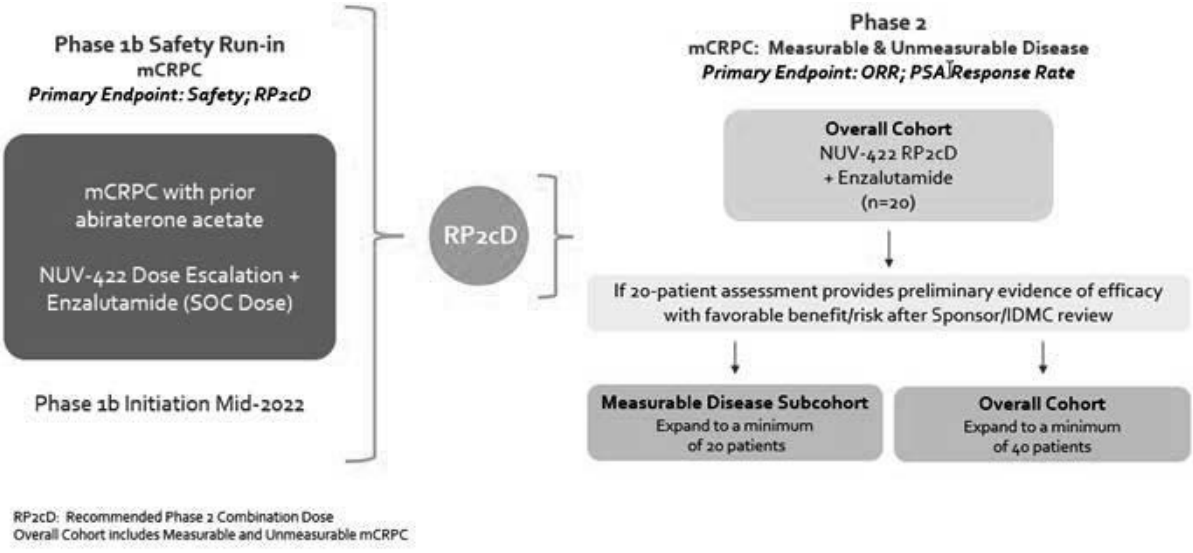
Development Plan for NUV-422 in mCRPC

For mCRPC, we are exploring NUV-422 as both a monotherapy and in combination with SOC agent, enzalutamide. We began a monotherapy Phase 1/2 study (Protocol NUV-422-02) in December 2020 in high grade gliomas and later amended the protocol in the second quarter of 2021 to include mCRPC. We are continuing to enroll patients in the monotherapy Phase 1 dose escalation portion of the study and data from this portion of the study. After the determination of the recommended Phase 2 dose, the Phase 2 portion will enroll up to 40 mCRPC patients who have disease progression or rising PSA on prior therapies that include prior anti-androgen therapies and at least 1 prior line of taxane-based chemotherapy for castration-resistant disease. The primary objective is ORR and DOR based on radiographic tumor assessments performed per RECIST 1.1 criteria and Prostate Cancer Clinical Trials Working Group 3 (PCWG3) guidelines as well as a decrease in the prostate-specific antigen (PSA) to $\geq$ 50% less than the baseline PSA.



In December 2021, the FDA cleared an IND for NUV-422 for the treatment of prostate cancer. In 2022, we plan to initiate a Phase 1b/2 study in patients with mCRPC who have received prior treatment with abiraterone acetate. This study will begin with a Phase 1b dose escalation portion designed to evaluate safety and tolerability of NUV-422 plus enzalutamide combination and to determine a recommended Phase 2 combination dose of NUV-422. The Phase 2 portion will be an open-label, single-arm study designed to evaluate safety and efficacy of NUV-422 in combination with enzalutamide in previously treated mCRPC patients who can have measurable or nonmeasurable disease. A minimum of 20 patients with measurable disease will be enrolled into the Phase 2 portion. The primary endpoint is ORR based on radiographic tumor assessments performed per RECIST 1.1 criteria and PCWG3 guidelines as well as PSA-response rate (PSA-RR) defined as the proportion of treated patients who achieve PSA response per PCWG3 guidelines.

NUV-422-04 Phase 1b/2 Study in mCRPC: NUV-422 combination with enzalutamide



Overview of NUV-868: BET Inhibitor Program

NUV-868 for Advanced Solid Tumors

NUV-868, a BD2-selective oral small molecule BET inhibitor, inhibits BRD4, a key member of the BET family that epigenetically regulates proteins that control tumor growth and differentiation. BETs consist of two sub-domains:

BD1, the inhibition of which is known to contribute to toxicity, and BD2, the inhibition of which is known to be important for efficacy. BET inhibitors have historically targeted both BD1 and BD2 less selectively, causing gastrointestinal toxicity and bone marrow suppressive effects like thrombocytopenia. NUV-868 is almost 1,500 times more selective for BD2 than BD1 and is designed to alleviate the therapeutic limiting toxicities observed by other non-BD2 selective BET inhibitors. NUV-868 in combination with androgen receptor-directed therapies may help to overcome resistance in prostate cancer. In addition, NUV-868 in combination with PARP inhibitors may have synergistic activity to increase efficacy across multiple solid tumors. We intend to initiate a Phase 1 trial of NUV-868 in patients with advanced solid tumors in mid-2022.

BET Inhibition in Advanced Solid Tumors

The BET family of proteins have critical biological functions and are found to be altered in many human cancers (Bechter and Schoffski, 2020). Genetic screening and nonclinical studies have implicated BET proteins in both hematologic malignancies and in solid tumors. BET proteins have been shown to drive transcription of a variety of oncogenes (reviewed in (Taniguchi, 2016)). For example, BRD4 was found to be enriched at super-enhancer regions of genes that play a major role in oncogenesis (Loven et al, 2013). Inhibition of BRD4 led to defects in transcription along with decreased mRNA of super-enhancer driven genes, including the *Myc*oncogene (Loven et al, 2013). Besides genetic alterations, overexpression and perturbation of physiological BET function have been described. Chromosomal translocations involving BRD4 and BRD3 have been identified in particularly aggressive forms of nuclear protein in testis (NUT) midline carcinomas (NMC) (French et al, 2001; French et al, 2008). Overexpression of both BRD2 and BRD4 have been observed in glioblastoma cell lines and stem cells (Pastori et al, 2014). Furthermore, gene amplification and overexpression of BRD4 have been observed in patients with some ovarian cancers (Goundiam et al, 2015). Together, these observations suggest that the BET protein family plays multiple roles in oncogenesis.

BET proteins are epigenetic readers that turn on specific genes by binding unique regions of the genome through their ability to read specific chemical tags on chromatin. In some instances, BET proteins turn on oncogenes that are abnormally expressed in a variety of human cancers, such as c-myc. C-myc is believed to play a role in promoting the growth of up to 70% of all cancers. BET inhibitors have the potential to downregulate the expression of such driver oncogenes. These observations have resulted in the generation and clinical investigation of BET inhibitors in several cancer subtypes.

BET Inhibition with Anti-Androgen Therapy

The androgen receptor (AR) plays a pivotal role in castration-resistant prostate cancer, and androgen deprivation therapy is an effective strategy for suppressing the progression of most prostate cancers (Fujita and Nonomura, 2019). Enzalutamide is a nonsteroidal antiandrogen approved for the treatment of castration-resistant and metastatic castration-sensitive prostate cancer. The drug has been studied extensively in the clinic and, along with available real-world data since its approval, shows strong evidence of its efficacy and tolerability (Scott, 2018). Many patients with castration-resistant prostate cancer eventually develop resistance to antiandrogens, including enzalutamide, through a variety of mechanisms related to the AR, including mutation and overexpression (Fujita and Nonomura, 2019). A potential therapeutic strategy to overcome antiandrogen resistance is through BET inhibition, specifically inhibition of BRD4, which has been shown to drive transcription of the AR (Faivre et al, 2017). Data from a nonclinical study showed that a dual AR and BET inhibitor reduced transactivation of the AR mutant that mediates enzalutamide resistance, inhibited proliferation of AR-positive prostate cancer cells, and suppressed growth of prostate cancer xenografts in vivo (Yu et al, 2020). Additional nonclinical data provide evidence that combining BET inhibitors with AR antagonists, such as enzalutamide, could prevent resistance to these antagonists (Asangani et al, 2016). Published results from a Phase 1b/2a study of ZEN-3694 in combination with enzalutamide in patients with mCRPC showed promising preliminary efficacy results (progression-free survival [PFS] of 9 months, with a PFS of 10 months in patients with prior progression on enzalutamide monotherapy) (Aggarwal et al, 2020).

BET Inhibition with PARP Inhibition

Poly (ADP-ribose) polymerase (PARP) inhibitors block DNA repair and replication in cancer cells. Originally, PARP inhibitors were shown to target cells deficient in breast cancer gene 1 or breast cancer gene 2 (BRCA)-dependent homologous recombination pathways (Farmer et al, 2005); however, nonclinical and clinical evidence suggests that PARP inhibitors may also be effective in cancers lacking BRCA 1/2 mutations through alternative mechanisms (Keung et al, 2020; Kim et al, 2019; Ledermann et al, 2014; Mirza et al, 2016), expanding the potential

population who might benefit from PARP inhibition. Several PARP inhibitors have now been approved for solid organ cancers, including ovarian, breast, prostate, and pancreatic cancers; however, their long-term use may be limited due to the development of resistance (reviewed in (Kim et al, 2021). Combination therapies that include drugs with other mechanisms of action are being investigated to potentially overcome common mechanisms of resistance to PARP inhibitors. Several nonclinical studies have provided evidence that BET inhibitors in combination with PARP inhibitors may provide synergistic activity against ovarian, breast, prostate, pancreatic, and small cell lung cancers and in cholangiocarcinoma (Fehling et al, 2020; Fiorentino et al, 2020; Karakashev et al, 2017; Lui et al, 2020; Miller et al, 2019; Mio et al, 2019; Pawar et al, 2018; Wilson et al, 2018; Yang et al, 2017). Two clinical studies are currently ongoing to test combination treatment using investigational BET inhibitors alongside approved PARP inhibitors: a Phase 2 study of ZEN-3694 + talazoparib in patients with metastatic or recurrent triple negative breast cancer (TNBC) (NCT03901469) and a Phase 1/2 study of PLX2853 + olaparib in patients with mCRPC (NCT04556617).

Our Solution—NUV-868

NUV-868, our lead candidate from our BET program, is a small molecule BD2-selective BETi for the treatment of solid tumors that is almost 1,500 times more selective for BD2 than BD1, which may potentially enable this molecule to reduce the toxicities associated with other non-BD2 selective inhibitors. Given BET's promise as an oncology target, there are several BET inhibitors in development for several cancers. Other BET inhibitors that are not as selective for BD2, have been associated with toxicities including gastrointestinal and thrombocytopenia. The selectivity of several BET inhibitors that are currently in development is shown in the table below.

NUV-868 IS A MORE SELECTIVE BD2 INHIBITOR

IC50 values of NUV-868 and other BET inhibitors in development

	BRD4 Affinity[2]		
	BD2	BD1	Selectivity
NUV-868	2	2920	1460x
ABBV-744[3]	1.05	340	234x
PLX-2853[4]	Modest BD2 selectivity		
CPI-0610[3]	17	85	5x
ABBV-075[1]	3	11	3.7x
MK-8628/OTX-015[5]	17	26	1.5x
BI-894999[6]	41	5	0.1x
ZEN-3694[7]	Non-selective		

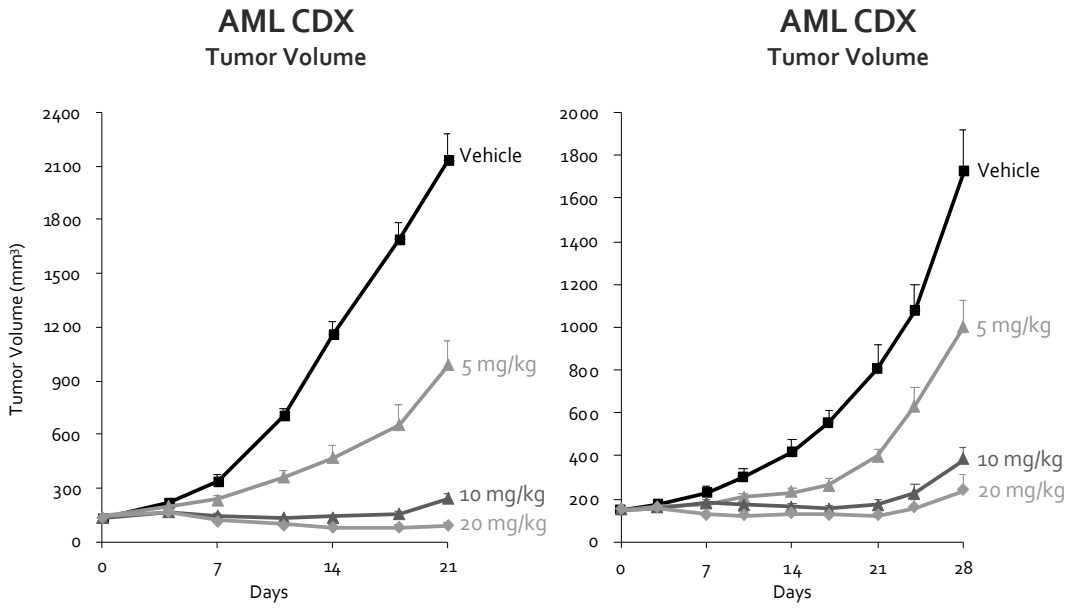
1. Faivre et al 2020; 2. Various assays used; 3. Internal Nuvation Bio data; 4. https://ash.confex.com/ash/2020/webprogram/Paper140138.html;5.https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5474678/; 6. https://www.nature.com/articles/s41388-018-0150-2; 7. 2016-EORTCposter-ZenithEpigenetics.pdf

Preclinical Data

In two AML xenograft models, including a Kasumi-1 and an MV-4-11 model, NUV-868 demonstrated anti-tumor activity as compared to vehicle across three doses (5 mg/kg, 10 mg/kg and 20 mg/kg twice daily (BID)) out to

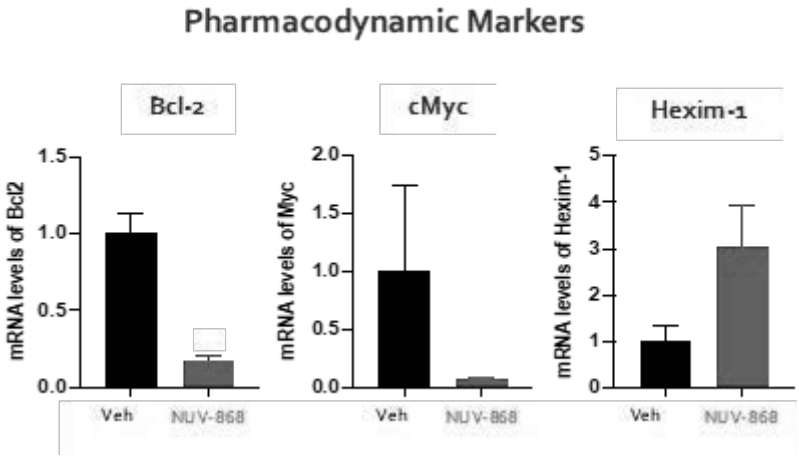
21 days, as shown in the graphs below. Notably, near complete tumor regression was observed in the 10-20 mg/kg NUV-868 groups.

NUV-868 IS HIGHLY POTENT IN KILLING AML CELLS IN *IN VIVO* XENOGRAFT MODELS



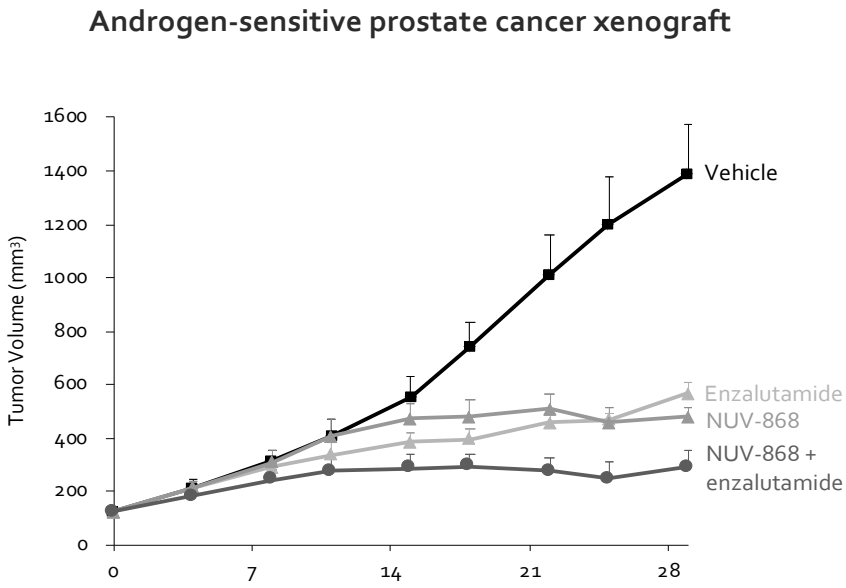
The pharmacodynamic effects of NUV-868 was evaluated in a systemic MV-4-11 model. NUV-868 was evaluated at a dose of 20 mg/kg BID. mRNA was isolated from control-treated and NUV-868 treated animals after 5 days of treatment. As demonstrated below, NUV-868 treatment reduced expression of tumor-promoting genes, c-Myc and BCL-2, and upregulated Hexim-1 which is indicative of BET inhibition.

NUV-868 DOWNREGULATES TUMOR PROMOTING GENES, SUCH AS C-MYC, AND UPREGULATES HEXIM-1, AN INDICATOR OF BET PROTEIN INHIBITION



The *in vivo* antitumor activity of NUV-868 alone and in combination with enzalutamide, an approved prostate cancer drug, was evaluated in an androgen-sensitive cell line-derived xenograft model, implanted subcutaneously in the flank of immunocompromised mice. NUV-868 was administered orally BID at 20 mg/kg. Treatment with NUV-868 alone, and in combination with enzalutamide, resulted in reduced tumor volume ($p<0.001$) compared to the vehicle-treated group. The combination resulted in significant growth inhibition than enzalutamide ($p<0.01$) or NUV-868 alone ($p<0.05$).

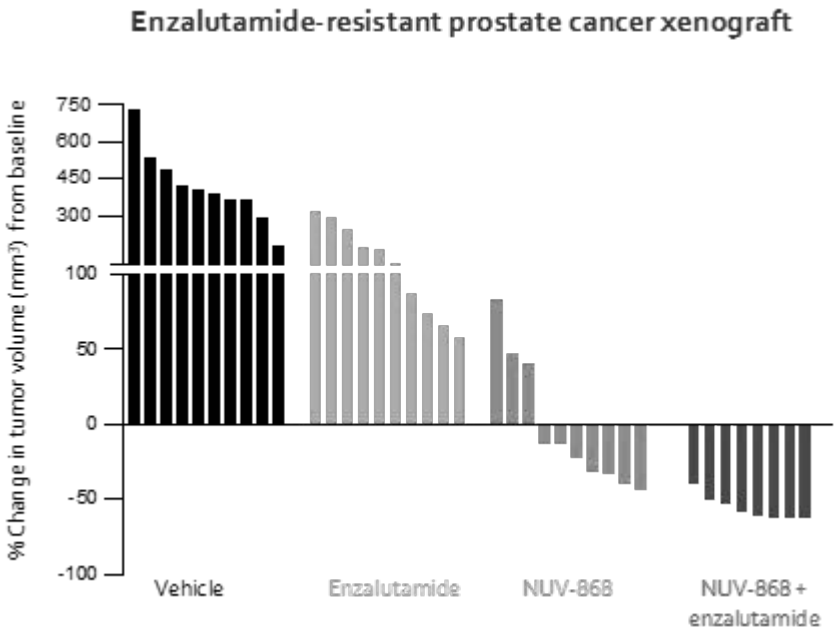
NUV-868 IN COMBINATION WITH ENZALUTAMIDE SIGNIFICANTLY INHIBITS GROWHT OF ANDROGEN-SENSITIVE PROSTATE CANCER XENOGRAFTS



NUV-868 in combination with AR directed therapies may help to overcome resistance in prostate cancer. Inhibition of BRD4 has been shown to drive transcription of the AR (Faivre et al, 2017). BET inhibitors given with AR antagonists, such as enzalutamide, may prevent resistance to these antagonists (Asangani et al, 2016).

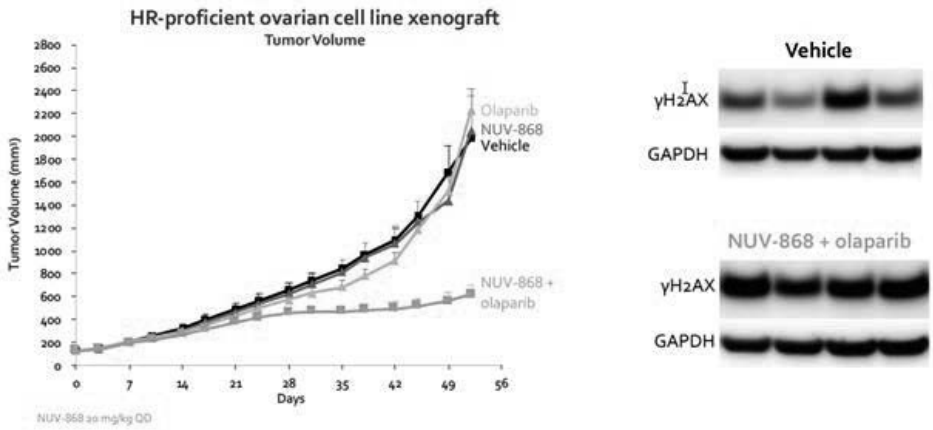
NUV-868 as a single agent causes tumor reductions in an enzalutamide-resistant patient-derived prostate cancer xenograft model as noted in the graph below. Additionally, NUV-868 re-sensitized tumors back to enzalutamide and the combination caused deep tumor reductions in this model.

NUV-868 CAUSES TUMOR REDUCTIONS IN AN ENZALUTAMIDE-RESISTANT PATIENT-DERIVED PROSTATE CANCER XENOGRAFT MODEL



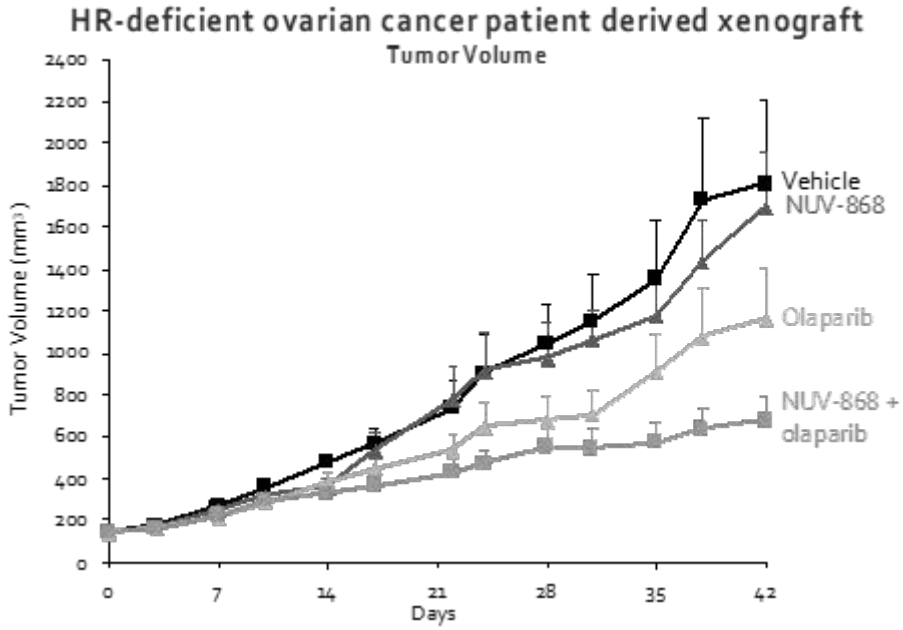
NUV-868 in combination with PARP inhibitors may have synergistic activity to increase efficacy across multiple solid tumors. Several nonclinical studies have provided evidence that BETi in combination with PARPi may provide synergistic activity against ovarian, breast, prostate, pancreatic, and small cell lung cancers (Fehling et al, 2020; Fiorentino et al, 2020; Karakashev et al, 2017; Lui et al, 2020; Miller et al, 2019; Mio et al, 2019; Pawar et al, 2018; Wilson et al, 2018; Yang et al, 2017). As noted in the figure below, NUV-868 + olaparib suppresses HR-proficient ovarian tumor growth better than olaparib alone. NUV-868 + olaparib increases double stranded DNA breaks (γH2AX) in an HR-proficient ovarian tumor model.

COMBINATION OF NUV-868 + OLAPARIB INCREASES DOUBLE STRANDED DNA BREAKS (γH2AX) IN AN HR-PROFICIENT OVARIAN TUMOR MODEL



The *in vivo* antitumor activity of NUV-868 alone and in combination with olaparib was evaluated in a patient-derived xenograft model, harboring a BRCA mutation derived from a patient that was previously treated with olaparib. NUV-868 was administered orally at 10 mg/kg BID. As illustrated in the graph below, while olaparib alone had very little effect on reducing tumor volume, the combination of NUV-868 and olaparib resulted in an enhanced antitumor effect when compared to the vehicle group ($p<0.05$).

COMBINATION OF NUV-868 AND OLAPARIB SUPPRESSES GROWTH OF A HR-DEFICIENT OVARIAN CANCER MODEL DERIVED FROM A PATIENT PREVIOUSLY TREATED WITH OLAPARIB

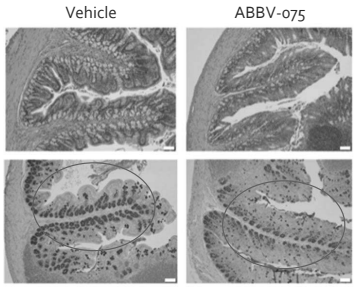


NUV-868's BD2 selectivity may limit gut toxicity observed with other dual BD1 / BD2 BET inhibitors. In tissue samples from a rat small intestine treated with vehicle and non-selective BET inhibitor, ABBV-075, treatment with ABBV-075 led to a marked reduction in healthy goblet cells, which are central in protecting the mucous membrane in the GI tract (Faivre et al 2020). By comparison, a notably higher dose (30 mg/kg) of NUV-868 showed no apparent evidence of goblet cell loss in mice. These results are shown in the images below. We believe this data supports the potential for NUV-868 to limit the gastrointestinal toxicities that are associated with other BET inhibitors.

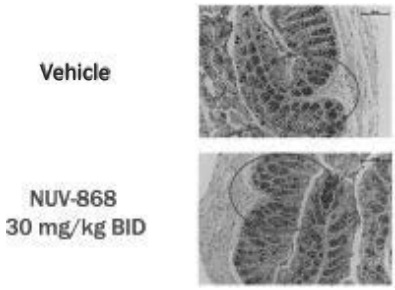
HIGH SELECTIVITY FOR BD2 OVER BD1 REDUCES THE GUT TOXICITY OBSERVED WITH OTHER BET INHIBITORS

ABBV-075 (Dual BD1 / BD2)

Faivre et al 2020



NUV-868 (BD2 Selective)



The other main toxicity associated with BET inhibitors is thrombocytopenia. While most non-selective BET inhibitors lower platelet levels and cause thrombocytopenia, NUV-868 has demonstrated higher platelet levels as a function of reversing platelet suppression associated with untreated tumor burden and a lack of bone marrow-suppressive side effects. In the table below, platelet counts are measured in a MV 4-11 AML xenograft hematology panel 24 hours post the final dose of NUV-868 on day 21 across three dose levels. As compared to treatment with vehicle, platelet counts are higher for the NUV-868 cohorts across the low (5 mg/kg), medium (10 mg/kg) and high (20 mg/kg) doses.

NUV-868 REVERSES PLATELET SUPPRESSION IN AML

MV 4-11 AML Xenograft Hematology Panel
(24-hours post final dose on Day 21)

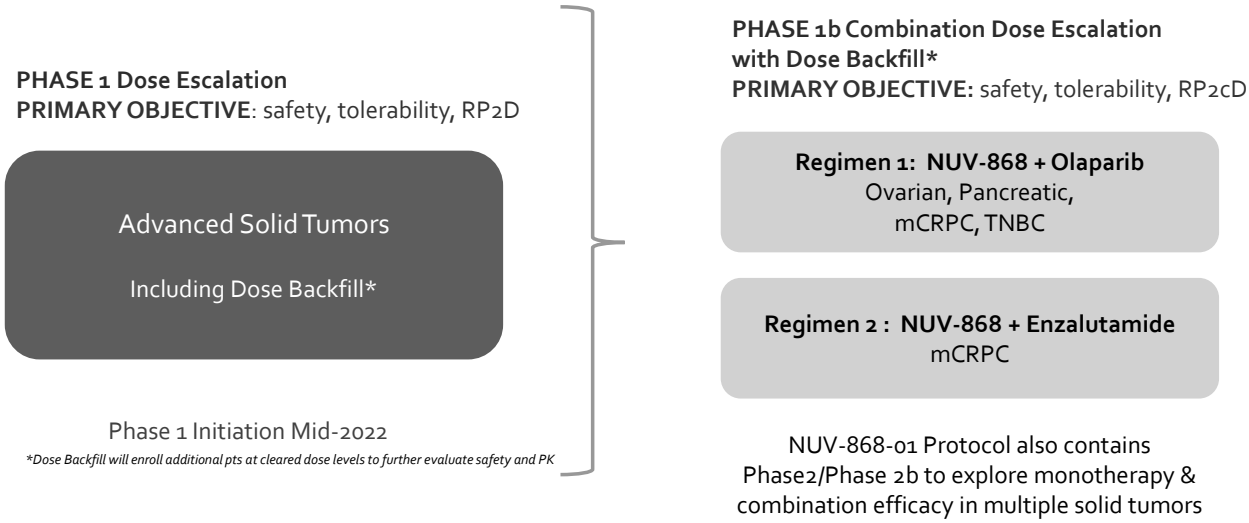
	Dose (mg/kg)	RBC (10^6/ul)	PLT (10^3/ul)	NEUT (10^3/ul)	LYM (10^3/ul)	RET (10^9/L)
Vehicle	-	10.4	842	0.20	7.45	361
NUV-868	5	9.6	893	0.19	3.98	438
NUV-868	10	10.2	1290	0.15	5.53	463
NUV-868	20	10.2	1460	0.07	5.93	505

Clinical Development Plan for NUV-868 in Advanced Solid Tumors

In January 2022, the FDA cleared an IND for NUV-868 for the treatment of advanced solid tumors. With the clearance of this IND, we will be initiating a Phase 1/2 study of NUV-868 as a monotherapy and in combination with olaparib or enzalutamide in multiple tumor types. This protocol (NUV-868-01) will initiate in mid-2022 with a Phase 1 monotherapy dose escalation study in advanced solid tumor patients. A Phase 1b study will then be initiated exploring NUV-868 in combination with olaparib in previously treated ovarian cancer, pancreatic cancer, mCRPC, and TNBC patients and in combination with enzalutamide for mCRPC patients followed by a Phase 2b study to further explore safety and efficacy once the recommended Phase 2 combination dose is determined. A Phase 2 monotherapy study will also be initiated in mCRPC patients as well to further explore safety and efficacy. The primary endpoints

for the Phase 1 and Phase 1b portions will be safety, tolerability, and the determination of the recommended phase 2 monotherapy or combination dose. In the Phase 2 and 2b portions, the primary objective is PSA-RR for the mCRPC cohorts and ORR by RECIST 1.1 for the ovarian, pancreatic, and TNBC cohorts.

NUV-868-01 Phase 1/1b Study: Monotherapy & Combination



Overview of NUV-569: Wee1 Program

NUV-569 is a differentiated oral small molecule selective inhibitor of Wee1 kinase, an important regulator of DNA damage repair. Wee1 inhibitors increase the efficacy of DNA-damaging therapies by forcing cancers to replicate before they can repair their damaged DNA. NUV-569 is a highly potent Wee1 kinase inhibitor that synergizes with DNA-damaging agents to enhance cancer cell death. NUV-569 is designed to limit off-target effects by improving its kinase selectivity. NUV-569 has low inhibition of PLK1, which may improve tolerability including reduction of bone marrow and GI toxicity.

Background on Wee1 and DNA Damage Repair

DNA damage occurs frequently throughout the cell cycle, and even more frequently in rapidly dividing cancer cells, as a result of the challenge of endogenous and exogenous DNA insults and stressors. In response to DNA damage, cells have evolved a network of complex, coordinated DNA damage response ("DDR"). The DDR involves a network of DNA repair pathways and DNA damage checkpoints that are linked through various signaling mechanisms responsible for sensing and responding to specific types of DNA damage that affect DNA repair, cell cycle regulation replication stress responses and apoptosis. Defects in the DDR result in genomic instability and ultimately promote the cloning of cancer cells.

Wee1 is one of many kinases involved in regulation of signaling within the cell cycle and DNA damage identification and repair within the DDR. Specifically, Wee1 is a tyrosine kinase that allows cells with DNA damage to repair and survive by activating the G2/M cell cycle checkpoint through inhibition of the phosphorylation of CDK1/2, thus suspending the process of cell division in healthy cells. In cancer cells, tumors activate their Wee1 checkpoint in order to arrest the process of cell division, thus allowing them to repair their damaged DNA and replicate, resulting in tumor growth. Inhibition of cellular regulation and repair mechanisms within the cell cycle and DDR, such as Wee1, may potentially play a crucial role in the induction of apoptosis, improve the efficacy of DNA-damaging cancer therapies to which cancer cells have already developed multiple mechanisms of resistance, and may improve the efficacy of DNA-damaging radiation treatment. Specifically, Wee1 inhibitors force tumor cells to replicate prior to DNA repair, leading to incorrect DNA replication and ultimately tumor cell death.

Wee1 Inhibitors in Clinical Development and Limitations

We are aware of several clinical-stage and preclinical-stage Wee1 inhibitors being developed for patients with solid tumors, including product candidates from AstraZeneca, Zentalis, DebioPharm, Impact Therapeutics, and

Schrodinger. To our knowledge, there is not a commercially available Wee1 inhibitor and the most advanced Wee1 inhibitor is currently in Phase 2 development with Phase 3s in the planning stages. There are 15 industry sponsored ongoing trials evaluating molecules targeting Wee1 inhibitors with several Phase 1 signal-seeking basket trials are ongoing (ClinicalTrials.gov; Citeline).

Adavosertib (AZD1775), which is manufactured by AstraZeneca (AZD), is currently the most advanced, being studied as a monotherapy and in combination with chemotherapy, anti-PD-L1 (durvalumab), and PARPi. AZD is planning a Phase 3 pivotal study for adavosertib in uterine carcinoma. Data from adavosertib Phase 1 and 2 trials have been published and have demonstrated the following efficacy data:

- Adavosertib with multiple chemotherapy regimens in platinum-refractory ovarian cancer, Phase 2: NCT02272790
    - In the 94 pts treated (median treatment duration 3 months; range 0–16 months), outcomes were greatest with adavosertib (weeks [W]1–3) + carboplatin cohort with ORR of 67% and median PFS (mPFS) of 10.1 months for this cohort (Moore et al, ASCO, 2019).
- Adavosertib monotherapy in advanced refractory solid tumors with CCNE1 amplification; Phase 2: NCT03253679
    - ORR of 25.9% and a median PFS of 4.7 mos; OS rate was 55% (Fu et al., AACR, 2021)
- Adavosertib + durvalumab in advanced solid tumors; Phase 1: NCT02617277
    - Two confirmed PR (soft tissue and esophageal tumors) with DCR of 36% (Patel et al, ASCO 2019)
- Adavosertib + olaparib in PARPi-resistant ovarian cancer; Phase 2 (EFFORT): NCT03579316 (Westin et al, ASCO 2021)
    - Adavosertib monotherapy demonstrated ORR of 23%, SD of 66%, and mPFS of 5.5 mos
    - Adavosertib + olaparib demonstrated ORR of 29%, SD of 66%, and mPFS of 6.4 mos
- Adavosertib vs. active monitoring for TP53 and RAS mutant metastatic colorectal cancer, Phase 2: EudraCT Number 2012-005111-1
    - Adavosertib arm demonstrated a mPFS of 3.6mos (HR 0.35; p=0.0022) with an immature mOS of 13.1 mos while the active monitoring arm demonstrated a mPFS of 1.8mos and mOS of 11.3 mos (Seligmann et al, ESMO 2021)
- Adavosertib + carboplatin in Platinum-refractory ES-SCLC; Phase 2: NCT02937818
    - No responses observed; 30% of pts had disease control at 12 weeks with mPFS of 2.6 mos and mOS of 4.67 mos (Results posted on clinicaltrials.gov)

Although AZD1775 has shown encouraging clinical efficacy data in patients with uterine serous carcinoma and ovarian and pancreatic cancers, we believe it has the following limitations with regards to its safety profile.

- ***Potent inhibition of polo-like kinase 1 ("PLK1").*** PLK1 is a cell kinase that phosphorylates Wee1 as the cell approaches the G2/M cell cycle checkpoint thus promoting and enabling the cell replication process. Potent PLK1 inhibition may be responsible for gastrointestinal and bone marrow toxicity. AZD1775 is a highly potent inhibitor of PLK1, having demonstrated an IC50 of 15 nanomolar in biochemical studies, and thus may contribute to bone marrow and GI toxicity.
- ***Liver enzyme inhibition.*** AZD1775 inhibits liver enzyme CYP3A4, which is responsible for elimination of drug and drug metabolites from the body.
- ***Tolerability.*** In a Phase 1 clinical trial in patients with locally advanced pancreatic cancer, AZD1775 in combination with gemcitabine, an FDA-approved chemotherapy, and radiation, eight patients (24%) experienced a dose-limiting toxicity, most commonly anorexia, nausea, or fatigue, thus preventing continuous dosing of AZD1775.

Other Wee1 inhibitors are also currently in early phase development. Zentalis has multiple ongoing studies for ZN-c3 as a monotherapy and in combination. The company is pursuing a fast-to-market strategy in uterine serous

carcinoma (USC), where the ongoing Phase II trial has registrational intent. Zentalis is also planning to start a tumor agnostic biomarker-driven Phase II trial with registrational potential. In a Phase 1/2 study of ZN-c3 in advanced solid tumors an ORR of 43% in the USC population was observed (Zentalis PR 6/28/2021; Zentalis Nov 2021 presentation). Phase I solid tumor basket studies are ongoing for Debio-0123 + carboplatin (Debiopharm) and IMP7068 monotherapy (Impact Therapeutics) (ClinicalTrials.gov; Citeline).

Our Solution—NUV-569

NUV-569, our lead candidate from our Wee1 program, is a differentiated oral small molecule selective inhibitor of Wee1 kinase, an important regulator of DNA damage repair. NUV-569 is a highly potent Wee1 kinase inhibitor that synergizes with DNA-damaging agents to enhance cancer cell death. NUV-569 is designed to limit off-target effects by improving its kinase selectivity. NUV-569 has low inhibition of PLK1, which may improve tolerability including reduction of bone marrow and GI toxicity. Specifically, in our preclinical studies NUV-569 demonstrated single digit nanomolar inhibition of Wee1, an approximate 45-fold lower PLK1 inhibition than AZD1775 and 9-fold lower potency in inhibiting proliferation of rat gut epithelial cells (IEC6) than AZD1775, which we believe suggests NUV-569 may have better GI tolerability than AZD1775. The following table demonstrates the favorable potency and selectivity profile of NUV-569 compared to AZD1775.

NUV-569'S HIGHLY POTENT AND SELECTIVE PROFILE = LESS TOXICITY

Compound	Wee1	PLK1	IEC6
NUV-569	7	**687**	2362
AZD1775	4	**15**	251

IC_{50} (nM)

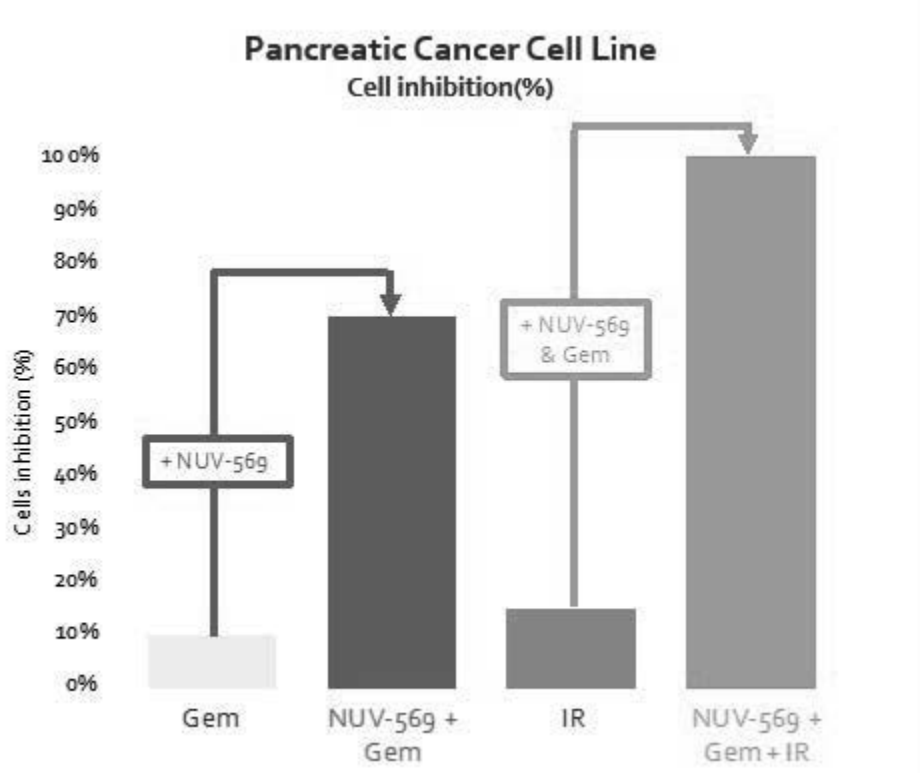
PLK1 is a ubiquitous cell kinase that may be responsible for gut and bone marrow toxicity

- NUV-569 is highly potent against Wee1 but avoids PLK1 unlike AZD1775
- 10X reduced potency on rat gut epithelial cells (IEC6), relative to AZD1775, suggests these new compounds have significantly improved tolerability

Preclinical Results

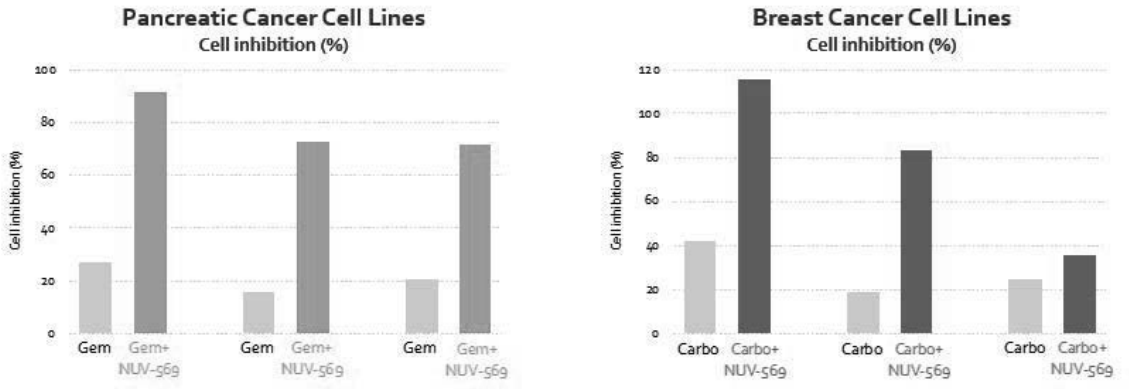
Wee1 inhibition can synergize with chemotherapy and radiation therapy leading to mitotic catastrophe and eventually, cell death. In an *in vitro* preclinical study of pancreatic cancer in combination with gemcitabine and radiation therapy, we observed NUV-569's anti-tumor activity and potency in inducing apoptosis in pancreatic cancer cells, as shown in the figure below.

NUV-569 FURTHER ENHANCES CANCER CELL DEATH IN COMBINATION WITH BOTH GEMCITABINE AND RADIATION



Enhancement of chemotherapy cytotoxicity by NUV-569 was observed in additional pancreatic models and triple negative breast cancer (TNBC) models. As demonstrated in the figure below, the cytotoxicity of SOC agent, gemcitabine, was enhanced by NUV-569 addition in several pancreatic cancer cell lines. Similarly, the addition of NUV-569 enhanced the cytotoxicity of SOC, carboplatin, in several TNBC models.

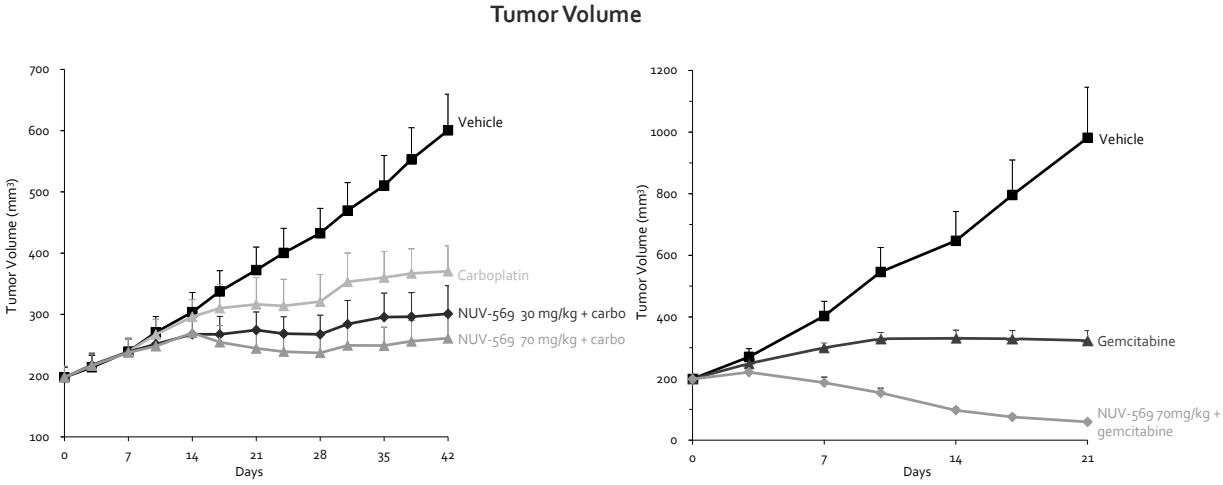
NUV-569 SYNERGIZES WITH SOC GEMCITABINE IN PANCREATIC CANCER CELLS AND CARBOPLATIN IN BREAST CANCER CELLS TO ENHANCE CANCER CELL DEATH



The *in vivo* antitumor activity of NUV-569 alone and in combination with carboplatin, was evaluated in a TNBC cell line-derived xenograft model. NUV-569 was administered orally BID at 30 mg/kg and 70 mg/kg, in combination with carboplatin. As illustrated in the figure below, while carboplatin alone had very little effect on reducing tumor volume, the combination of NUV-569 and carboplatin resulted in an enhanced antitumor effect when compared to the vehicle-treated and the carboplatin-treated group. In an *in vivo* model of ovarian cancer, the combination treatment of

NUV-569 and gemcitabine resulted in tumor regressions when compared to the vehicle-treated and gemcitabine-treated groups.

NUV-569 SYNERGIZES WITH SOC CARBOPLATIN AND GEMCITABINE TO INHIBIT TUMOR GROWTH IN BREAST AND OVARIAN CANCER XENOGRAFTS



Next Steps

We intend to submit an IND for NUV-569 by the end of 2022 and initiate Phase 1 trials in patients with advanced solid tumors following IND clearance. We are also continuing to evaluate additional Wee1 inhibitors for the potential to increase efficacy and further widen the therapeutic window.

Overview of Our A_{2A} Adenosine Receptor Program

Our adenosine receptor inhibitors are designed to have high affinity for the A_{2A} adenosine receptor, which plays multiple critical roles in human physiology and pathophysiology including anti-cancer immunity. We intend to nominate a clinical development candidate by year end 2022.

NUV-1182, an A_{2A} adenosine receptor inhibitor, boosts immune function and may enhance the efficacy of IO-targeted therapies. A_{2A} adenosine receptor plays multiple critical roles in human physiology and pathophysiology including anti-cancer immunity. Accumulation of adenosine in the tumor microenvironment may be a critical factor in limiting the activity of currently available immuno-oncology drugs, including anti-PD1/PD-L1 drugs and anti-cancer chimeric T cells. Targeting A_{2A} adenosine receptor may overcome this blockade, leading to improved anti-cancer activity in tumors which are resistant to immuno-oncology drugs and T cell therapies.

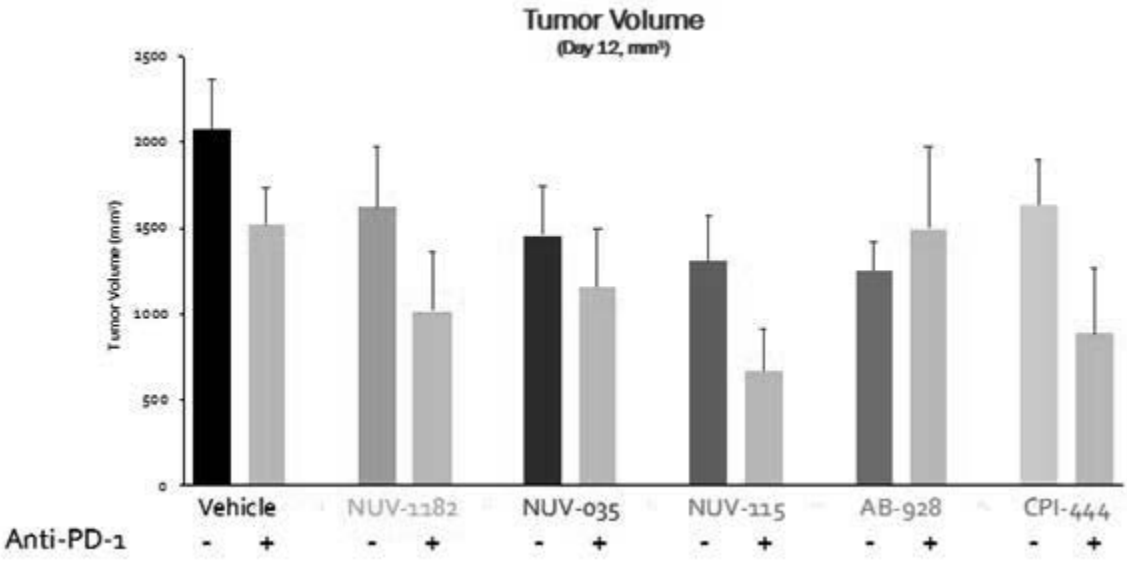
In our preclinical studies, our adenosine receptor inhibitors, NUV-035, NUV-115 and NUV-1182, have high affinity for the A_{2A} adenosine receptor demonstrating single digit nanomolar binding affinity. Our preclinical studies demonstrate that NUV-035, NUV-115 and NUV-1182 have desirable pharmacokinetic profiles, with high exposure following a single oral dose in mice. Furthermore, in a melanoma cell line derived xenograft model, daily oral dosing with NUV-1182 enhanced the tumor suppressive activity when combined with either an anti-PD1 antibody or an anti-PD-L1 antibody.

NUV-1182 IS A POTENT AND SELECTIVE A2A ADENOSINE RECEPTOR INHIBITOR

IC50 (nM)	AZD4635	CPI444	AB928	NUV-115	NUV-035	NUV-1182
A2A binding	~20	~7	~3	~1	~3	~3
A1 binding	>300	>100	>10	~2	~10	>200
A2A Selectivity (A2A/A1)	~20	~15	~10	~2	~4	>75
A2A cAMP (40 nM NECA)	>100	>50	>10	>10	>10	>50

The *in vivo* antitumor activity of NUV-1182 and other adenosine inhibitors include competitor molecules such as AB-928 (Arcus Biosciences) and CPI-444 (Corvus Pharmaceuticals), was evaluated in a melanoma cell line derived syngeneic xenograft model. As demonstrated in the figure below, NUV-1182 enhanced the tumor suppressive activity when combined with an anti-PD1 antibody, compared to anti-PD1 alone. NUV-035 and NUV-115, other adenosine receptor antagonists, also demonstrated enhanced anti-tumor activity when combined with anti-PD1.

NUVATION A2A ADENOSINE RECEPTOR INHIBITORS INCREASE THE ANTI-TUMOR ACTIVITY OF IMMUNE CHECKPOINT INHIBITORS IN AN IN VIVO MELANOMA XENOGRAFT MODEL



Our A_{2A} adenosine receptor inhibitors have an attractive PK profile, with good oral bioavailability and do not effectively cross the blood-brain barrier. Brain to plasma ratios range from 0.02 to 0.2, demonstrating that our compounds do not effectively cross the blood-brain barrier. Our compounds are currently being tested in several syngeneic tumor models, with tumor volume and tumor infiltrating immune cell profiling and mechanism of action studies.

NUVATION A2A INHIBITORS HAVE AN ATTRACTIVE ORAL PHARMACOKINETIC PROFILE AND DO NOT CROSS THE BLOOD-BRAIN BARRIER

Mouse Oral Pharmacokinetic Profile

Compound	Dose	Cmax (nM)	Tmax (h)	AUC_{INF} (nM*h)	t1/2 (h)
NUV-035	10 mg/kg	>900	0.25	>50000	~6
NUV-115	10 mg/kg	>500	0.5	>900	~1.5
NUV-1182	50 mg/kg	>15000	0.5	>30000	~1.5

Overview of Our DDC Technology Platform

The foundations of our DDCs are built by employing tissue-targeting small molecules fused to anti-cancer warheads of existing drugs with well-understood mechanisms of action. For example, our PARP-AR DDC, NUV-1156, is composed of the AR binder Xtandi (enzalutamide) fused to the warhead of the PARP inhibitor Lynparza® (olaparib) to address advanced stage prostate cancers with the potential to move into earlier lines typically treated with surgical prostatectomy. Our PARP-ER DDC, NUV-1176, is composed of a PARP inhibitor warhead that is fused to the binding domain of an ER-targeting small molecule to address ER+ breast and ovarian cancer. NUV-1511 is a DDC that fuses a targeting agent to a widely used chemotherapy agent. In preclinical models, NUV-1156 and NUV-1176 potently kill tumor cell lines without killing healthy cells in the bone marrow and the gastrointestinal tract. In in vivo models of prostate and breast cancer, NUV-1511 caused significant tumor growth inhibition and regression when compared to the targeting ligand or the chemotherapy-treated groups. We intend to nominate our first clinical development candidate from our DDC platform in the second half of 2022.

Traditional Cancer Therapeutics

Cancer treatment has traditionally included chemotherapy, radiation, surgery or a combination of these approaches. Over the last twenty years, new paradigms of cancer research and treatment have emerged to address the limitations of existing treatments. Monoclonal antibodies, or proteins that bind to antigen targets on tumor cells and inhibit tumor growth, represent one of the most successful approaches. More recently, engineered versions of monoclonal antibody-based therapies have emerged, including ADCs and bispecific antibodies, which collectively aim to exert the tumor-specific power of monoclonal antibodies to drive a larger clinical impact than conventional approaches.

ADCs

ADCs exert their antitumor activity by using monoclonal antibodies to deliver potent cytotoxins directly to tumors. ADCs have three primary components: (1) a monoclonal antibody that recognizes an antigen on the tumor and is responsible for directing the therapy to the tumor; (2) a cytotoxic molecule that causes cell death, typically by interrupting a critical cell function such as replication; and (3) a linker that attaches the cytotoxin to the antibody. The two main attributes of ADC therapeutics are:

- ***Targeting Only Diseased Tissue.*** ADCs are designed with a monoclonal antibody that binds to antigen targets that are preferably expressed on the outside of tumor cells and not on healthy tissues.
- ***Increased Therapeutic Window.*** The cytotoxin payload of the ADC attached to the targeting monoclonal antibody is directed to specific cancer epitopes on the cell surface, allowing an improved therapeutic index by delivering the cytotoxin to the cancer more than non-target tissues.

As a result of these two main attributes, ADCs can offer greater antitumor potency while still maintaining an acceptable tolerability profile. Despite these benefits, limitations remain, including:

- ***Intravenous Delivery.*** ADCs are administered intravenously into the systemic circulation where they home to tumors. While the cytotoxic payload is designed to only cleave when internalized by the targeted

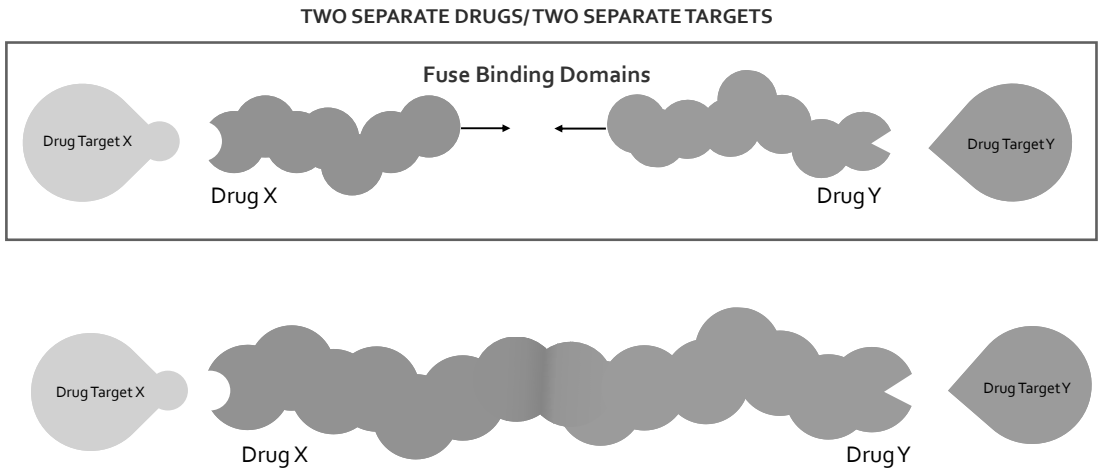
tumor cell, challenges with linker chemistry can result in instability and cause the cytotoxic payload to be released within circulation, causing systemic toxicities.

- ***Inability to Reach Intracellular Targets.*** Monoclonal antibodies are not capable of penetrating the cell membrane due to their size and are limited to targeting antigens that are present on the surface of a tumor cell.
- ***Complex Manufacturing.*** ADCs are complex biologics that require the refinement of several properties in tandem and are expensive to manufacture. They often present significant manufacturing challenges, particularly at a large scale, and generally have a lower gross margin than a small molecule.

Our Solution—DDCs

Our DDC platform has generated orally bioavailable or IV small molecules that fuse the binding domains of two different drugs to target two different targets, simultaneously. Our platform leverages our drug discovery and chemistry expertise to find the minimum target binding sites of drug X and drug Y and fuse them together, while maintaining activity. Our DDCs are designed to selectively bind to intracellular as well as surface cell membrane targets that are expressed more highly in specific target tissues and to potently deliver anti-cancer warheads to these target tissues. The figure below depicts our DDC approach.

DRUG-DRUG CONJUGATES ARE DESIGNED TO BIND TWO DIFFERENT TARGETS SIMULTANEOUSLY



Key benefits of our DDCs include:

- Tissue-selective targeting improves therapeutic index vs. untargeted warhead;
- Oral or IV delivery;
- Binds intracellular and cell membrane targets;
- Highly cell permeable; and
- Simpler and less expensive to manufacture

We believe our DDC technology will be broadly applicable and can be replicated across many other existing therapies to transform the SOC across multiple indications for oncology.

We are currently in preclinical development and intend to nominate our first lead clinical development candidate in the second half of 2022.

NUV-1156: Targeting AR and PARP for Prostate Cancer

NUV-1156 is an oral small molecule that is composed of a PARP inhibitor warhead that is fused to the binding domain of an AR-targeting small molecule. In preclinical models, NUV-1156 demonstrated the ability to kill tumor

cells associated with high AR-expression, sparing healthy cells in bone marrow and the gastrointestinal tract that do not have high levels of AR expression.

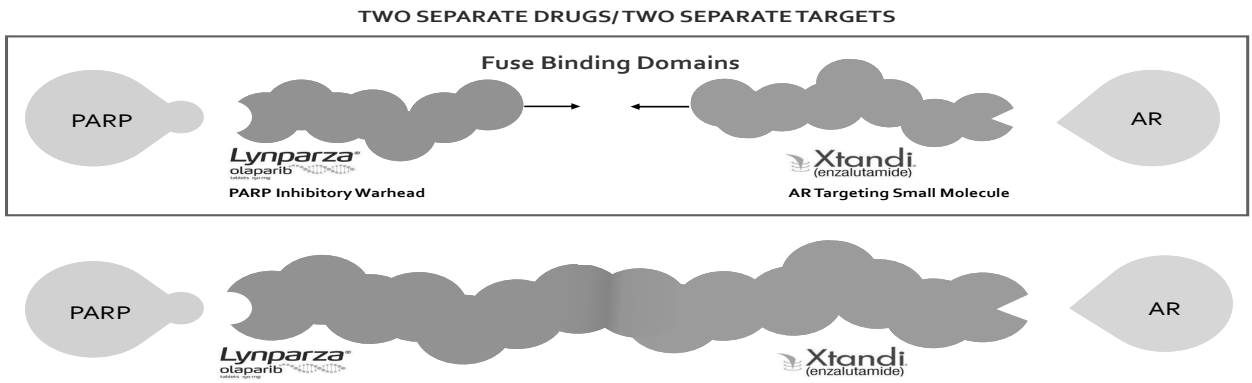
We are exploring the use of PARP-AR DDCs in prostate cancer, initially focused on mCRPC where there is an urgent unmet medical need. The ability of our PARP-AR DDC to kill prostate cancer cells resistant to current therapies suggests that this drug could play a role in advanced stage prostate cancer, particularly in the Xtandi and Zytiga resistant setting.

Additionally, we believe PARP-AR DDCs could play a role in early-stage prostate cancer where the SOC for newly diagnosed, early-stage patients is radical prostatectomy and radiation therapy which often results in serious side effects, including urinary incontinence, erectile dysfunction and fecal incontinence. We believe a PARP-AR DDC could potentially allow early-stage patients to avoid surgical radical prostatectomy and radiation therapy, which we believe could be a major transformation for the treatment of prostate cancer.

NUV-1156 Drug Design and Mechanism of Action

Our PARP-AR DDCs kill cells via an AR-targeted mechanism. NUV-1156 consists of the warhead from the PARP inhibitor Lynparza (olaparib) which is fused to an AR-binding domain of Xtandi (enzalutamide). We believe this drug design will potentially allow for a PARP inhibitor to be potently delivered to high AR-expressing tumors, like prostate cancer, while potentially reducing the off-target toxicities associated with other PARP inhibitors, namely toxicity in the bone marrow and gastrointestinal tract, which are low AR-expressing tissues. The figure below depicts the components of NUV-1156.

NUV-1156 IS A DDC THAT TARGETS AR AND PARP



PARP Inhibitor Overview

Mechanisms of Action

The rapid cell division and attendant required DNA replication seen in cancers causes an increase in single stranded DNA breaks. PARP is the most abundant DNA repair enzyme in the nucleus. Because cancers have an increase in DNA breaks related to their rapid division, their DNA breaks must be repaired by PARP if the cancers are to be able to faithfully replicate their DNA. Furthermore, approximately one-third of tumors have intrinsic DNA repair defects, such as BRCA-mutations and other HR-D. Tumors with HR-D struggle to repair and faithfully replicate DNA. When HR-D is combined with PARP inhibition, DNA repair is so compromised that cancer cells can no longer survive. This is the fundamental reason that all current commercially available PARP inhibitors have superior outcomes in HR-D vs. homologous recombination proficient ("HR-P") cancers. This mechanism of action of PARP inhibitors has been shown to further enhance the effects of DNA-damaging anti-cancer therapies, such as chemotherapy or radiation.

Existing PARP Inhibitors and Our Opportunity

PARP inhibitors Lynparza (olaparib), Rubraca (rucaparib camsylate), Zejula (niraparib) and Talzenna (talazoparib tosylate) have been approved by the FDA for multiple oncology indications, including ovarian, breast, prostate and pancreatic cancer. Sales of these FDA-approved PARP inhibitors were approximately $1.7 billion in 2019 and are forecasted to be over $7.0 billion in 2025, with Lynparza (olaparib) accounting for $1.2 billion and over $4.0 billion in the 2019 and 2025 totals, respectively.

Despite the commercial success of PARP inhibitors, broader adoption is limited by their high rates of GI and bone marrow toxicity which is largely a result of off-target cell killing. Adverse grade 3-4 events from this class of drugs include anemia, thrombocytopenia, neutropenia and alopecia. Other common adverse reactions include nausea, vomiting, diarrhea, fatigue and decreased appetite. We believe a DDC that fuses the warhead of a PARP inhibitor to an AR-binding domain of Xtandi (enzalutamide) will allow us to take advantage of the powerful and proven selectivity of AR therapy in AR-driven tumors by possibly minimizing the toxicities associated with PARP inhibitors in low AR-expressing cells in the gastrointestinal tract and bone marrow and broadening the tumor types (both HR-D and HR-P) in which this approach could be effective.

AR Selectively Expressed in AR-Specific Tissue

The growth and survival of prostate cancer cells depends heavily on the AR. Testosterone fuels prostate cancer cell growth by using the binding of androgens to ARs to trigger abnormal cell growth and tumor progression. In men, AR protein expression is limited primarily to the sex organs, with medium to high AR expression levels seen across the testis, prostate, epididymis and seminal vesicle tissues. In contrast, AR expression is either low or not detected in the bone marrow and the gastrointestinal tract, two organs strongly associated with PARP-inhibitor toxicity.

Existing AR Inhibitors and Our Opportunity

Xtandi (enzalutamide) is an AR inhibitor that acts on different steps in the AR signaling pathway. Xtandi has been shown to potently bind to the AR and effectively compete for this receptor against its native ligand testosterone. Zytiga (abiraterone) is an inhibitor of androgen synthesis and results in decreased AR signaling through ligand depletion. Between 15% and 25% of patients do not respond to either AR signaling pathway inhibitors abiraterone or enzalutamide, and the vast majority of the responsive patients will ultimately become resistant, resulting in limited survival. Zytiga was approved for the treatment of mCRPC in 2011 and generated sales of $2.8 billion in 2019. Xtandi was approved for the treatment of mCRPC in 2012 and generated sales of approximately $3.7 billion in 2019.

Prostate Cancer Overview

See “Prostate Cancer Overview” for NUV-422, above.

Preclinical Data

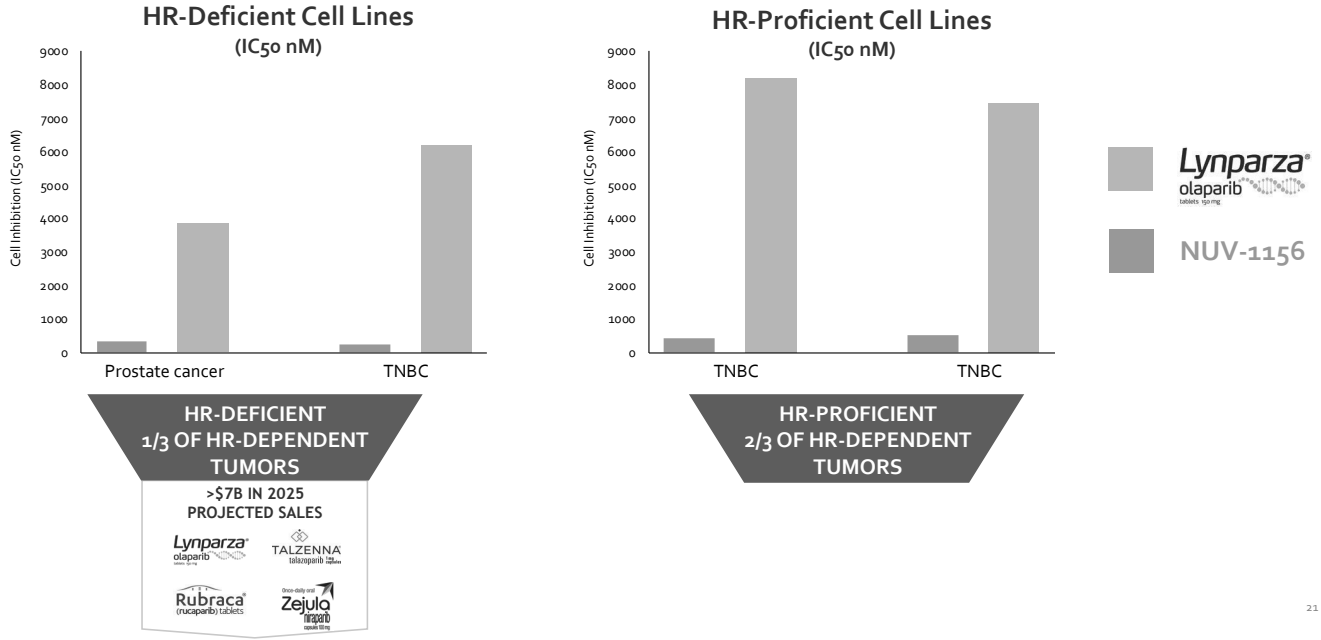
In an Xtandi (enzalutamide)-resistant prostate cancer model, NUV-1156 demonstrated the ability to inhibit growth of enzalutamide-resistant prostate cancer cells more than Lynparza (olaparib), Xtandi (enzalutamide) or the combination of olaparib and enzalutamide. Cell proliferation, as measured by IC50, was more than 30,000 nanomolar for enzalutamide, nearly 8,000 nanomolar for olaparib and over 6,000 nanomolar for olaparib + enzalutamide. In contrast, NUV-1156 had an IC50 of 201 nanomolar, demonstrating that forming a DDC of a PARP inhibitor with a targeting agent that targets a receptor highly expressed in prostate cancer leads to orders of magnitude superior therapeutic effects compared to either agent alone, or even a combination of the two agents given in their native state. These results are shown in the table below.

NUV-1156 DDC POTENTLY KILLS PROSTATE CANCER CELLS RESISTANT TO CURRENT SOC

	CELL PROLIFERATION IC_{50} (nM)
Xtandi (enzalutamide)	>30,000
Lynparza olaparib	7844
Xtandi (enzalutamide) + Lynparza olaparib	6152
NUV-1156 (PARP-AR DDC)	**201**

As shown in the figure below, unlike Lynparza (olaparib) which is only approved in HR-D cancers and is not effective in HR-P tumors, NUV-1156 potently kills prostate cancer cells and triple negative breast cancer cells, whether they are HR-D or HR-P. We believe this underscores the superior potency of NUV-1156 as well as the potential for NUV-1156 to be used more broadly than current commercially available PARP inhibitors, which are limited to HR-D driven tumor types.

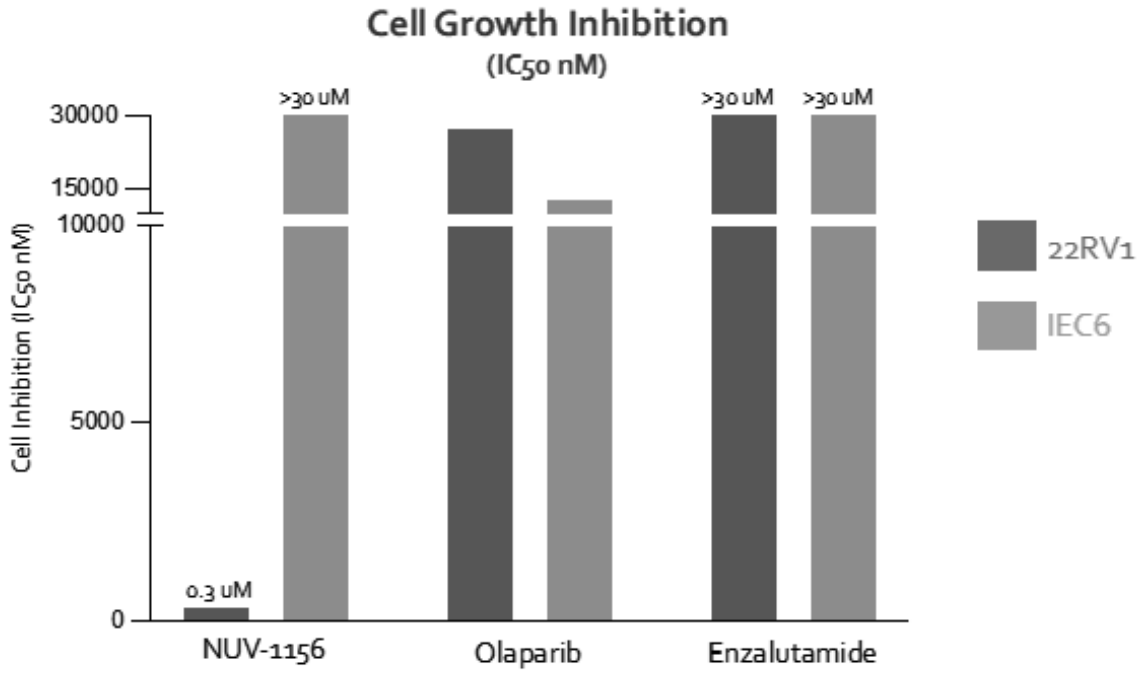
UNLIKE CURRENT PARP INHIBITORS, NUV-1156 KILLS HR-DEFICIENT AND HR-PROFICIENT CANCER CELL LINES WITH EQUALLY HIGH POTENCY



In an Xtandi (enzalutamide)-resistant prostate cancer cell model, NUV-1156 demonstrated the ability to kill cancer cells while sparing healthy gastrointestinal cells in vitro. In the figure below, the grey bars represent prostate cancer cells (22Rv1 prostate cancer cell line model) and the blue bars represent gastrointestinal epithelial cells, or healthy tissue (IEC-6, a standard model for healthy rat gastrointestinal epithelial cells). In this enzalutamide-resistant model, Xtandi (enzalutamide) had no toxicity on IEC-6 gastrointestinal cells but had little efficacy on Xtandi-resistant prostate cancer cells, a suboptimal effect. Lynparza (olaparib) fared even worse, having little efficacy on Xtandi-resistant prostate cancer, but killing gastrointestinal epithelial cells three times more potently than it kills prostate

cancer cells. As compared to Lynparza (olaparib) and Xtandi (enzalutamide), NUV-1156 was observed to be significantly more potent and selective for prostate cancer cells than either Lynparza or Xtandi alone, killing Xtandi-resistant prostate cancer with low nanomolar potency while having little toxicity on healthy gastrointestinal epithelial cells. These results are shown in the figure below.

NUV-1156 KILLS ENZALUTAMIDE-RESISTANT PROSTATE CANCER (HIGH AR) CELLS BUT SPARES HEALTHY COLON (LOW AR) CELLS IN VITRO



In addition to NUV-1156, several other PARP-AR DDCs have demonstrated potent growth inhibition of prostate cancer cells lines, while sparing healthy gastrointestinal cells in vitro. In the figure below, the in vitro IC50 values for several PARP-AR DDCs are shown ranging from less than <150 nM to <250 nM in the prostate cancer cell line 22RV1, and from <30 nM to <150 nM in the prostate cancer cell line LNCaP. In contrast, in vitro IC50 values for the normal gastrointestinal epithelial cell line IEC6 are >30,000 nM. This leads to 22RV1/IEC6 selectivity ratios of up to 250-fold.

NEW AR-DDCS ARE EVEN MORE POTENT AND SELECTIVE THAN NUV-1156 AT KILLING PROSTATE CANCER CELLS (22RV1 AND LNCAP) COMPARED TO GUT EPITHELIAL CALLS (IEC6)

In Vitro Cell Growth Inhibition

Compound	Targeting Receptor	Warhead	Cell Potency (IC50 nM)			Selectivity Ratio
			22RV1	LNCaP	IEC6	IEC6/22RV1
NUV-1546	AR	PARPi	<150	<30	>30000	>250
NUV-1541	AR	PARPi	<200	<150	>30000	>150
NUV-1448	AR	PARPi	<200	<150	>30000	>150
NUV-1552	AR	PARPi	<250	<150	>30000	>125
NUV-1536	AR	PARPi	<250	<150	>30000	>100
NUV-1156	AR	PARPi	<300	<350	>30000	>100

Thus, in preclinical models, PARP-AR DDCs have demonstrated the ability to kill high AR-expressing tissues like prostate cancer while sparing low AR-expressing tissues like healthy gastrointestinal epithelial cells. This level

of specificity may potentially allow a prostate-specific DDC to kill prostate cancer cells in the prostate while sparing other low AR-expressing cells like nerve and blood vessel cells, which are directly impacted during prostate ablation procedures like radical prostatectomy and radiation therapy, the current SOC for early stage prostate cancer. While prostatectomy and radiation ablation are potentially curative, these interventions can result in serious side effects, including erectile dysfunction, urinary incontinence and/or fecal incontinence, or other sequelae of invasive surgery, as a result of damage to the tissues surrounding or within the prostate like healthy blood vessels and nerve cells. We believe that PARP-AR DDCs have the potential to become a non-surgical/non-radiation curative alternative for these patients, representing a large potential market opportunity.

NUV-1176: Targeting ER and PARP for ER+ Breast Cancers

NUV-1176 is an oral small molecule that is composed of a PARP inhibitor warhead that is fused to the binding domain of an ER targeting small molecule. In preclinical models, NUV-1176 potently kills both HR-D and HR-P ER+ tumor cell lines without killing healthy gastrointestinal epithelial cells. We are exploring the use of NUV-1176 for ER+ breast cancer and ovarian cancer. We are currently in preclinical development and intend to nominate our first lead clinical development candidate in the second half of 2022.

Overview of ER+ Breast Cancers

See “Overview of Breast Cancer” for NUV-422, above.

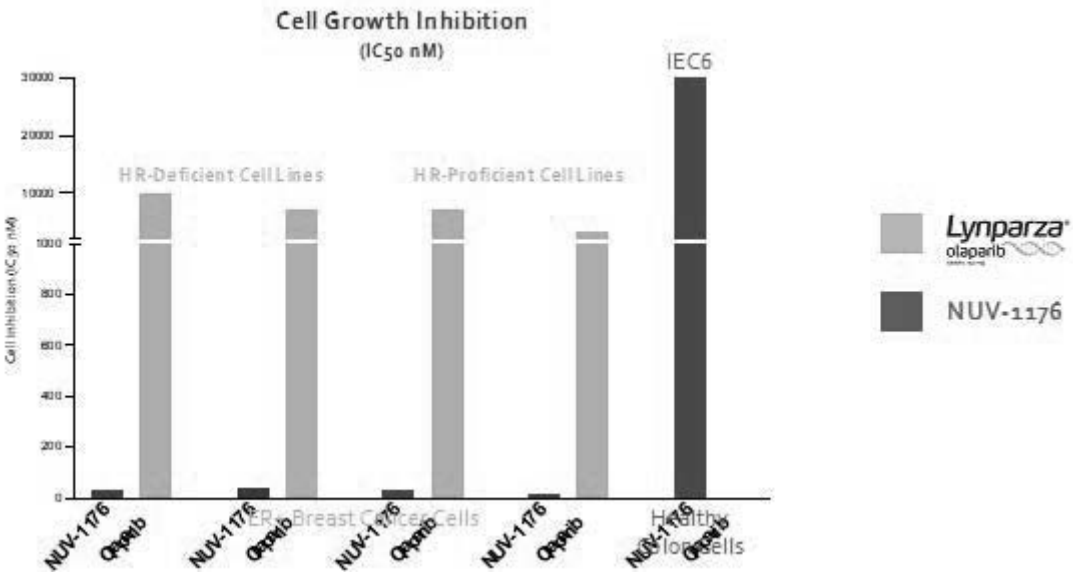
ER Selectively Expressed in ER-Specific Tissue

In women, ER protein expression is limited primarily to the sex organs, with median to high ER expression levels seen across the fallopian tube, breast, vagina, uterine, cervix and endometrium tissues. In contrast, ER expression is either low or not detected in the bone marrow and intestine, organs strongly associated with current commercially available PARP-inhibitor toxicity. Given that ER is more highly expressed in tumors that arise in female sex organ tissues like breast or ovarian cancer than tissues like the bone marrow or gastrointestinal tract, we believe an ER-targeted DDC will have improved anti-tumor activity while limiting the toxicity profile associated with current commercially available PARP inhibitors.

Preclinical data

We have developed NUV-1176, an ER-targeted DDC that is composed of a PARP inhibitor warhead that is fused to the binding domain of an ER-targeting small molecule. In preclinical models, as shown below, NUV-1176 has demonstrated the ability to potently kill both HR-D and HR-P ER+ tumor cell lines with minimal effects on healthy gastrointestinal cells.

NUV-1176, AN ER-TARGETED DDC, POTENTLY KILLS BOTH HR-D AND HR-P ER+ BREAST CANCER CELLS WITH MINIMAL EFFECTS ON HEALTHY COLON CELLS



NUV-1511: A Targeted DDC Derived from a Widely Used Chemotherapy Agent for Prostate and Breast Cancer

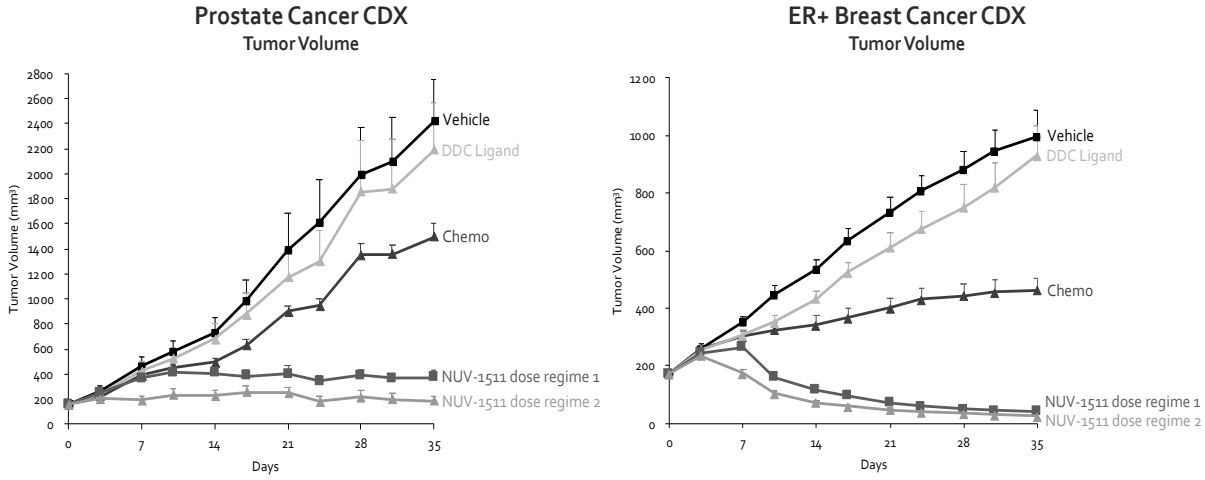
NUV-1511 is a DDC that fuses a targeting agent to a widely used chemotherapy agent that suppresses the growth of prostate and breast cancer. We believe NUV-1511 may be able to limit the adverse side effects of the chemotherapy agent while effectively targeting prostate and breast tumors.

Preclinical data

The anti-tumor efficacy of NUV-1511 was evaluated in a prostate cancer cell line derived xenograft model. As shown in the figure below, NUV-1511 demonstrated significant tumor growth inhibition with IV dosing and two different dosing regimens. Of note, the DDC targeting ligand or chemotherapy agent alone did not inhibit tumor growth to the extent of NUV-1511.

NUV-1511 was also examined in an ER+/PR+ breast cancer cell line derived xenograft model. As shown below, both dosing regimens of NUV-1511 caused significant tumor regressions. The DDC targeting ligand or the chemotherapeutic agent were less effective in inhibiting tumor growth.

NUV-1511, A DDC DERIVATIVE OF A WIDELY USED CHEMO AGENT, CAUSES REGRESSIONS OF PROSTATE AND BREAST CANCER XENOGRAFTS



DDCs have the Potential to Achieve Significant Plasma Exposure Following Oral Dosing in Preclinical Models

As shown in the figure below, following single oral dosing in mice, several new DDCs, with various nuclear hormone receptor targeting and various warheads, have achieved enhanced plasma concentrations and exposure compared with NUV-1156, with plasma exposure, (AUC), exceeding 1000 nM*hr.

NEW DDCS HAVE IMPROVED ORAL BIOAVAILIBILITY COMPARED WITH NUV-1156

Mouse Pharmacokinetics

Compound	Targeting Receptor	Warhead	Dose (mg/kg)	Cmax (nM)	AUC (nM*h)	T1/2 (h)
NUV-1469	undisclosed	undisclosed	10	>50	>500	~5
NUV-1500	undisclosed	undisclosed	10	>300	>1000	~2
NUV-1484	undisclosed	undisclosed	10	>400	>2000	~3
NUV-3064	AR	PARPi	10	>1500	>3000	~3
NUV-1602	AR	PARPi	10	>1000	>4000	~4
NUV-3056	AR	PARPi	10	>2000	>5000	~3
NUV-1156	AR	PARPi	30	<20	>100	~12

Intellectual Property

Our commercial success depends in large part on our ability to obtain and maintain patent protection in the U.S. and other countries for our investigational products, to operate without infringing valid and enforceable patents and proprietary rights of others, and to prevent others from infringing on our proprietary or intellectual property rights.

We seek to protect our proprietary position by pursuing patents that cover the compositions of matter, formulations, methods of use or methods of synthesis relating to our investigational products, as well as other discoveries, technologies, inventions and improvements that may be commercially important to our business. We generally seek patent protection in the U.S. and in foreign jurisdictions such as Australia, Brazil, Canada, Europe, China, Japan, India, Israel, New Zealand, Mexico, Singapore, South Africa, Republic of Korea, Hong Kong and Taiwan.

As of December 31, 2021, our company-owned patent portfolio consists of approximately 6 issued U.S. patents, 35 pending U.S. patent applications, 9 pending PCT applications, and 168 pending foreign patent applications.

NUV-422, our lead investigational product, is covered by an issued patent in the U.S. that claims the composition of matter of NUV-422. This patent is expected to expire in 2039 (not including patent term extension that

may be available to extend the term of the patent). Corresponding patent applications covering the composition of matter of NUV-422 are pending in certain foreign jurisdictions. We also have pending patent applications directed towards specific therapeutic indications and certain solid forms of NUV-422, which if issued, are anticipated to expire in 2042.

Because of the extensive time required for development, testing and regulatory review of an investigational product, it is possible that, before a product can be commercialized, any patent protection for such product may expire or remain in force for only a short period following commercialization, thereby reducing the commercial advantage the patent provides. In the U.S., the term of a patent covering an FDA-approved product may, in certain cases, be eligible for a patent term extension under the Hatch-Waxman Act as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years, but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension may be extended and the amount of available extension to any patent term extension-eligible patent depends on a variety of factors, including the date on which the patent issues and certain dates related to the regulatory review period. Possible extensions may be available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved product. While we intend to seek patent term extensions in any jurisdictions where they are available to us, there is no guarantee that the applicable authorities, including the FDA or the USPTO, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

We also rely on trade secrets to protect our technology and product candidates, especially where we do not believe patent protection is appropriate or obtainable. We seek to protect our proprietary information, in part, using confidentiality agreements with our partners, collaborators, employees and consultants.

Our commercial success may depend in part on not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third party patent would require us to alter our development or commercial strategies, obtain licenses or cease certain activities. Our failure to obtain a license to proprietary rights that we may require to develop or commercialize our future drug products may have a material adverse impact on us.

The intellectual property positions for biotechnology and pharmaceutical companies like us are generally uncertain and can involve complex legal, scientific and factual issues. For information regarding the risks related to our intellectual property, please see "Risk Factors—Risks Related to Our Intellectual Property."

Manufacturing and Supply

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of our investigational products for preclinical and clinical testing, as well as for commercial manufacture if any of our investigational products obtain marketing approval. We also rely, and expect to continue to rely, on third parties to package, label, store and distribute our investigational products, as well as for our commercial products if marketing approval is obtained. We believe that this strategy allows us to maintain a more efficient infrastructure by eliminating the need for us to invest in our own manufacturing facilities, equipment and personnel while also enabling us to focus our expertise and resources on the development of our investigational products.

To date, we have obtained APIs and drug product for our investigational products from single-source third-party CMOs. We are in the process of developing our supply chain for each of our investigational products and intend to put in place framework agreements under which CMOs will generally provide us with necessary quantities of API and drug product on a project-by-project basis based on our development needs, and which agreements will provide us with intellectual property rights necessary to conduct the business. We seek to use a different CMO for each investigational product and will consider further diversification of drug product and supply organizations as circumstances warrant. Overall, as we advance our investigational products through development, we will start by seeking multiple sources for raw materials and address other potential points of concern over time.

Commercialization

We intend to retain significant development and commercial rights to our investigational products and, if marketing approval is obtained, to commercialize our investigational products on our own, or potentially with a partner, in the U.S. and other regions. We intend to build the necessary infrastructure and sales, marketing and commercial product distribution capabilities for the U.S., and potentially other regions, following further advancement

of our investigational products. Clinical data, the size of the addressable patient population and the size of the commercial infrastructure and manufacturing needs and economics related to the foregoing may all influence or alter our commercialization plans.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including large pharmaceutical and biotechnology companies, academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for the research, development, manufacturing and commercialization of cancer therapies. Any investigational products that we successfully develop and commercialize will compete with new therapies that may become available in the future.

We compete in the segments of the pharmaceutical, biotechnology and other related markets that develop small molecules and drug conjugates as treatments for cancer patients. There are many other companies that have commercialized and/or are developing such treatments for cancer including large pharmaceutical and biotechnology companies, such as AstraZeneca plc, Bristol-Myers Squibb Company (“BMS”), Eli Lilly, Merck, Novartis Pharmaceuticals Corporation ("Novartis"), Pfizer, Regeneron Pharmaceuticals, Inc. in partnership with Sanofi Genzyme (“Sanofi”) and Roche.

For our CDK2/4/6 and/or CDK 2 alone inhibitors, we are aware of several clinical-stage and preclinical stage CDK inhibitors being developed as monotherapy or in combination with other drugs, including, but not limited to, product candidates being developed by Pfizer, Fosun Pharma, Cyclacel, Adastra/Cothera Bio, Blueprint Medicines, Aucentra, ARC Therapeutics, and Regor Therapeutics.. In addition, CDK 4/6 inhibitors from Pfizer, Novartis and Eli Lilly are commercially available for patients with breast cancer and are also in clinical trials for other types of cancer. G1 Therapeutics received approval with its CDK4/6 inhibitor to decrease the incidence of chemotherapy-induced myelosuppression extensive-stage small cell lung cancer and is exploring trilaciclib in other oncology indications, including additional breast indications.

For our BET inhibitor, we are aware of several clinical-stage BET inhibitors being developed for patients with hematological malignancies and solid tumors, including, but not limited to, product candidates from Constellation Pharma/MorphoSys Company, Plexxikon, Zenith Epigenetics, Incyte, Boehringer Ingelheim, Abbvie, BMS, Jacobio, Foghorn Therapeutics, Sierra Oncology, Betta Pharmaceuticals and Ranok Therapeutics. In addition, there are a number of BET inhibitors at the preclinical stage. To our knowledge, there is currently no commercially available BET inhibitor and the most advanced BET inhibitor is in a Phase 3 clinical trial (pelabresib for myelofibrosis).

For our Wee1 inhibitor, we are aware of several clinical-stage and preclinical-stage Wee1 inhibitors being developed for patients with solid tumors, including product candidates from AstraZeneca, Zentalis, DebioPharm, Impact Therapeutics, and Schrodinger. To our knowledge, there is currently no commercially available Wee1 inhibitor and the most advanced Wee1 inhibitor is currently in Phase 2 development with Phase 3s in the planning stages.

For our adenosine receptor antagonist, we are aware of several other clinical-stage adenosine antagonists being developed, including, but not limited to, product candidates from Ligand Pharmaceuticals/Corvus Pharmaceuticals, CStone Pharmaceuticals, Dizal (Jiangsu) Pharmaceuticals, Arcus Biosciences/Gilead, Evotec/Exscientia, Incyte, iTeos Therapeutics, Palobiofarma, and Novartis. To our knowledge, there is currently no adenosine receptor antagonist approved for the treatment of cancer and the most advanced adenosine receptor antagonist is in Phase 2 development.

Our DDC programs targeting hormone receptors in cancer cells apply to types of cancer that may depend on hormone receptors for their growth, such as ER+ mBC, prostate cancer and ovarian cancer. All of these tumors have commercially available therapies including therapies from AstraZeneca, Bayer, Clovis Oncology, Dendreon, Eli Lilly, GSK, Janssen Pharmaceutical Companies, Novartis, Pfizer, Roche and Sanofi. In addition, many new product candidates are being developed as monotherapy or in combination with other drugs for these tumors type, and the most advanced of these development programs are in Phase 3 and may lead to near-term regulatory approval and subsequent commercialization. These development programs include those of the companies named above as well as numerous others. Some of these drugs and drug candidates target hormone receptor pathways directly, while many others may affect cancer cell growth through different mechanisms of action.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and enrolling subjects for our clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We could see a reduction or elimination of our commercial opportunity if our competitors develop and commercialize products that are safer or more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we or our collaborators may develop. Our competitors also may obtain FDA or foreign regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we or our collaborators are able to enter the market. The key competitive factors affecting the success of all of our investigational products, if approved, are likely to be their degree of efficacy, tolerability profile, convenience and price, the effectiveness of companion diagnostics (if required), the level of biosimilar or generic competition and the availability of reimbursement from government and other third-party payors.

Government Regulation

Government authorities in the U.S. at the federal, state and local level and in other countries regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and biological products. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. Drug Development

In the U.S., the FDA regulates drugs under the Food, Drug, and Cosmetic Act ("FDCA"). Drugs also are subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post-market may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Our product candidates are considered small molecule drugs and must be approved by the FDA through the new drug application ("NDA") process before they may be legally marketed in the U.S. The process generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with GLP;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board ("IRB") or ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well controlled human clinical trials in accordance with applicable IND regulations, current Good Clinical Practice ("GCP") requirements and other clinical trial-related protocols and regulations to establish substantial evidence of the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of an NDA after completion of all pivotal trials;

- determination by the FDA within 60 days of its receipt of an NDA to accept the filing for substantive review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug will be produced to assess compliance with current good manufacturing practices ("cGMP") requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA audit of the preclinical study and/or clinical trial sites that generated the data in support of the NDA filing to assess compliance with GCP;
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the U.S.; and
- compliance with any post-approval requirements, including the potential requirement to implement a risk evaluation and mitigation strategy ("REMS") and the potential requirement to conduct post-approval studies.

The data required to support an NDA are generated in two distinct developmental stages: preclinical and clinical. The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any current and future product candidates will be granted on a timely basis, or at all.

Preclinical Studies and IND

The preclinical developmental stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. The sponsor must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before human clinical trials may begin.

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vitro* and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

The clinical-stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB must also approve the informed consent form that must be provided to each clinical trial

subject or his or her legal representative and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside of the U.S. may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA. The FDA will generally accept a well-designed and well conducted foreign clinical trial not conducted under an IND if the clinical trial is conducted in compliance with GCP and the FDA is able to validate the data through an onsite inspection, if deemed necessary. An NDA based solely on foreign clinical data meeting U.S. criteria for marketing approval may be approved if (1) the foreign data are applicable to the U.S. population and U.S. medical practice, (2) the studies have been performed by clinical investigators of recognized competence and (3) the FDA is able to validate the data through an onsite inspection or other appropriate means, if deemed necessary

Clinical trials in the U.S. generally are conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and may overlap.

- Phase 1 clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, tolerability and safety of the drug.
- Phase 2 clinical trials involve studies in disease-affected patients to determine the dose and dosing schedule required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified, and a preliminary evaluation of efficacy is conducted.
- Phase 3 clinical trials generally involve a large number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, are conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA. Sponsor is also responsible for submitting written IND safety reports, including reports of serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the drug, findings from animal or *in vitro* testing that suggest a significant risk for human subjects, and any clinically significant increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides recommendations for whether a trial may move forward at designated check-points based on access to certain data from the trial.

Concurrent with clinical trials, companies usually complete additional animal safety studies and also must develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process, as performed by the manufacturing facility, must be capable of consistently producing quality batches of our product candidates. Additionally, appropriate packaging must be selected and tested, and stability studies must be

conducted to demonstrate that our product candidates do not undergo unacceptable deterioration over their labeled shelf life.

NDA Review Process

Following completion of the clinical trials, data is analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical trials are then submitted to the FDA as part of an NDA, along with proposed labeling, chemistry and manufacturing information to ensure product quality and other relevant data. In short, the NDA is a request for approval to market the drug in the U.S. for one or more specified indications and must contain proof of safety and efficacy for a drug.

The application must include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of FDA. FDA approval of an NDA must be obtained before a drug may be legally marketed in the U.S.

Under the Prescription Drug User Fee Act ("PDUFA"), as amended, each NDA must be accompanied by a user fee. FDA adjusts the PDUFA user fees on an annual basis. PDUFA also imposes an annual program fee for each marketed human drug. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all submitted NDAs before it accepts them for filing and may request additional information rather than accepting the NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has 10 months, from the filing date, in which to complete its initial review of a new molecular-entity NDA and respond to the applicant, and six months from the filing date of a new molecular-entity NDA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often extended by FDA requests for additional information or clarification.

Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. The FDA likely will reanalyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, preclinical studies and/or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals

in the U.S., or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making the product available in the U.S. for this type of disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care or in instances of drug supply issues. However, competitors may receive approval of either a different product for the same indication or the same product for a different indication but that could be used off-label in the orphan indication. Orphan drug exclusivity also could block the approval of one of our product candidates for seven years if a competitor obtains approval before we do for the same product, as defined by the FDA, for the same indication we are seeking approval, or if a product candidate is determined to be contained within the scope of the competitor's product for the same indication. If one of our product candidates designated as an orphan drug receives marketing approval for an indication broader than that which is designated, it may not be entitled to orphan drug exclusivity. Orphan drug status in the European Union has similar, but not identical, requirements and benefits.

Expedited Development and Review Programs

The FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request the FDA to designate the product for fast track status any time before receiving NDA approval, but ideally no later than the pre-NDA meeting with the FDA.

Any product submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies.

A product may also be eligible for accelerated approval, if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality ("IMM"), which is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. FDA may withdraw drug approval or require changes to the labeled indication of the drug if confirmatory post-market trials fail to verify clinical benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug. If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it may require such post-marketing restrictions as it deems necessary to assure safe use of the product.

Additionally, a drug may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as fast track designation, plus intensive guidance from the FDA to ensure an efficient drug development program. Fast track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Post-approval Requirements

Following approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping requirements, requirements to report adverse events and comply with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations, known as "off-label promotion," and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Further, if there are any modifications to the drug, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may also place other conditions on approvals including the requirement for REMS, to assure the safe use of the product. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market, or product recalls;
- fines, warning letters, or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications;
- suspension or revocation of product approvals;
- product seizure or detention;
- refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and such promotion must be consistent with FDA-approved labelling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Other U.S. Regulatory Matters

Pharmaceutical manufacturers are subject to various healthcare laws, regulation, and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Our conduct, including those of our employees, as well as our business operations and relationships with third parties, including current and future arrangements with healthcare providers, third-party payors, customers, and others may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, which may constrain the business or financial arrangements and relationships through which we research, as well as, sell, market, and distribute any products for which we obtain marketing approval. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include, but are not limited to:

- The federal Anti-Kickback Statute, which makes it illegal for any person or entity, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit,

receive, offer or pay any remuneration that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Moreover, the Patient Protection and Affordable Care Act, as amended by the Health Care Education and Reconciliation Act, (collectively, the "Affordable Care Act") provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

- The federal false claims laws, including the civil False Claims Act that can be enforced by private citizens through civil whistleblower or *qui tam* actions, and civil monetary penalties law prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government.
- The federal Health Insurance Portability and Accountability Act ("HIPAA") prohibits, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), and their implementing regulations also impose obligations on covered entities such as health insurance plans, healthcare clearinghouses, and certain healthcare providers and their respective business associates and their covered subcontractors, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.
- The federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to annually report to the Centers for Medicare & Medicaid Services ("CMS") information regarding certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals as well as information regarding ownership and investment interests held by physicians and their immediate family members.
- Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, state laws that require biotechnology companies to comply with the biotechnology industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state and local laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and require the registration of their sales representatives, state laws that require biotechnology companies to report information on the pricing of certain drug products, and state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pricing and rebate programs must also comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the Affordable Care Act. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Manufacturing, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws. In addition, the distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act as well as other applicable consumer safety requirements.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in significant civil, criminal and administrative penalties, including damages, fines, disgorgement, imprisonment,

exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings, injunctions, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals or refusal to allow a firm to enter into supply contracts, including government contracts.

U.S. Patent-Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of any future product candidates, some of our U.S. patents, if issued, may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits restoration of the patent term of up to five years as compensation for patent term lost during product development and FDA regulatory review process. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent-term restoration period is generally one-half the time between the effective date of an IND or the issue date of the patent, whichever is later, and the submission date of an NDA plus the time between the submission date of an NDA or the issue date of the patent, whichever is later, and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application ("ANDA"), or a 505(b)(2) NDA submitted by another company for a generic version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness or generate such data themselves.

European Union Drug Development

In the European Union, medicinal products are subject to extensive regulatory requirements. As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained.

The various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the EU Member States have transposed and applied the provisions of the Directive differently into their national laws. This has led to significant variations in the member state regimes.

The Clinical Trials Regulation (EU) No 536/2014 entered into application on January 31, 2022. The Regulation is intended to harmonize and streamline clinical trial authorizations, simplify adverse-event reporting procedures, improve the supervision of clinical trials and increasing their transparency. Specifically, the new Regulation, which is directly applicable in all EU Member States, introduces a streamlined application procedure via a single entry point, the "EU portal"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors. A harmonized procedure for the assessment of applications for clinical

trials is divided into two parts. Part I is assessed by the competent authorities of a reference member state selected by the trial sponsor largely of the type of clinical trial, risk-benefit analysis, and compliance with technical requirements. This assessment, which is valid for the entire EU, is then in Part II submitted to the competent authorities of all the concerned member states in which the trial is to be conducted.

European Union Drug Review and Approval

In the European Economic Area ("EEA"), which comprises the 27 Member States of the European Union and three European Free Trade Association States (Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization ("MA"). There are two types of MAs.

- The Community MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, of the EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State ("RMS"). The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics ("SOPC"), and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SOPC, labeling or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above-described procedures, before granting the MA, EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. Similar to the U.S. patent term-restoration, Supplementary Protection Certificates ("SPCs") serve as an extension to a patent right in Europe for up to five years. SPCs apply to specific pharmaceutical products to offset the loss of patent protection due to the lengthy testing and clinical trials these products require prior to obtaining regulatory marketing approval.

Coverage and Reimbursement

Sales of our products, if approved, will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. In the U.S., for example, principal decisions about reimbursement for new products are typically made by CMS. CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third-party payors often follow CMS's decisions regarding coverage and reimbursement to a substantial degree. However, no uniform policy of coverage and reimbursement for drug products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor-by-payor basis.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Further, such payors are increasingly

challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical product candidates. There may be especially significant delays in obtaining coverage and reimbursement for newly approved drugs. Third-party payors may limit coverage to specific product candidates on an approved list, known as a formulary, which might not include all FDA-approved drugs for a particular indication. We may need to conduct expensive pharmacoeconomic studies to demonstrate the medical necessity and cost effectiveness of our products. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained. Additionally, coverage policies and third party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA"), established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan likely will be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private third-party payors often follow Medicare coverage policy and payment limitations in setting their own payment rates.

In addition, in case a drug product needs companion diagnostics, then companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics.

In addition, in most foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the U.S. and generally prices tend to be significantly lower.

Healthcare Reform

The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price-controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the Affordable Care Act substantially changed the way healthcare is financed by both the government and private insurers, and continues to significantly impact the U.S. pharmaceutical industry. The Affordable Care Act contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal healthcare programs. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the HHS Secretary as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. The Affordable Care Act made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price ("AMP"), to 23.1% of AMP and adding a new rebate

calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The Affordable Care Act also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by enlarging the population potentially eligible for Medicaid drug benefits. Additionally, for a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer.

Since its enactment, there have been executive, judicial and Congressional challenges to certain aspects of the Affordable Care Act, as well as efforts by the administration to repeal or replace certain aspects of the Affordable Care Act. For example, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the Affordable Care Act will remain in effect in its current form. Moreover, prior to the U.S. Supreme Court ruling on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace, which began on February 15, 2021 and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and other litigation, and the healthcare reform measures of the Biden administration will impact the Affordable Care Act.

Other legislative changes have been proposed and adopted in the U.S. since the Affordable Care Act was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, effective April 1, 2013, which, due to subsequent legislative amendments, will stay in effect through 2031, except for a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic, unless additional congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. Further, Congress is considering additional health reform measures. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and accordingly, our financial operations.

Additionally, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Presidential executive orders, Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drug products. For example, at the federal level, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to drug pricing that sought to implement several of the administration's proposals. Additionally, the FDA concurrently released a final rule and guidance in September 2020 providing pathways for states to build and submit importation plans for drugs from Canada. Additionally, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. It is unclear whether these or similar policy initiatives will be implemented in the future. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries

and bulk purchasing. It is possible that additional governmental action is taken in response to the ongoing COVID-19 pandemic, which may impact our business. We are unable to predict the future course of federal or state healthcare legislation in the U.S. directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. These and any further changes in the law or regulatory framework that reduce our revenue or increase our costs could also have a material and adverse effect on our business, financial condition and results of operations.

Facilities

Our principal executive office is located in New York, New York, where we lease approximately 7,900 square feet of office space under a lease that terminates in 2027. We also occupy approximately 8,200 square feet of office space in San Francisco, California, under a lease that terminates in 2022. We are currently evaluating potential options to meet our future San Francisco office space needs. We believe that our existing facilities will be adequate for our current needs and that suitable additional or alternative space will be available in the future on commercially reasonable terms, if required.

Human Capital

Employees

As of December 31, 2021, we had 64 full-time employees, 20 of whom hold Ph.D.s, M.D.s or both. Of our total workforce, 21 employees are engaged in research and development, and 14 employees in general and administrative. We have no collective bargaining agreements with our employees and we have not experienced any work stoppages nor are we aware of any employment circumstances that are likely to disrupt work at any of our facilities. We consider our relationship with our employees to be good.

Human Capital Management

We recognize that attracting, motivating and retaining talent at all levels is vital to our continued success. Our employees are a significant asset and we aim to create an environment that is equitable, inclusive and representative in which our employees can grow and advance their careers, with the overall goal of developing, expanding and retaining our workforce to support our current pipeline and future business goals. By focusing on employee retention and engagement, we also improve our ability to support our clinical-stage platform, business and operations, and also protect the long-term interests of our securityholders. Our success also depends on our ability to attract, engage and retain a diverse group of employees. Our efforts to recruit and retain a diverse and passionate workforce include providing competitive compensation and benefits packages and ensuring we listen to our employees.

We value agility, passion and teamwork, and are building a diverse environment where our employees can thrive and one that inspires exceptional contributions and professional and personal development in order to achieve our mission to significantly change the practice of oncology. Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel through the granting of stock-based and cash-based compensation awards, in order to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives. We are committed to providing a competitive and comprehensive benefits package to our employees. Our benefits package provides a balance of protection along with the flexibility to meet the individual health and wellness needs of our employees.

Diversity and Inclusion

Diversity and inclusion are priorities for us. We believe that a rich culture of inclusion and diversity enables us to create, develop and fully leverage the strengths of our workforce. Our workforce is comprised approximately 55% female employees and approximately 44% racial/ethnic minority employees.

Legal Proceedings

From time to time, we may become involved in legal proceedings or be subject to claims arising in the ordinary course of our business. We are not currently a party to any material legal proceedings. Regardless of outcome, such proceedings or claims can have an adverse impact on us because of defense and settlement costs, diversion of resources and other factors, and there can be no assurances that favorable outcomes will be obtained.

Available Information

We were incorporated in Delaware in April 2020 as a blank check company under the name Panacea Acquisition Corp. On February 10, 2021, Nuvation Bio and Panacea consummated the transactions contemplated under the Merger Agreement, following the approval at a special meeting of our stockholders. In connection with the closing of the Merger, we changed our name to Nuvation Bio Inc.

We file electronically with the U.S. Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended. We make available on our website at www.nuvationbio.com, free of charge, copies of these reports as soon as reasonably practicable after filing these reports with, or furnishing them to, the SEC.

Item 1A. Risk Factors.

Our business and investing in our securities involve significant risks, some of which are described below. Before you make a decision to buy our securities, in addition to the risks and uncertainties discussed in the section titled "Cautionary Information Regarding Forward-Looking Statements," you should carefully consider the risks and uncertainties described below together with all of the other information contained in this Annual Report on Form 10-K, including our financial statements and related notes and in the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations." The occurrence of any of the events or developments described in the following risk factors and the risks described elsewhere in this report could harm our business, financial condition, results of operations, cash flows, the trading price of our common stock and our growth prospects. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. This report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described in the following risk factors and the risks described elsewhere in this report.

Risks Related to Our Financial Position and Need for Additional Capital

We have a limited operating history and have incurred significant losses since inception and anticipate that we may continue to incur losses for the foreseeable future, and may never achieve or maintain profitability.

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are an oncology company with a limited operating history upon which you can evaluate our business and prospects. We commenced operations in 2018, and to date, we have focused primarily on organizing and staffing our company, business planning, raising capital, identifying product candidates, establishing our intellectual property portfolio and conducting research, preclinical studies and clinical trials. Our approach to the discovery and development of product candidates is unproven, and we do not know whether we will be able to develop any product candidates that succeed in clinical development or products of commercial value. As an organization, we have not yet completed any clinical trials, obtained regulatory approvals, manufactured a commercial-scale product (or arranged for a third party to do so on our behalf), or conducted sales and marketing activities necessary for successful product commercialization. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing biopharmaceutical products.

Since inception, we have not generated any product revenue and have incurred significant operating losses. Our net losses were $41.7 million and $86.8 million in 2020 and 2021, respectively. As of December 31, 2021, we had an accumulated deficit of $162.8 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. Since inception, we have devoted substantially all of our efforts to research and preclinical and clinical development of our product candidates, as well as to building our management team and infrastructure. It could be at least several years, if ever, before we have a commercialized drug. The net losses we incur may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if, and as, we:

- continue to advance our research and preclinical and clinical development of our product candidates;
- expand and initiate further clinical trials for our product candidates;
- seek to identify additional product candidates;

- seek marketing approvals for our product candidates that successfully complete clinical trials, if any;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- maintain, expand, protect and enforce our intellectual property portfolio and obtain licenses to third-party intellectual property;
- attract, hire and retain additional administrative, clinical, regulatory and scientific personnel;
- enter into third-party relationships for clinical trials, manufacturing and supply; and
- incur additional legal, accounting and other expenses in operating our business, including the additional costs associated with operating as a public company.

In addition, because of the numerous risks and uncertainties associated with pharmaceutical products and development, we are unable to accurately predict the timing or amount of increased expenses and when, or if, we will be able to achieve profitability. Our expenses could increase and profitability could be further delayed if we decide to or are required by the FDA or other regulatory authorities such as the European Medicines Agency ("EMA"), or the U.K. Medicines & Healthcare Products Regulatory Agency (the "MHRA"), to perform studies or trials in addition to those currently expected, or if there are any delays in the development or completion of any current or future preclinical studies or clinical trials of our current and future product candidates. Even if we complete the development and regulatory processes described above, we anticipate incurring significant costs associated with launching and commercializing our current and future product candidates.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease our value and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in value also could cause you to lose all or part of your investment.

We will need substantial funding to pursue our business objectives. If we are unable to raise capital when needed or on favorable terms, we could be forced to delay, reduce or terminate our product development, other operations or commercialization efforts.

Identifying and developing potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and begin selling any approved products. We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct our ongoing and planned preclinical studies and clinical trials, initiate additional clinical trials for our product candidates and seek regulatory approval for our current product candidates and any future product candidates we may develop. Our expenses could increase beyond our current expectations if the FDA requires us to perform clinical trials and other studies in addition to those that we currently anticipate. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we will be forced to delay, reduce or terminate our research and development programs or future commercialization efforts.

As of December 31, 2021, we had $765.4 million in cash and investments, and an accumulated deficit of $162.8 million. Based upon our current operating plan, we believe that our existing cash, cash equivalents and marketable securities, including the net proceeds from the PIPE Investment, will be sufficient to fund our operations for at least the next 12 months. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we expect. Changes may occur beyond our control that would cause us to consume our available capital before that time, including changes in and progress of our development activities and changes in regulation. Our future capital requirements will depend on many factors, including:

- the scope, rate of progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the number and development requirements of product candidates that we may pursue, and other indications for our current product candidates that we may pursue;

- the costs, timing and outcome of regulatory review of our product candidates;
- the scope and costs of manufacturing development and commercial manufacturing activities;
- the cost associated with commercializing any approved product candidates;
- the cost and timing of developing our ability to establish sales and marketing capabilities, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining, enforcing and protecting our intellectual property rights, defending intellectual property-related claims and obtaining licenses to third-party intellectual property;
- our ability to establish and maintain collaborations on favorable terms, if at all; and
- the extent to which we acquire or in-license other product candidates and technologies and associated intellectual property.

We may require additional capital to complete our planned clinical development programs for our lead product candidate NUV-422 and our other product candidates to obtain regulatory approval. Any additional capital raising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our current and future product candidates, if approved.

In addition, we cannot guarantee that future financing will be available on a timely basis, in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and our issuance of additional securities, whether equity or debt, or the market perception that such issuances are likely to occur, could cause the market price of our common stock to decline. If we are unable to obtain funding on a timely basis on acceptable terms, we may be required to delay, reduce or terminate one or more of our research and development programs or the commercialization of any product candidates that may be approved. This could harm our business and could potentially cause us to cease operations.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish proprietary rights.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, reduce or terminate our product development or future commercialization efforts or grant rights to third parties to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our ability to use our net operating loss carryforwards and certain other tax attributes to offset taxable income or taxes may be limited.

As of December 31, 2021, we had federal and state net operating loss, ("NOL"), carryforwards of $42.7 million and $76.2 million, respectively. Under current law, federal NOLs incurred in taxable years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of such federal net operating losses in taxable years beginning after December 31, 2020 is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to federal tax laws.

Separately, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Internal Revenue Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes, such as research

tax credits, to offset its post-change income or taxes may be limited. The completion of the Merger, together with private placements and other transactions that have occurred since our inception, may trigger such an ownership change pursuant to Section 382. We have not completed a Section 382 analysis, and therefore, there can be no assurances that our NOLs are not already limited.

We may experience ownership changes as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. As a result, if we earn net taxable income, our ability to use our pre-change NOL carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. If an ownership change occurs and our ability to use our net operating loss carryforwards is materially limited, this could harm our future operating results by effectively increasing our future tax obligations. In addition, due to changes in laws and regulations, including changes proposed or implemented by the current U.S. presidential administration, such as alternative minimum taxes, or other unforeseen reasons, our existing net operating losses could become unavailable to reduce future income tax liabilities. Further, at the state level, there may be periods during which the use of NOL carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Risks Related to the Development of our Product Candidates

If we do not obtain regulatory approval for and successfully commercialize our product candidates in one or more indications or we experience significant delays in doing so, we may never generate any revenue or become profitable.

We do not have any products that have received regulatory approval and may never be able to develop marketable product candidates. We are very early in our development efforts. We have invested substantially all of our efforts in developing and identifying potential product candidates and conducting preclinical studies. We expect that a substantial portion of our efforts and expenses over the next several years will be devoted to the development of NUV-422 in our current and planned clinical trials in patients for the treatment of high-grade gliomas, HR+ HER2- advanced breast cancer (with and without brain metastases), mCRPC and other types of cancers, as well as the development of our other product candidates. As a result, our business currently depends heavily on the successful development, regulatory approval and, if approved, commercialization of NUV-422. We cannot be certain that NUV-422 or any other product candidate will receive regulatory approval or will be successfully commercialized even if we receive regulatory approval. The research, testing, manufacturing, safety, efficacy, labeling, approval, sale, marketing and distribution of product candidates is, and will remain, subject to comprehensive regulation by the FDA and similar foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through preclinical studies and clinical trials that the product candidate is safe and effective for use in each target indication. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our preclinical studies or clinical trials. Failure to obtain regulatory approval for our product candidates will prevent us from commercializing and marketing our product candidates. The success of our product candidates will depend on several additional factors, including:

- successful completion of preclinical studies;
- successful initiation of clinical trials;
- successful patient enrollment in, and completion, of clinical trials that demonstrate their safety and efficacy;
- receiving marketing approvals from applicable regulatory authorities;
- obtaining, maintaining, protecting and enforcing patent, trade secret and other intellectual property rights and regulatory exclusivity for our product candidates;
- completing any post-marketing studies required by applicable regulatory authorities;
- making and maintaining arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our product candidates;
- establishing sales, marketing and distribution capabilities and successfully launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- the prevalence and severity of adverse events experienced with our product candidates;

- acceptance of our product candidates by patients, the medical community and third-party payors;
- a continued acceptable safety profile following approval;
- obtaining and maintaining healthcare coverage and adequate reimbursement for our product candidates;
- competing effectively with other cancer therapies, including with respect to the sales and marketing of our product candidates, if approved; and
- obtaining licenses to any third-party intellectual property we deem necessary or desirable.

Many of these factors are beyond our control, including the time needed to adequately complete preclinical studies, clinical testing and the regulatory submission process, our ability to obtain and protect intellectual property rights and changes in the competitive landscape. It is possible that none of our product candidates will ever obtain regulatory approval, even if we expend substantial time and resources seeking such approval. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully complete clinical trials, obtain regulatory approval or, if approved, commercialize our product candidates, which would materially harm our business, financial condition, results of operations and prospects.

In addition, the clinical trial requirements of the FDA, the EMA, the MHRA and other regulatory agencies and the criteria these regulators may use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates.

Our approach to the discovery and development of product candidates based on our DDC platform is unproven, and we do not know whether we will be able to develop any products of commercial value, or if competing technological approaches will limit the commercial value of our product candidates or render our platform obsolete.

The success of our business depends in part upon our ability to identify, develop and commercialize products based on our proprietary Drug-Drug Conjugate ("DDC") platform, which leverages a novel and unproven therapeutic approach within the drug-conjugate class of anti-cancer therapies. While we have had favorable preclinical study results based on our technology, we have not yet succeeded and may not succeed in demonstrating safety and efficacy for any product candidates in clinical trials or in obtaining marketing approval thereafter. Our product candidates arising from our DDC platform are in pre-clinical development and we have not yet completed any clinical trials for any such product candidate. Our research methodology and novel approach to oncology using our DDC platform may be unsuccessful in identifying additional product candidates, and any product candidates based on our technology may be shown to have harmful side effects or may have other characteristics that may necessitate additional clinical testing, or make the product candidates unmarketable or unlikely to receive marketing approval. In addition, adverse developments with respect to one of our DDC platform-based programs may have a significant adverse impact on the actual or perceived likelihood of success and value of similar programs.

In addition, the biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies. Our future success will depend in part on our ability to maintain a competitive position with our DDC platform. If we fail to stay at the forefront of technological change in utilizing our DDC platform to create and develop product candidates, we may be unable to compete effectively. Our competitors may render our DDC platform obsolete, or limit the commercial value of our product candidates, by advances in existing technological approaches or the development of new or different approaches, potentially eliminating the advantages in our drug discovery process that we believe we derive from our research approach and proprietary technologies. By contrast, adverse developments with respect to other companies that attempt to use a similar approach to our approach may adversely impact the actual or perceived value of our DDC platform and potential of our DDC platform-based product candidates. If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would harm our business.

Our DDC platform-based product candidates are based on a novel technology, which makes it difficult to predict the time and cost of product candidate development.

We have concentrated our product research and development efforts on our novel DDC platform, and our future success depends in part on the successful development of product candidates arising from our DDC platform. There

can be no assurance that any development problems we may experience in the future related to our DDC platform will not cause significant delays or unanticipated costs, or that such development problems can be efficiently solved. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical trials or commercializing our product candidates on a timely or profitable basis, if at all.

We may in the future develop product candidates in combination with other therapies and that may expose us to additional risks.

We may develop future product candidates for use in combination with one or more currently approved cancer therapies. Even if any product candidate we develop was to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or similar foreign regulatory authorities could revoke approval of the therapy used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. Combination therapies are commonly used for the treatment of cancer, and we would be subject to similar risks if we develop any of our product candidates for use in combination with other drugs or for indications other than cancer. This could result in our own products being removed from the market or being less successful commercially.

We may also evaluate our product candidates in combination with one or more other cancer therapies that have not yet been approved for marketing by the FDA or similar foreign regulatory authorities. We will not be able to market and sell our product candidates we develop in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval.

If the FDA or similar foreign regulatory authorities do not approve or revoke the approval of these other drugs, or if safety, efficacy, manufacturing or supply issues arise with the drugs we choose to evaluate in combination with our product candidates, we may be unable to obtain approval of or market our product candidates.

Clinical trials are very expensive, time-consuming and difficult to design and implement, and involve uncertain outcomes. Furthermore, results of earlier preclinical studies and clinical trials may not be predictive of results of future preclinical studies or clinical trials.

The risk of failure for our product candidates is high. It is impossible to predict when or if any of our product candidates will prove safe or effective in humans or will receive regulatory approval. To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe and effective in humans for use in each target indication. Preclinical investigation and clinical testing is expensive and can take many years to complete, and the outcome is inherently uncertain. Failure can occur at any time during the preclinical investigation or clinical trial process.

In addition, the results of preclinical studies and earlier clinical trials may not be predictive of the results of later-stage preclinical studies or clinical trials. The results generated to date in preclinical studies for our product candidates do not ensure that later preclinical studies or clinical trials will demonstrate similar results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical and earlier stage clinical trials. In later-stage clinical trials, we will likely be subject to more rigorous statistical analyses than in completed earlier stage clinical trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in later-stage clinical trials due to adverse safety profiles or lack of efficacy, notwithstanding promising results in earlier trials, and we cannot be certain that we will not face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in clinical trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen and other clinical trial protocols, and the rate of dropout among clinical trial participants. If we fail to produce positive results in our planned preclinical studies or clinical trials of any of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be materially and adversely affected.

Interim, "topline," and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial.

We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular drug candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for and commercialize our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

We may encounter substantial delays in our preclinical studies or clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidate for its intended indications. Preclinical studies and clinical trials are expensive, time-consuming and uncertain as to outcome. We cannot guarantee that any preclinical studies or clinical trials will be conducted as planned or completed on schedule, if at all. A failure of one or more preclinical studies or clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of preclinical or clinical development include:

- delays in conducting experiments or preclinical studies or unsatisfactory results from such experiments or studies;
- delays in reaching a consensus with regulatory authorities on trial design;
- delays in reaching agreement or failing to agree on acceptable terms with prospective CROs and clinical trial sites;
- delays in opening sites and recruiting suitable patients to participate in our clinical trials;
- delays in enrollment due to travel or quarantine policies, or other factors, related to COVID-19, other pandemics or other events outside our control;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event, concerns with a class of product candidates or after an inspection of our clinical trial operations or trial sites;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;

- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

For instance, the ongoing COVID-19 pandemic and the measures taken by the governmental authorities could disrupt the supply chain and the manufacture or shipment of drug substances and finished drug products for our product candidates for use in our research and clinical trials, delay, limit or prevent our employees and CROs from continuing research and development activities, impede the ability of patients to enroll or continue in clinical trials, or impede testing, monitoring, data collection and analysis or other related activities, any of which could delay our clinical trials and increase our development costs, and have a material adverse effect on our business, financial condition and results of operations.

Any inability to timely and successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to achieve regulatory and commercialization milestones. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional testing to bridge our modified product candidate to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates, if approved, or allow our competitors to bring comparable drugs to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects.

Additionally, if the results of our clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product candidates, we may:

- be delayed in obtaining marketing approval, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the drug or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy, or REMS;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Our drug development costs will also increase if we experience delays in testing or obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, need to be restructured or be completed on schedule, if at all.

Further, we, the FDA or an IRB may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, including the FDA's current Good Clinical Practice, ("GCP"), regulations that we are exposing participants to unacceptable health risks or if the FDA finds deficiencies in our INDs, or the conduct of these trials. Therefore, we cannot predict with any certainty the schedule for commencement and completion of future clinical trials. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our product candidates could be negatively impacted, and our ability to generate revenues from our product candidates may be delayed or eliminated entirely.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons, including challenges resulting from the ongoing COVID-19 pandemic, labor shortages, and global supply chain interruptions.

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. The enrollment of patients depends on many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size and health of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to study sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial site. Moreover, because our product candidates represent a departure from more commonly used methods for cancer treatment, potential patients and their doctors may be inclined to use conventional therapies rather than enroll patients in any future clinical trial.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our current or planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our product candidates.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications, even those that we have begun investigating and that may have shown promise, that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial therapies or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

If any of our product candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability to market the drug could be compromised.

Clinical trials of our product candidates are conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If one or more of our product candidates receives regulatory approval, and we, or others, later discover

that they are less effective than previously believed, or cause undesirable side effects, a number of potentially significant negative consequences could result, including:

- withdrawal or limitation by regulatory authorities of approvals of such product;
- product candidate is approved under 21 CFR 314 (Subpart H, accelerated approval) but required confirmatory trials may fail to verify clinical benefit;
- seizure of the product by regulatory authorities;
- recall of the product;
- restrictions on the marketing of the product or the manufacturing process for any component thereof;
- requirement by regulatory authorities of additional warnings on the label, such as a "black box" warning or contraindication;
- requirements that we implement a REMS or create a medication guide outlining the risks of such side effects for distribution to patients;
- commitment to expensive additional safety studies prior to approval or post-marketing studies required by regulatory authorities of such product;
- adverse impact on the product's competitiveness;
- initiation of regulatory investigations and government enforcement actions;
- initiation of legal action against us to hold us liable for harm caused to patients; and
- harm to our reputation and resulting harm to physician or patient acceptance of our products.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could harm our business, financial condition, results of operations and prospects.

We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or at the commercial stage, and our product liability insurance may not cover all damages from such claims.

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of pharmaceutical products. We currently have no products that have been approved for commercial sale. However, the current and future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients who use the product, healthcare providers, pharmaceutical companies or others selling such products. Any claims against us, regardless of their merit, could be difficult and costly to defend or settle, and could compromise the market acceptance of our product candidates or any prospects for commercialization of our product candidates, if approved. For more information regarding the risks associated with intellectual property-related litigation, see "Risk Factors—Risks Related to Our Intellectual Property."

Although the clinical trial process is designed to identify and assess potential side effects, it is always possible that a drug, even after regulatory approval, may exhibit unforeseen or rare side effects. If any of our product candidates were to cause adverse side effects during clinical trials or after approval of the product candidate, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates.

Although we maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. As the expense of insurance coverage is increasing, we may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Although we have received Fast Track designation for NUV-422 for the treatment of high-grade gliomas, there is no guarantee that NUV-422 will experience a faster regulatory review or obtain regulatory approval.

If a product is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address an unmet medical need for this condition, the product sponsor may apply for Fast Track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. We have received Fast Track designation for NUV-422 for the treatment of high-grade gliomas, however we may not experience a faster development process, review or approval compared to conventional FDA approval timelines, and the FDA may still decline to approve NUV-422. The FDA may rescind the Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program or for any other reason.

Although we have received Orphan Drug designation for NUV-422 for the treatment of malignant glioma, we may be unable to maintain the benefits associated with such designation, including the potential for market exclusivity.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as Orphan Drugs. Under the Orphan Drug Act, the FDA may designate a drug as an Orphan Drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, Orphan Drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax credits for certain clinical trial costs and user-fee waivers. Generally, if a drug with an Orphan Drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. The applicable period is seven years in the United States.

Although we have obtained Orphan Drug designation for NUV-422 for the treatment of malignant glioma, there is no guarantee that we will obtain approval or Orphan Drug exclusivity for this product. Even if we obtain Orphan Drug exclusivity for NUV-422, that exclusivity may not effectively protect the product candidate from competition because different therapies can be approved for the same condition and the same therapy could be approved for different conditions. Even after an Orphan Drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, a designated Orphan Drug may not receive Orphan Drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, Orphan Drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. Orphan Drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Risks Related to Commercialization of Our Product Candidates

We have never commercialized a product candidate and we may lack the necessary expertise, personnel and resources to successfully commercialize any of our products that receive regulatory approval on our own or together with collaborators.

We have never commercialized a product candidate. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, undertaking preclinical studies of our product candidates and enrolling patients in a clinical trials for our lead product candidate, NUV-422. We currently have no sales force, marketing, manufacturing or distribution capabilities. To achieve commercial success of our product candidates, if any are approved, we will have to develop our own sales, marketing and manufacturing capabilities or outsource these activities to a third party.

Factors that may affect our ability to commercialize our product candidates on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, persuading adequate numbers of physicians to prescribe our product candidates and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization requires significant investment, is time-consuming and could delay the launch of our product candidates. We may not be able to build an effective sales and

marketing organization in the U.S., the European Union or other key global markets. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our product candidates, we may have difficulties generating revenue from them.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical, specialty pharmaceutical and biotechnology companies among others. We compete in the segments of the pharmaceutical, biotechnology and other related markets that develop immunotherapies for the treatment of cancer. There are other companies working to develop immunotherapies for the treatment of cancer including divisions of large pharmaceutical and biotechnology companies of various sizes. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

We are developing our initial product candidates for the treatment of cancer, and currently none of these therapies are approved. There are already a variety of available drug therapies marketed for cancer and some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic products. This may make it difficult for us to achieve our business strategy of replacing existing therapies with our product candidates.

Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop. In addition, most of these companies have substantially greater sales, marketing and other experience and reserves than we do. Competition may further increase as a result of advances in the commercial applicability of technologies for drug discovery and development and greater availability of capital for investment in cancer therapies.

Established pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make our product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, discovering, developing, receiving FDA approval for or commercializing drugs before we do, which would have an adverse impact on our business and results of operations.

The availability of our competitors' products could limit the demand and the price we are able to charge for any product candidate we commercialize, if any. The inability to compete with existing or subsequently introduced drugs would harm our business, financial condition, results of operations and prospects.

Even if any of our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If NUV-422 and our other current and future product candidates receive marketing approval, whether as a single agent or in combination with other therapies, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current approved immunotherapies, and other cancer treatments like chemotherapy and radiation therapy, are well established in the medical community, and doctors may continue to rely on these therapies. If any of our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may never become

profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the ability of NUV-422 and our other product candidates to treat cancer, as compared with other available drugs, treatments or therapies;
- the prevalence and severity of any adverse side effects associated with NUV-422 and our other product candidates;
- limitations or warnings contained in the labeling approved for NUV-422 or our other product candidates by the FDA;
- availability of alternative treatments;
- the size of the target patient population, and the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity for our product candidates and competing products and treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies; and
- our ability to obtain sufficient third-party coverage and adequate reimbursement.

The successful commercialization of certain of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels and pricing policies. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford products such as our product candidates, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our product candidates and, if desired, attract collaboration partners to invest in the development of our product candidates. Coverage under certain government programs, such as Medicare, Medicaid, the 340B drug pricing program and TRICARE, may not be available for certain of our product candidates. Assuming we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the U.S., the European Union or elsewhere will be available for any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates and other therapies as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing drugs may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on products that we may develop.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the U.S., third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may

require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Obtaining and maintaining reimbursement status is time-consuming and costly. No uniform policy for coverage and reimbursement for products exists among third-party payors in the U.S. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely.

Moreover, increasing efforts by governmental and third-party payors in the U.S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. The continuing efforts of the government, insurance companies, managed care organizations and other payors of health care services to contain or reduce costs of health care may adversely affect:

- the demand for any products for which we may obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain coverage and reimbursement approval for a product;
- our ability to generate revenues and achieve or maintain profitability; and
- the level of taxes that we are required to pay.

Even if we obtain regulatory approval for our product candidates, they will remain subject to ongoing regulatory oversight.

Even if we obtain regulatory approval for any of our product candidates, they will be subject to extensive and ongoing regulatory requirements for manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, sampling and record-keeping. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP, regulations and GCPs, for any clinical trials that we conduct post-approval, all of which may result in significant expense and limit our ability to commercialize such products. In addition, any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for any future product candidates we may develop, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. However, if we are found to have promoted such off-label uses, we may become subject to significant liability. The FDA may also require a REMS as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability. Moreover, if there are changes in the application of legislation or regulatory policies, or if problems are discovered with a product or our manufacture

of a product, or if we or one of our distributors, licensees or co-marketers fails to comply with regulatory requirements, the regulators could take various actions. These include:

- issuing warning or untitled letters;
- seeking an injunction or imposing civil or criminal penalties or monetary fines;
- suspension or imposition of restrictions on operations, including product manufacturing;
- seizure or detention of products, refusal to permit the import or export of products or request that we initiate a product recall;
- suspension or withdrawal of our marketing authorizations;
- suspension of any ongoing clinical trials;
- refusal to approve pending applications or supplements to applications submitted by us; or
- requiring us to conduct additional clinical trials, change our product labeling or submit additional applications for marketing authorization.

If any of these events occurs, our ability to sell such product may be impaired, and we may incur substantial additional expense to comply with regulatory requirements, which could harm our business, financial condition, results of operations and prospects.

If any of our product candidates are approved for marketing and commercialization and we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we will be unable to successfully commercialize our product candidates if and when they are approved.

We have no sales, marketing or distribution capabilities or experience. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization, which would be expensive and time consuming, or outsource these functions to other third parties. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or educate adequate numbers of physicians on the benefits of prescribing any future product candidates;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues to us are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. In entering into third-party marketing or distribution arrangements, any revenue we receive will depend upon the efforts of the third parties and we cannot assure you that such third parties will establish adequate sales and distribution capabilities or devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Risks Related to Our Dependence on Third Parties

We rely on third parties to perform the chemistry work associated with our drug discovery and preclinical activities and to conduct our preclinical studies and future clinical trials, and our business could be substantially harmed if these third parties cease performing services or perform in an unsatisfactory manner.

We do not have any laboratory facilities and have relied on CROs to perform most of the medicinal chemistry work associated with our drug discovery activities.

We also do not currently have the ability to independently conduct preclinical studies or clinical trials without outside assistance. We have relied on CROs to conduct all of our preclinical studies to date and intends to conduct our future clinical trials by leveraging expertise and assistance from CROs as appropriate. We plan to rely upon medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct or assist us in conducting GCP-compliant clinical trials on our product candidates properly and on time, and may not currently have all of the necessary contractual relationships in place to do so. Once we have established contractual relationships with such third-party CROs, we will have only limited control over their actual performance of these activities.

We and our CROs and other vendors are required to comply with cGMP, GCP, and good laboratory practice ("GLP"), which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Union and any comparable foreign regulatory authorities for all of our product candidates in preclinical and clinical development. Regulatory authorities enforce these regulations through periodic inspections of trial sponsors, principal investigators, clinical trial sites and other contractors. Although we will rely on CROs to conduct any current or planned GLP-compliant preclinical studies and GCP-compliant clinical trials and has limited influence over their actual performance, we remain responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with our investigational plan and protocol and applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities. If we or any of our CROs or vendors fail to comply with applicable regulations, the data generated in our preclinical studies and clinical trials may be deemed unreliable and the FDA, EMA, MHRA or any comparable foreign regulatory agency may require us to perform additional preclinical studies and clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory agency, such regulatory agency will determine that all of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with products produced under cGMP requirements. Our failure to comply with these requirements may require us to repeat clinical trials, which would delay the regulatory approval process.

While we or our CROs have or will have agreements governing their activities, we will not be able to control whether or not they devote sufficient time and resources to our future chemistry work and preclinical and clinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other chemistry or drug discovery or development activities. We face the risk of potential unauthorized disclosure, infringement, misappropriation or other violation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors, and other third parties, to access and exploit our proprietary technology. CROs also may use our proprietary information and intellectual property in such a way as to invite litigation or other intellectual property-related proceedings that could jeopardize or invalidate our proprietary information and intellectual property. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reason, our clinical trials or other drug discovery or development activities may be extended, delayed or terminated, the clinical data generated in our clinical trials may be deemed unreliable, and we may not be able to obtain regulatory approval for, or successfully commercialize any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

If our relationships with our CROs were to terminate, we might not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial cost and requires management time and focus, and could delay the discovery, development and commercialization of our product candidates. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can negatively impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a negative impact on our business and financial condition.

We do not have our own manufacturing capabilities and will rely on third parties to produce clinical and commercial supplies of NUV-422 and our other current and future product candidates.

We have limited experience in drug formulation and manufacturing and do not own or operate, and we do not expect to own or operate, facilities for drug manufacturing, storage, distribution or testing. To date, we have obtained active pharmaceutical ingredients ("APIs") and drug product for our investigational products mostly from single-source third-party CMOs. We are in the process of developing our supply chain for each of our investigational products and intend to put in place framework agreements under which CMOs will generally provide us with necessary quantities of API and drug product on a project-by-project basis based on our development needs. We seek to use a different CMO for each investigational product and will consider further diversification of drug product and supply organizations as circumstances warrant.

Third-party CMOs may be unable or unwilling to supply us with sufficient clinical and commercial grade quantities of our clinical materials due to production shortages or other supply interruptions resulting from the ongoing COVID-19 pandemic or otherwise, because they are purchased by one of our competitors or another company that decides not to continue supplying us with these materials, or for other reasons. If one or more of these events occur and we are unable to timely establish an alternate supply from one or more third-party CMOs, we could experience delays in our development efforts as we locate and qualify new manufacturers. Under such circumstances, we may be required to receive drug substance for use on a purchase order basis, and as such, there can be no assurance that we actually receive sufficient quantities. See also the risk factor titled "—Our business, operations and clinical development plans and timelines and supply chain could be adversely affected by the effects of health epidemics, including the ongoing COVID-19 pandemic, on the manufacturing, clinical trial and other business activities performed by us or by third parties with whom we conduct business, including our CMOs, CROs, shippers and others."

Further, our reliance on third-party manufacturers exposes us to risks beyond our control, including the risk of:

- inability to meet our product specifications and quality requirements consistently;
- delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and quality issues, including related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for additional scale-up;
- failure of the manufacturer to comply with cGMP and similar foreign standards;
- inability to negotiate manufacturing agreements with third parties on commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- reliance on a limited number of sources, and in some cases, single sources for components, such that if we are unable to secure a sufficient supply of these drug components, we will be unable to manufacture and sell NUV-422 or other product candidates in a timely fashion, in sufficient quantities or under acceptable terms;
- lack of qualified backup suppliers for those components that are currently purchased from a sole or single source supplier;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier or the issuance of a FDA Form 483 notice, warning letter, or cease and desist order;
- carrier disruptions or increased costs that are beyond our control; and
- failure to deliver our products under specified storage conditions and in a timely manner.

Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production. In addition, our third-party manufacturers and suppliers are subject to FDA inspection from time to time. Failure by our third-party manufacturers and suppliers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our product candidate may result in regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses. In addition, our third-party manufacturers and suppliers are subject to numerous environmental,

health and safety laws and regulations, including those governing the handling, use, storage, treatment and disposal of waste products, and failure to comply with such laws and regulations could result in significant costs associated with civil or criminal fines and penalties for such third parties. Based on the severity of the regulatory action, our clinical or commercial supply of drug and packaging and other services could be interrupted or limited, which could harm our business.

In addition, our CMOs are or may be engaged with other companies to supply and manufacture materials or products for such companies, which also exposes our suppliers and manufacturers to regulatory risks for the production of such materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may also affect the regulatory clearance of a contract supplier's or manufacturer's facility. If the FDA or a comparable foreign regulatory agency does not approve these facilities for the supply or manufacture of our product candidates, or if it withdraws its approval in the future, we may need to find alternative supply or manufacturing facilities, which would negatively impact our ability to develop, obtain regulatory approval of or market our product candidates, if approved.

As we prepare for later-stage clinical trials and potential commercialization, we will need to take steps to increase the scale of production of our product candidates, which may include transferring production to new third-party suppliers or manufacturers. In order to conduct larger or late-stage scale clinical trials for our product candidates and supply sufficient commercial quantities of the resulting drug product and our components, if that product candidate is approved for sale, our CMOs and suppliers will need to produce our product candidates in larger quantities, more cost effectively and, in certain cases, at higher yields than they currently achieve. These third-party contractors may not be able to successfully increase the manufacturing capacity for any such product candidates in a timely or cost-effective manner or at all. Significant scale up of manufacturing may require additional processes, technologies and validation studies, which are costly, may not be successful and which the FDA and foreign regulatory authorities must review and approve. In addition, quality issues may arise during those scale-up activities because of the inherent properties of a product candidate itself or of a product candidate in combination with other components added during the manufacturing and packaging process, or during shipping and storage of the APIs or the finished product. If our third-party CMOs are unable to successfully scale up the manufacture of any of our product candidates in sufficient quality and quantity and at commercially reasonable prices, and we are unable to find one or more replacement suppliers or manufacturers capable of production at a substantially equivalent cost in substantially equivalent volumes and quality, and we are unable to successfully transfer the processes on a timely basis, the development of that product candidate and regulatory approval or commercial launch for any resulting products may be delayed, or there may be a shortage in supply, either of which could significantly harm our business, financial condition, results of operations and prospects.

If we are not able to establish collaborations, we may have to alter some of our future development and commercialization plans.

Our product development programs and the potential commercialization of our product candidates will require substantial additional capital to fund expenses. We may enter into collaboration agreements with pharmaceutical and biotechnology companies for the future development and potential commercialization of our product candidates. If we enter into one or more such collaborations, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of any product candidates we may seek to develop with them. We cannot predict the success of any collaboration that we may enter into.

We face significant competition in seeking appropriate collaborators, and a number of more established companies may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, financial resources and greater clinical development and commercialization experience and capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, EMA, MHRA or similar foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be

available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaboration agreements on a timely basis, on acceptable terms, or at all. Even if we are able to obtain a license to intellectual property of interest, we may not be able to secure exclusive rights, in which case others could use the same rights and compete with us. Our collaboration partners, if any, may not prioritize our product candidates or otherwise not effectively pursue the development of our product candidates which may delay, reduce or terminate the development of such product candidate, reduce or delay its development program or delay its potential commercialization. Further if we are unable to successfully obtain rights to required third-party intellectual property rights or maintain and protect the existing intellectual property rights we have, we may have to delay, reduce or terminate the development of our product candidates, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. Doing so will likely harm our ability to execute our business plans. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Risks Related to Regulatory Compliance

Enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may charge for such product candidates.

The U.S. and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product for which we obtain marketing approval.

The Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "Affordable Care Act"), includes measures that have significantly changed the way healthcare is financed by both governmental and private insurers. There have been judicial, executive and congressional challenges to certain aspects of the Affordable Care Act. For example, while Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the Affordable Care Act such as removing penalties, effective January 1, 2019, for not complying with the Affordable Care Act's individual mandate to carry health insurance. On June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the Affordable Care Act will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace, which began on February 15, 2021 and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and the healthcare reform measures of the Biden administration will impact the Affordable Care Act and our business. We continue to evaluate the effect that the Affordable Care Act and its possible repeal and replacement has on our business.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, the Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction, which triggered the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of, on average, 2% per fiscal year through 2031 unless Congress takes additional action. However, COVID-19 relief legislation suspended the 2% Medicare sequester from May 1, 2020, through March 31, 2022. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. Additionally,

on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. Further, Congress is considering additional health reform measures.

Recently, there has been increasing legislative and enforcement interest in the U.S. with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. presidential executive orders, congressional inquiries and legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. For example, at the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders to lower drug prices that attempt to implement several of the Trump administration's proposals. Additionally, the FDA released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, the Department of Health and Human Services ("HHS") finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of this rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been until January 1, 2023. On November 20, 2020, the Centers for Medicare & Medicaid Services ("CMS") issued an interim final rule implementing President Trump's Most Favored Nation ("MFN") executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. As a result of litigation challenging the MFN Model, on December 27, 2021, CMS published a final rule that rescinds the MFN Model interim final rule. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. It is possible that additional governmental action is taken in response to the COVID-19 pandemic, which may impact our business. We are unable to predict the future course of federal or state healthcare legislation in the U.S. directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. These and any further changes in the law or regulatory framework that reduce our revenue or increase our costs could also have a material and adverse effect on our business, financial condition and results of operations.

We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors and customers will be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, health information privacy and security laws and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Although we do not currently have any products on the market, our current and future operations may be, directly or indirectly through our prescribers, customers and third-party payors, subject to various U.S. federal and

state healthcare laws and regulations, including, without limitation, the U.S. federal Anti-Kickback Statute, the U.S. federal civil and criminal false claims laws and the Physician Payments Sunshine Act and regulations. Healthcare providers and others play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. These laws may impact, among other things, our current business operations, including our clinical research activities, and proposed sales, marketing and education programs and constrain the business of financial arrangements and relationships with healthcare providers and other parties through which we may market, sell and distribute our products for which we obtain marketing approval. In addition, we may be subject to patient data privacy and security regulation by both the U.S. federal government and the states in which we conduct our business. Finally, we may be subject to additional healthcare, statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. The laws that may affect our ability to operate include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the U.S. federal false claims, including the False Claims Act, which can be enforced through whistleblower actions, and Civil Monetary Penalties Laws, which, among other things, impose criminal and civil penalties against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

- the U.S. federal Health Insurance Portability and Accountability Act of 1996, ("HIPAA"), which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, ("HITECH"), and its implementing regulations, and as amended again by the Modifications to the HIPAA Privacy, Security, Enforcement and Breach Notification Rules Under HITECH and the Genetic Information Nondiscrimination Act; Other Modifications to the HIPAA Rules, commonly referred to as the Final HIPAA Omnibus Rule, published in January 2013, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the Final HIPAA Omnibus Rule, i.e. health plans, healthcare clearinghouses and certain healthcare providers, as well as their business associates and covered subcontractors that perform certain services for or on their behalf involving the use or disclosure of individually identifiable health information;

- the U.S. Federal Food, Drug and Cosmetic Act, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;

- the U.S. federal legislation commonly referred to as Physician Payments Sunshine Act, enacted as part of the Affordable Care Act, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the CMS information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists,

podiatrists and chiropractors), certain other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;

- analogous state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including, but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the delay, reduction, termination or restructuring of our operations. Further, defending against any such actions can be costly and time-consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business is found to not be in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations.

Failure to comply with current or future federal, state and foreign laws and regulations and industry standards relating to privacy and data protection laws could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.

We and our collaborators and third-party providers may be subject to federal, state and foreign data privacy and security laws and regulations. In the U.S., numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws and federal and state consumer protection laws, such as Section 5 of the Federal Trade Commission Act, that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators and third-party providers.

In many jurisdictions, enforcement actions and consequences for noncompliance are rising. In the U.S., these include enforcement actions in response to rules and regulations promulgated under the authority of federal agencies and state attorneys general and legislatures and consumer protection agencies. In addition, privacy advocates and industry groups have regularly proposed, and may propose in the future, self-regulatory standards that may legally or contractually apply to us. If we fail to follow these security standards, even if no customer information is compromised, we may incur significant fines or experience a significant increase in costs. Many state legislatures have adopted legislation that regulates how businesses operate online, including measures relating to privacy, data security and data

breaches. Laws in all 50 states require businesses to provide notice to customers whose personally identifiable information has been disclosed as a result of a data breach. The laws are not consistent, and compliance in the event of a widespread data breach is costly. States are also constantly amending existing laws, requiring attention to frequently changing regulatory requirements. Furthermore, California recently enacted the California Consumer Privacy Act (the "CCPA"), which became effective in January 2020. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. At this time, we do not collect personal data on residents of California but should we begin to do so, the CCPA will impose new and burdensome privacy compliance obligations on our business and will raise new risks for potential fines and class actions.

Foreign data protection laws, including EU General Data Protection Regulation (the "GDPR"), may also apply to health-related and other personal information obtained outside of the U.S. The GDPR, which came into effect in 2018, introduced new data protection requirements in the European Union, as well as potential fines for noncompliant companies of up to the greater of €20.0 million or 4% of annual global revenue. The regulation imposes numerous new requirements for the collection, use and disclosure of personal information, including more stringent requirements relating to consent and the information that must be shared with data subjects about how their personal information is used, the obligation to notify regulators and affected individuals of personal data breaches, extensive new internal privacy governance obligations and obligations to honor expanded rights of individuals in relation to their personal information (e.g., the right to access, correct and delete their data). Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the U.S., and the efficacy and longevity of current transfer mechanisms between the EU and the U.S. remains uncertain. For example, in 2016, the EU and U.S. agreed to a transfer framework for data transferred from the EU to the U.S., called the Privacy Shield, but the Privacy Shield was invalidated in July 2020 by the Court of Justice of the European Union. At this time, we do not believe we are subject to the GDPR, but should this change, the GDPR will increase our responsibility and potential liability in relation to personal data that we process, and we may be required to put in place additional mechanisms to ensure compliance with the new EU data protection rules.

Compliance with U.S. and foreign data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure by us or our collaborators and third-party providers to comply with U.S. and foreign data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties), private litigation and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws or breached our contractual obligations, even if we are not found liable, could be expensive and time consuming to defend, could result in adverse publicity and could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Our Intellectual Property

If we are unable to obtain, maintain, protect and enforce sufficient patent and other intellectual property rights for our product candidates and technology, or if the scope of patent and other intellectual property rights obtained is not sufficiently broad, we may not be able to compete effectively in our market.

Our success depends in significant part on our ability and the ability of any licensors and collaborators to obtain, maintain, protect and enforce patents and other intellectual property rights with respect to our product candidates and technology and to operate our business without infringing, misappropriating or otherwise violating the intellectual property rights of others.

The patent prosecution process is uncertain, expensive and time-consuming. We and our current or future licensors, licensees or collaborators may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our licensors will fail to identify patentable aspects of our research and development output in time to obtain patent protection or fail to file patent applications covering inventions made in the course of development and commercialization activities before a

competitor or another third party files a patent application covering, or publishes information disclosing, a similar, independently-developed invention. Such competitor's or other third party's patent application may pose obstacles to our ability to obtain patent protection or limit the scope of the patent protection we may obtain. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection in certain jurisdictions. In addition, publications of discoveries in the scientific literature often lag behind actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to conceive the inventions claimed in our owned or licensed patents or pending patent applications, or were the first to file for patent protection of such inventions.

The patent position of biotechnology and pharmaceutical companies generally is uncertain, involves complex legal and factual questions and is the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our and our current or future licensors' patent rights are uncertain. Our and our licensors' pending and future patent applications may not mature into patents or result in issued patents that protect our technology or product candidates, in whole or in part, or which effectively exclude others from commercializing competitive technologies and product candidates. The patent examination process may require us or our licensors to narrow the scope of the claims of our pending and future patent applications, and therefore, even if such patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our and our licensors' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications, and then only to the extent the issued claims cover such technology. Any patents that we hold or in-license may be challenged, narrowed, circumvented or invalidated by third parties. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Any of the foregoing could harm our competitive position, business, financial condition, results of operations and prospects.

The patent protection we obtain for our product candidates and technology may be challenged or not sufficient to provide us with any competitive advantage.

Even if our owned patent applications issue as patents, the issuance of any such patents is not conclusive as to their inventorship, scope, validity or enforceability, and such patents may be challenged, invalidated, narrowed or held to be unenforceable, including in the courts or patent offices in the U.S. and abroad, or circumvented. We may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office (the "USPTO"), a federal court or equivalent foreign bodies, or become involved in opposition, derivation, revocation, re-examination, post-grant and inter partes review or interference proceedings, or other similar proceedings, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, we, or one of our licensors, may have to participate in interference or derivation proceedings declared by the USPTO to determine priority or ownership of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of patentability. Such proceedings and any other patent challenges may result in loss of patent rights, loss of exclusivity, loss of priority or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. Moreover, there could be public announcements of the results of hearings, motions or other developments related to any of the foregoing proceedings. If securities analysts or investors perceive those results to be negative, it could cause the price of shares of our common stock to decline. Any of the foregoing could harm our business, financial condition, results of operations and prospects.

Moreover, some of our owned or in-licensed patents and patent applications may in the future be co-owned with third parties. If we are unable to obtain an exclusive license to any such co-owners' interest in such patents or patent

applications, such co-owners may be able to license their rights to other third parties, including our competitors, who could market competing products and technology. In addition, we may need the cooperation of any such co-owners in order to enforce such patents against third parties, and such cooperation may not be provided to us.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to discover, develop and manufacture our product candidates, we must, at times, share certain of our trade secrets with them. We seek to protect our proprietary technology in part by entering into agreements containing confidentiality provisions, including if applicable, confidentiality agreements, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite these agreements with third parties, sharing trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure could impair our competitive position and may harm our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets could impair our competitive position and have an adverse impact on our business.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful, and issued patents covering our technology and product candidates could be found invalid or unenforceable if challenged.

Competitors and other third parties may infringe, misappropriate or otherwise violate our issued patents or other intellectual property or the patents or other intellectual property of our licensors. In addition, our patents or the patents of our licensors may become involved in inventorship or priority disputes. Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. To counter infringement or other unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents or that our patents are invalid or unenforceable. In a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology. An adverse result in any litigation proceeding could put one or more of our owned or licensed patents at risk of being invalidated, held unenforceable, interpreted narrowly or interpreted in a manner that would not prevent competitors from entering the market. Further, we may find it impractical or undesirable to enforce our intellectual property against some third parties.

In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or insufficient written description. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO or an equivalent foreign body, even outside the context of litigation. Potential proceedings include re-examination, post-grant review, inter partes review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of, or amendment to our patents in such a way that they no longer cover our technology or any product candidates that we may develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on the applicable product candidates or technology covered by the patent rendered invalid or

unenforceable. Such a loss of patent protection could materially harm our business, financial condition, results of operations and prospects.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the ownership or priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Such licenses may not be available on commercially reasonable terms, or at all, or may be non-exclusive. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture and commercialization of one or more of the product candidates we may develop. In addition, if we or our licensors are unsuccessful in any inventorship disputes to which we or they are subject, we may lose valuable intellectual property rights, such as exclusive ownership of, or the exclusive right to use, our owned or in-licensed patents. The loss of exclusivity or the narrowing of our owned and licensed patent claims could limit our ability to stop others from using or commercializing similar or identical technology and products. Any of the foregoing could result in a material adverse effect on our business, financial condition, results of operations or prospects. Even if we are successful in any of the foregoing disputes, it could result in substantial costs and be a distraction to management and other employees. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or proceeding.

Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Most of our competitors are larger than we are and have substantially greater resources. They are, therefore, more likely to be able to sustain the costs of complex patent litigation or proceedings than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing, misappropriating or otherwise violating our intellectual property. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims could result in substantial costs and diversion of management resources, which could harm our business. In addition, the uncertainties associated with litigation could compromise our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs or in-license needed technology or other product candidates. There could also be public announcements of the results of the hearing, motions or other interim proceedings or developments. If securities analysts or investors perceive those results to be negative, it could cause the price of shares of our common stock to decline. Any of the foregoing events could harm our business, financial condition, results of operations and prospects.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, maintaining, defending and enforcing patents and other intellectual property rights on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. can be less extensive than those in the U.S. As such, we may choose not to seek to protect our intellectual property in certain jurisdictions which could leave us without recourse to prevent competitive products from being manufactured or commercialized in such jurisdictions. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the U.S.. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection or other intellectual property rights to develop their own products and may export otherwise infringing, misappropriating or violating products to territories where we have patent or other intellectual property protection, but enforcement rights are not as strong as those in the U.S.. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of some countries do not favor the enforcement of patents and other intellectual property rights, which could make it difficult for us to stop the infringement, misappropriation or other violation of our intellectual property rights generally. Proceedings to enforce our intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful.

Many countries, including European Union countries, India, Japan and China, have compulsory licensing laws under which a patent owner may be compelled under specified circumstances to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In those countries, we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license, which could adversely affect our business, financial condition, results of operations and prospects.

We may not identify relevant third-party patents or pending patent applications or may incorrectly interpret the relevance, scope or expiration of a third-party patent which might adversely affect our ability to develop and market our product candidates.

We are developing certain product candidates in highly competitive areas and cannot guarantee that any patent searches or analyses that we may conduct, including the identification of relevant patents or pending patent applications, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending patent application in the U.S. and abroad that is or may be relevant to or necessary for the commercialization of our product candidates in any jurisdiction. For example, U.S. patent applications filed before November 29, 2000 and certain U.S. patent applications filed after that date that will not be filed outside the U.S. remain confidential until patents issue. Patent applications in the U.S. and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patents or pending patent applications covering our product candidates could have been or may be filed in the future by third parties without our knowledge. Additionally, patents and pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the manufacturing or use of our product candidates. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending patent application may be incorrect, which may negatively impact our ability to market our product candidates. We may incorrectly determine that our product candidates are not covered by a third-party patent or pending patent application or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the U.S. or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents or pending patent applications may negatively impact our ability to develop and market our product candidates.

If we fail to identify or correctly interpret relevant patents or pending patent applications or if we are unable to obtain licenses to relevant patents or pending patent applications, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to pay damages, potentially including in the form of future royalties, which may be significant, we may be temporarily or permanently prohibited from commercializing any of our product candidates that are held to be infringing. We might, if possible, also be forced to redesign product candidates so that we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business and could adversely affect our business, financial condition, results of operations and prospects.

If we are unable to obtain licenses from third parties on commercially reasonable terms or fail to comply with our obligations under such agreements, our business could be harmed.

It may be necessary for us to use the patented or other proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license or ownership from these third parties. The licensing or acquisition of third-party intellectual property rights is a competitive area, and more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources or greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. If we are unable to license or acquire such intellectual property or technology, or if we are forced to in-license such intellectual property or technology, on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may

be unable to develop or commercialize the affected product candidates, or the cost of development, manufacture or commercialization may be materially increased, which could materially harm our business, and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us.

If we fail to comply with our obligations under any future license agreements, such counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or commercialize, or may be forced to cease developing, manufacturing or marketing, any product that is covered by these agreements or may face other penalties under such agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, cause us to lose our rights under these agreements, including our rights to important intellectual property or technology, or impede, delay or prohibit the further development or commercialization of one or more product candidates that rely on such agreements. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing our product candidates, if approved. If we breach any of the agreements under which we license the use, development and commercialization rights to our product candidates or technology from third parties or, in certain cases, we fail to meet certain development deadlines, we could lose license rights that are important to our business.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the U.S., if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product candidate, we may be open to competition from competitive products, including generic medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours.

Depending upon the timing, duration and conditions of any FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and one or more of our foreign patents may be eligible for patent term extension under similar legislation, for example, in the European Union. In the U.S., the Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process provided other requirements are met. However, there are no assurances that the FDA, USPTO or any comparable foreign regulatory authority or national patent office will grant such extensions, in whole or in part and the length of any available extension may vary based on a number of factors. For example, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. Only one patent per approved product can be extended, the extension cannot extend the total patent term beyond 14 years from approval, and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for the applicable product candidate will be shortened, and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case, and our competitive position, business, financial condition, results of operations and prospects could be adversely affected.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

Obtaining and enforcing patents in the pharmaceutical industry is inherently uncertain, due in part to ongoing changes in the patent laws. Depending on decisions by Congress, the federal courts, and the USPTO and equivalent institutions in other jurisdictions, the laws and regulations governing patents, and interpretation thereof, could change in unpredictable ways that could weaken our and our licensors' or collaborators' ability to obtain new patents or to enforce existing or future patents. For example, in recent years the U.S. Supreme Court has ruled on several patent cases that have been interpreted to have either narrowed the scope of patent protection or weakened the rights of patent owners in certain situations. Therefore, there is increased uncertainty with regard to our and our licensors' or collaborators' ability to obtain patents in the future, as well as uncertainty with respect to the value of patents once obtained.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our and our licensors' or collaborators' patent applications and the enforcement or defense of our or our licensors' or collaborators' issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the U.S., the first to invent the claimed invention was entitled to the patent, while outside the U.S., the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act enacted in September 2011 (the "Leahy-Smith Act"), the U.S. transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. The Leahy-Smith Act also includes a number of significant changes that affect the way patent applications are prosecuted and may also affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO-administered post-grant proceedings, including post-grant review, inter partes review and derivation proceedings. The USPTO recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, particularly the first inventor-to-file provisions. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents, all of which could harm our business, financial condition, results of operations and prospects.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated if we fail to comply with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on any issued patents and certain pending patent applications are required to be paid to the USPTO or foreign patent agencies in several stages over the lifetime of a patent. In certain circumstances, we rely on our licensors to pay these fees. The USPTO and various foreign patent agencies also require compliance with a number of procedural, documentary, fee payment and other similar requirements during the patent application and prosecution process. Noncompliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official communications within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in irrevocable abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If we or our licensors or collaborators fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market with similar or identical products or technology, which would harm our business, financial condition, results of operations and prospects.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could negatively impact the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and other proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or be

threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technology, including re-examination, interference, post-grant review, inter partes review or derivation proceedings, or other similar proceedings, before the USPTO, a federal court or an equivalent foreign body. Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are developing our product candidates. In the event that any of these patents were asserted against us, we believe that we would have defenses against any such action, including that such patents are not valid, that our product candidates do not infringe such patents, or that we would be able to replace such technology with alternative, non-infringing technology. However, if any such patents were to be asserted against us and our defenses to such assertion were unsuccessful and such alternative technology was not available or technologically or commercially practical, unless we obtain a license to such patents, we could be liable for damages, which could be significant and include treble damages and attorneys' fees if we are found to willfully infringe such patents, and we could be precluded from commercializing any product candidates that were ultimately held to infringe such patents. Any potential future legal proceedings relating to these patents could cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. If we are unsuccessful in our challenges to these patents and become subject to litigation or are unable to obtain a license on commercially reasonable terms with respect to these patents, it could harm our business, financial condition, results of operations and prospects.

Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability or priority. A court of competent jurisdiction could hold that third-party patents asserted against us are valid, enforceable and infringed, which could materially and adversely affect our ability to commercialize any product candidates we may develop and any other product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe, misappropriate or otherwise violate a third party's intellectual property rights, and we are unsuccessful in demonstrating that such rights are invalid or unenforceable, we could be required to obtain a license from such a third party in order to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease commercializing the infringing technology or product candidates. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties and other fees, redesign our infringing drug or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. Any of the foregoing events would harm our business, financial condition, results of operations and prospects.

We may be subject to claims by third parties asserting that we or our employees have infringed upon, misappropriated or otherwise violated their intellectual property rights, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at other biotechnology or pharmaceutical companies. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's former employer. Litigation may be necessary to defend against these claims.

In addition, we or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents or other intellectual property as an inventor or co-inventor. While it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact conceives, develops or reduces to practice intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may

be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in litigating such claims, litigation could result in substantial costs, delay development of our product candidates and be a distraction to management. Any of the foregoing events would harm our business, financial condition, results of operations and prospects.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace, including compromising our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development collaborations that would help us commercialize our product candidates, if approved. Any of the foregoing events would harm our business, financial condition, results of operations and prospects.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

We rely on trade secrets and agreements containing confidentiality obligations to protect our unpatented know-how, technology and other proprietary information and to maintain our competitive position. With respect to our research and development programs, we consider trade secrets and know-how to be one of our important sources of intellectual property, including our extensive knowledge of certain drug delivery techniques and drug conjugation. Trade secrets and know-how can be difficult to protect. We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. We cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology and processes. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the U.S. are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

We may not be able to protect and enforce our trademarks and trade names, or build name recognition in our markets of interest thereby harming our competitive position.

We intend to rely on both registered and common law rights for our trademarks. We have applied to register certain of our trademarks with the USPTO and trademark authorities in certain other countries and may in the future seek to register additional trademarks in the U.S. or other countries. Our current and future trademark applications may not mature to registration in a timely fashion or at all, and our registered trademarks may not be maintained or enforced. In the U.S. and some foreign jurisdictions, our ability to obtain and maintain trademark registrations and acquire enforceable trademark rights depends on making use of our marks in commerce, meaning we must make a certain amount of progress, depending on the jurisdiction, in our clinical studies or in the commercialization of our

products. If we fail to satisfy these requirements or any other requirements of applicable regulatory authorities, we may not have enforceable trademark rights or registrations in such jurisdictions. We have yet to obtain trademark registrations for the NUVATION or NUVATION BIO trademarks in the U.S., and we have yet to apply to register any brand name for any product candidate in the U.S. or any other jurisdiction.

In addition, the registered or unregistered trademarks or trade names that we own may be challenged, infringed, circumvented, declared generic, lapsed or determined to be infringing on or dilutive of other marks. We may be unable to develop any enforceable trademark rights in relevant countries, or to protect the rights that we do develop. We may be forced to stop using our trademarks or trade names, which we need for name recognition by potential partners and customers in our markets of interest, and spend time and money rebranding. In addition, third parties have filed, and may in the future file, for registration of trademarks similar or identical to our trademarks, thereby impeding our ability to build brand identity and possibly leading to market confusion. If they succeed in registering or developing common law rights in such trademarks, and if we are not successful in enforcing our rights, we may not be able to use these trademarks to develop brand recognition of our company, technologies, products or services. In addition, there could be potential trade name or trademark infringement litigation brought against us by owners of other trademarks that incorporate variations of our registered or unregistered trademarks or trade names.

During the trademark registration process, we may receive office actions from the USPTO or from comparable agencies in foreign jurisdictions refusing to register our trademarks. Although we would be given an opportunity to respond to those refusals, we may be unable to overcome them. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek the cancellation of registered trademarks. Opposition or cancellation proceedings may in the future be filed against our trademark applications or registrations, and our trademark applications or registrations may not survive such proceedings. In addition, third parties may file first for our trademarks or similar variations thereof in certain countries. If they succeed in registering such trademarks, and if we are not successful in challenging such third party rights, we may not be able to use these trademarks to market our products in those countries. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would. If we are unable to establish name recognition based on our trademarks and trade names, we may be unable to compete effectively, which could have an adverse effect on our business, financial condition, results of operations and prospects.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to any product candidates we may develop or utilize similar technology but that are not covered by the claims of the patents that we own or license now or in the future;
- we, or our current or future licensors, might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or license now or in the future;
- we, or our current or future licensors, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending owned or licensed patent applications or those that we may own or license in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by other persons;
- our competitors might conduct research and development activities in the U.S. under FDA-related safe harbor patent infringement exemptions and/or in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;

- we may not develop additional proprietary technologies that are patentable;
- the patents or pending patent applications of others may harm our business; and
- we may choose not to file a patent application in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent application covering such intellectual property.

Should any of these events occur, they could harm our business, financial condition, results of operations and prospects.

Risks Related to Our Business Operations, Employee Matters and Managing Growth

Our business, operations and clinical development plans and timelines and supply chain could be adversely affected by the effects of health epidemics, including the ongoing COVID-19 pandemic, on the manufacturing, clinical trial and other business activities performed by us or by third parties with whom we conduct business, including our CMOs, CROs, shippers and others.

Our business could be adversely affected by health epidemics wherever we have clinical trial sites or other business operations. In addition, health epidemics could cause significant disruption in the operations of CMOs, CROs and other third parties upon whom we rely. For example, the COVID-19 pandemic has presented a substantial public health and economic challenge around the world and is affecting employees, patients, communities and business operations, as well as the U.S. economy and financial markets. Many geographic regions have imposed, or in the future may impose, "shelter-in-place" orders, quarantines or similar orders or restrictions to control the spread of COVID-19. Our headquarters are located in the New York, New York and San Francisco, California areas and at present, we have implemented work-from-home policies for all employees. The effects of the executive order and our work-from-home policies may negatively impact productivity, disrupt our business and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, operating results and financial condition.

We are dependent on a worldwide supply chain for products to be used in our clinical trials and, if approved by the regulatory authorities, for commercialization. Quarantines, shelter-in-place and similar government orders, or the expectation that such orders, shutdowns or other restrictions could occur, whether related to COVID-19 or other infectious diseases, could impact personnel at third-party manufacturing facilities in the U.S. and other countries, or the availability or cost of materials or supplies, which could disrupt our supply chain or our ability to enroll patients in or perform testing for our clinical trials. In addition, closures of transportation carriers and modal hubs could materially impact our clinical development and any future commercialization timelines.

If our relationships with our suppliers or other vendors are terminated or scaled back as a result of the COVID-19 pandemic or other health epidemics, we may not be able to enter into arrangements with alternative suppliers or vendors or do so on commercially reasonable terms or in a timely manner. Switching or adding additional suppliers or vendors involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new supplier or vendor commences work. As a result, delays generally occur, which could adversely impact our ability to meet our desired clinical development and any future commercialization timelines. Although we carefully manage our relationships with our suppliers and vendors, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have an adverse impact on our business, financial condition and prospects. See "Risk Factors—Risks Related to Our Dependence on Third Parties."

In addition, our clinical trials may be affected by the COVID-19 pandemic. In the future, clinical site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID-19 pandemic or concerns among patients about participating in clinical trials during a pandemic and public health measures imposed by the respective national governments of countries in which the clinical sites are located. Some patients may have difficulty following certain aspects of clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Similarly, our inability to successfully recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 or experience additional restrictions by their institutions, city or state governments could adversely impact our clinical trial operations.

The spread of COVID-19 has also led to disruption and volatility in the global capital markets, which increases the cost of, and adversely impacts access to, capital and increases economic uncertainty. The trading prices for the common stock of other biopharmaceutical companies have, at times, been highly volatile as a result of COVID-19.

To the extent the COVID-19 pandemic adversely affects our business, financial results and value of our common stock, it may also affect our ability to access capital, which could in the future negatively affect our liquidity.

The global pandemic of COVID-19 continues to evolve rapidly. The ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material impact on our operations, and we will continue to monitor the COVID-19 situation closely.

Our future success depends on our ability to retain Dr. Hung and our other key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

We are highly dependent on the management, research and development, clinical, financial and business development expertise of Dr. Hung and our executive officers, as well as the other members of our scientific and clinical teams. Although we have employment offer letters with each of our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or employees.

Recruiting and retaining qualified scientific and clinical personnel and, if we are successful in obtaining marketing approval for our product candidates, sales and marketing personnel, is critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy.

In particular, in light of Dr. Hung's central role in the discovery of all of our current product candidates, our ongoing discovery activities and development programs, the recruitment of our other executives and key employees and all other aspects of our strategy and operations, we believe our loss of Dr. Hung's services for any reason would severely impair our business and prospects. Replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval for and commercialize our product candidates.

Competition to hire qualified personnel in our industry is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. Furthermore, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited, and could harm our business, financial condition, results of operations and prospects.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2021, we had 64 employees. As our preclinical and clinical development progresses, we expect to experience growth in the number of our employees and the scope of our operations, particularly in the areas of research, clinical operations, regulatory affairs, general and administrative and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless or negligent conduct or unauthorized activities that violates (1) the laws and regulations of the FDA, the EMA, the MHRA and other similar regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities, (2) manufacturing standards, (3) federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the U.S. and abroad and (4) laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of individually identifiable information, including information obtained in the course of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of product candidates, which could result in regulatory sanctions and serious harm to our reputation.

We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, including damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm and the delay, reduction, termination or restructuring of our operations.

International operations may expose us to business, regulatory, political, operational, financial, pricing and reimbursement risks associated with doing business outside of the U.S.

Our business will be subject to risks associated with conducting business internationally. Some of our suppliers, industry partners and clinical study centers are located outside of the U.S. Furthermore, our business strategy incorporates potential international expansion as we seek to obtain regulatory approval for, and commercialize, our product candidates in patient populations outside the U.S. If approved, we may hire sales representatives and conduct physician and patient association outreach activities outside of the U.S. Doing business internationally involves a number of risks, including but not limited to:

- multiple, conflicting and changing laws and regulations such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements and other governmental approvals, permits and licenses;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- rejection or qualification of foreign clinical trial data by the competent authorities of other countries;
- delays or interruptions in the supply of clinical trial materials resulting from any events affecting raw material supply or manufacturing capabilities abroad, including those that may result from the ongoing COVID-19 pandemic;
- additional potentially relevant third-party patent and other intellectual property rights;
- complexities and difficulties in obtaining, maintaining, protecting and enforcing our intellectual property;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors or patient self-pay systems;

- limits in our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our product candidates and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism and political unrest, outbreak of disease, including COVID-19 and related shelter-in-place orders, travel, social distancing and quarantine policies, boycotts, curtailment of trade and other business restrictions;
- certain expenses including, among others, expenses for travel, translation and insurance; and
- regulatory and compliance risks that relate to anti-corruption compliance and record-keeping that may fall within the purview of the U.S. Foreign Corrupt Practices Act, its accounting provisions or its anti-bribery provisions or provisions of anti-corruption or anti-bribery laws in other countries.

Any of these factors could harm our future international expansion and operations and, consequently, our results of operations.

Our internal computer systems, or those used by our CROs or other contractors or consultants, may fail or experience security breaches or other unauthorized or improper access.

Despite the implementation of security measures, our internal computer systems, and those of our CROs and other third parties on which we rely, are vulnerable to privacy and information security incidents, such as data breaches, damage from computer viruses and unauthorized access, malware, natural disasters, fire, terrorism, war and telecommunication, electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. While we have not experienced any such material system failure or security breach to our knowledge to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business.

Unauthorized disclosure of sensitive or confidential data, including personally identifiable information, whether through a breach of computer systems, systems failure, employee negligence, fraud or misappropriation, or otherwise, or unauthorized access to or through our information systems and networks, whether by our employees or third parties, could result in negative publicity, legal liability and damage to our reputation. Unauthorized disclosure of personally identifiable information could also expose us to sanctions for violations of data privacy laws and regulations around the world. To the extent that any disruption or security breach resulted in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

As we become more dependent on information technologies to conduct our operations, cyber incidents, including deliberate attacks and attempts to gain unauthorized access to computer systems and networks, may increase in frequency and sophistication. These threats pose a risk to the security of our systems and networks, the confidentiality and the availability and integrity of our data and these risks apply both to us, and to third parties on whose systems we rely for the conduct of our business. Because the techniques used to obtain unauthorized access, disable or degrade service or sabotage systems change frequently and often are not recognized until launched against a target, we and our partners may be unable to anticipate these techniques or to implement adequate preventative measures. Further, we do not have any control over the operations of the facilities or technology of our cloud and service providers, including any third party vendors that collect, process and store personal data on our behalf. Our systems, servers and platforms and those of our service providers may be vulnerable to computer viruses or physical or electronic break-ins that our or their security measures may not detect. Individuals able to circumvent such security measures may misappropriate our confidential or proprietary information, disrupt our operations, damage our computers or otherwise impair our reputation and business. We may need to expend significant resources and make

significant capital investment to protect against security breaches or to mitigate the impact of any such breaches. There can be no assurance that we or our third party providers will be successful in preventing cyber attacks or successfully mitigating their effects. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our future product candidates could be delayed.

Risks Related to Ownership of Our Securities

The market price of our securities may be volatile and fluctuate substantially, which could result in substantial losses for our investors and may subject us to securities litigation suits.

The market price of our securities may be volatile. The stock market in general and the market for pharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their securities or above the price they paid. The market price for our securities may be influenced by many factors, including:

- adverse regulatory decisions;
- any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- the impact of the continued effects of and responses to the ongoing COVID-19 pandemic;
- the commencement, enrollment or results of any future clinical trials we may conduct, or changes in the development status of our product candidates;
- adverse results from, delays in or termination of clinical trials;
- unanticipated serious safety concerns related to the use of our product candidates;
- lower than expected market acceptance of our product candidates following approval for commercialization;
- changes in financial estimates by us or by any securities analysts who might cover our securities;
- conditions or trends in our industry;
- changes in the market valuations of similar companies;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the pharmaceutical industry;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- investors' general perception of our company and our business;
- recruitment or departure of key personnel;
- overall performance of the equity markets;
- trading volume of our securities;
- disputes or other developments relating to intellectual property rights, including patents, litigation matters and our ability to obtain, maintain, defend, protect and enforce patent and other intellectual property rights for our technologies;
- significant lawsuits, including patent or stockholder litigation;

- proposed changes to healthcare laws in the U.S. or foreign jurisdictions, or speculation regarding such changes including changes in the structure of healthcare payment systems;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

The dual-class structure of our common stock has the effect of concentrating voting power with our Chief Executive Officer, which limits other stockholders' ability to influence the outcome of important transactions, including a change in control.

Dr. Hung holds all of the outstanding shares of our Class B common stock and 27.2% of our Class A and Class B common stock outstanding. In addition to voting together with the Class A common stock (with one vote per share) on all matters, the holders of Class B common stock have (i) the right to elect and remove without cause three of our directors plus at least 50% of all directors in excess of seven and (ii) an approval right over any acquisition (whether by merger, sale of shares or sale of assets) or our liquidation. Accordingly, Dr. Hung has the ability to control or exert substantial influence over all matters submitted to our stockholders for approval, including the election of directors and amendments of our organizational documents, and an approval right over any acquisition or liquidation of our company. Dr. Hung may have interests that differ from those of the other stockholders and may vote in a way with which the other stockholders disagree and which may be adverse to their interests. This concentrated control may have the effect of delaying, preventing or deterring a change in control, could deprive our stockholders of an opportunity to receive a premium for their capital stock as part of a sale of our company, and might ultimately affect the market price of shares of our Class A common stock

We cannot predict the impact our dual-class structure may have on the market price of our Class A common stock.

We cannot predict whether our dual-class structure, combined with the concentrated voting power of Dr. Hung by virtue of his ownership of 100% of the outstanding shares of our Class B common stock, will result in a lower or more volatile market price of our Class A common stock in the future, or in adverse publicity or other adverse consequences. Certain index providers have announced restrictions on including companies with multi-class share structures in certain of their indices. For example, in July 2017, FTSE Russell and Standard & Poor's announced that they would cease to allow most newly public companies utilizing dual or multi-class capital structures to be included in their indices. Under the announced policies, our dual-class capital structure makes us ineligible for inclusion in any of these indices. Given the sustained flow of investment funds into passive strategies that seek to track certain indices, exclusion from stock indices would likely preclude investment by many of these funds and could make our securities less attractive to other investors. As a result, the market price of our Class A common stock could be adversely affected.

There can be no assurance that we will be able to comply with the continued listing standards of the NYSE.

Our Class A common stock and Public Warrants are listed on the NYSE under the symbols "NUVB" and "NUVBW," respectively. Our continued eligibility for listing will depend on our compliance with the continued listing standards of the NYSE and may depend on the number of our shares that are redeemed. If the NYSE delists our securities from trading on its exchange for failure to meet the listing standards, we and our stockholders could face significant negative consequences including:

- limited availability of market quotations for our securities;
- a determination that our common stock is a "penny stock" which will require brokers trading in our common stock to adhere to more stringent rules, possibly resulting in a reduced level of trading activity in the secondary trading market for shares of our common stock;
- a limited amount of analyst coverage; and
- a decreased ability to issue additional securities or obtain additional financing in the future.

Future sales, or the perception of future sales, by us or our stockholders in the public market following the merger could cause the market price for our securities to decline.

The sale of our securities in the public market, or the perception that such sales could occur, could harm the prevailing market price of our securities. These sales, or the possibility that these sales may occur, also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deems appropriate.

As of the consummation of the Merger, we had a total of approximately 217,650,055 shares of Class A common stock outstanding, consisting of approximately 216,650,055 shares of Class A common stock and 1,000,000 shares of Class B common stock. All shares issued in the merger are freely tradable without registration under the Securities Act, and without restriction by persons other than our "affiliates" (as defined under Rule 144 of the Securities Act, "Rule 144"), including our directors, executive officers and other affiliates.

In connection with the Merger, Legacy Nuvation Bio entered into certain agreements restricting the transfer of our securities held by such contracting parties, including agreements with the Sponsor, Dr. Hung, purchasers under the forward purchase agreement and certain of Legacy Nuvation stockholders. All of these lock-up agreements have now expired.

In addition, the shares of Class A common stock reserved for future issuance under our equity incentive plans will become eligible for sale in the public market once those shares are issued, subject to provisions relating to various vesting agreements, lock-up agreements and, in some cases, limitations on volume and manner of sale applicable to affiliates under Rule 144, as applicable. Our compensation committee of our board of directors may determine the exact number of shares to be reserved for future issuance under our equity incentive plans at its discretion. We have filed and expect to file registration statements on Form S-8 under the Securities Act to register shares of Class A common stock or securities convertible into or exchangeable for shares of Class A common stock issued pursuant to our equity incentive plans. Any such Form S-8 registration statements will automatically become effective upon filing. Accordingly, shares registered under such registration statements will be available for sale in the open market.

In the future, we may also issue our securities in connection with investments or acquisitions. The amount of shares of Class A common stock issued in connection with an investment or acquisition could constitute a material portion of our then-outstanding shares of Class A common stock. Any issuance of additional securities in connection with investments or acquisitions may result in additional dilution to our stockholders.

Because we do not anticipate paying any cash dividends on our Class A common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment.

We may retain future earnings, if any, for future operations, expansion and debt repayment and have no current plans to pay any cash dividends for the foreseeable future. Any decision to declare and pay dividends as a public company in the future will be made at the discretion of our board of directors and will depend on, among other things, our results of operations, financial condition, cash requirements, contractual restrictions and other factors that our board of directors may deem relevant. In addition, our ability to pay dividends may be limited by covenants of any existing and future outstanding indebtedness we or our subsidiaries incur. As a result, you may not receive any return on an investment in our securities unless you sell your securities for a price greater than that which you paid for it.

There is no guarantee that our warrants will be in the money at the time they become exercisable, and they may expire worthless.

The exercise price for our warrants, including our Public Warrants, is $11.50 per share of Class A common stock. There is no guarantee that any of our warrants will be in the money following the time they become exercisable and prior to their expiration, and as such, the warrants may expire worthless.

We may issue additional shares securities without your approval, which would dilute your ownership interests and may depress the market price of our securities.

As of December 31, 2021, we have options outstanding to purchase approximately 11,216,275 shares of Class A common stock. Pursuant to the 2021 Equity Incentive Plan (the "2021 Plan") and the Employee Stock Purchase Plan (the "2021 ESPP"), we may issue an aggregate of up to 52,107,724 shares of Class A common stock and Class B common stock, which amount will be subject to increase from time to time. We may also issue additional shares of Class A common stock or other equity securities of equal or senior rank in the future in connection with, among other

things, future acquisitions or repayment of outstanding indebtedness, without stockholder approval, in a number of circumstances.

The issuance of additional shares or other equity securities of equal or senior rank would have the following effects:

- existing stockholders' proportionate ownership interest in our company will decrease;
- the amount of cash available per share, including for payment of dividends in the future, may decrease;
- the relative voting strength of each previously outstanding common stock may be diminished; and
- the market price of our securities may decline.

Anti-takeover provisions in our amended and restated certificate of incorporation and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult, and may prevent attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation contains provisions that may delay or prevent an acquisition of the company or change in our management in addition to the significant rights of Dr. Hung as the holder of 100% of the outstanding shares of our Class B common stock. These provisions may make it more difficult for stockholders to replace or remove members of our board of directors. Because the board of directors is responsible for appointing the members of the management team, these provisions could in turn frustrate or prevent any attempt by our stockholders to replace or remove our current management. In addition, these provisions could limit the price that investors might be willing to pay in the future for shares of our Class A common stock. Among other things, these provisions include:

- the limitation of the liability of, and the indemnification of, our directors and officers;
- a prohibition on actions by our stockholders except at an annual or special meeting of stockholders;
- a prohibition on actions by our stockholders by written consent; and
- the ability of the board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by the board of directors.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law (the "DGCL"), which prohibits a person who owns 15% or more of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired 15% or more of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. This could discourage, delay or prevent a third party from acquiring or merging with us, whether or not it is desired by, or beneficial to, our stockholders. This could also have the effect of discouraging others from making tender offers for our Class A common stock, including transactions that may be in our stockholders' best interests. Finally, these provisions establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings. These provisions would apply even if the offer may be considered beneficial by some stockholders.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America are the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative action or proceeding brought on our behalf;
- any action asserting a breach of fiduciary duty;

- any action asserting a claim against us arising under the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine or otherwise related to our internal affairs.

To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find either exclusive-forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could harm our business.

We are eligible to report as a "smaller reporting company," and as a result of the reduced reporting requirements applicable to "smaller reporting companies," our securities may be less attractive to investors.

We are eligible to report as a smaller reporting company, although we ceased to qualify as a "smaller reporting company" at the end of 2021 and will cease to report as a "smaller reporting company" commencing with our Quarterly Report on Form 10-Q for the quarter ending March 31, 2022. For as long as we continue to be eligible to report as a "smaller reporting company," including with respect to any portions of our 2022 proxy statement that are incorporated by reference into this report, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not "smaller reporting companies," including exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. If some investors find our securities less attractive because we rely on any of these exemptions, there may be a less active trading market for our securities and the price of our securities may be more volatile.

General Risk Factors

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, the Sarbanes-Oxley Act and the rules and regulations of the NYSE. Section 302 of the Sarbanes-Oxley Act requires, among other things, that public companies report on the effectiveness of our disclosure controls and procedures in our quarterly and annual reports and, beginning with this report, Section 404 of the Sarbanes-Oxley Act requires that we perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting in our Annual Report on Form 10-K for that year. This has required us to incur substantial additional professional fees and internal costs to expand our accounting and finance functions and to expend significant management efforts.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be

subject to sanctions or investigations by the NYSE, the SEC or other regulatory authorities. In addition, our securities may not be able to remain listed on the NYSE or any other securities exchange.

We will incur costs and demands upon our management as a result of complying with the laws and regulations affecting public companies in the U.S., which may harm our business.

As a public company listed in the U.S., we will incur significant additional legal, accounting and other expenses. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the SEC and the NYSE may increase legal and financial compliance costs and make some activities more time consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from regular business activities to compliance activities. If, notwithstanding our efforts, we fail to comply with new laws, regulations and standards, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Failure to comply with these rules might also make it more difficult for us to obtain certain types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management.

If securities or industry analysts cease publishing research or reports about us, our business or our market, or if they change their recommendations regarding our securities adversely, the price and trading volume of our securities could decline.

Equity research analysts may cease providing research coverage of our securities at any time, and such lack of research coverage may adversely affect the market price of our securities. In any event, we do not have any control over the analysts or the content and opinions included in their reports and the price of our stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our securities' prices or trading volume to decline.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our principal executive office is located in New York, New York, where we lease approximately 7,900 square feet of office space under a lease that terminates in 2027. We also occupy approximately 8,200 square feet of office space in San Francisco, California, under a lease that terminates in 2022. We are currently evaluating potential options to meet our future San Francisco office space needs. We believe that these existing facilities will be adequate for our current needs and that suitable additional or alternative space will be available in the future on commercially reasonable terms, if required.

Item 3. Legal Proceedings.

From time to time, we may become involved in legal proceedings or be subject to claims arising in the ordinary course of our business. We are not currently a party to any material legal proceedings. Regardless of outcome, such proceedings or claims can have an adverse impact on us because of defense and settlement costs, diversion of resources and other factors, and there can be no assurances that favorable outcomes will be obtained.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

On February 10, 2021, Panacea and Legacy Nuvation Bio completed the Merger. Following the Merger, we changed the name of the combined company to Nuvation Bio Inc.

Our Class A common stock and warrants to purchase Class A common stock originally began trading as units on The New York Stock Exchange on July 1, 2020. Prior to July 1, 2020, there was no public market for our securities. Following the Merger, beginning February 11, 2021, our Class A common stock and warrants to purchase Class A common stock continued trading on The New York Stock Exchange under the symbols "NUVB" and "NUVB.WS," respectively.

Holders of Record

As of February 18, 2022, there were approximately 91 holders of record of our Class A common stock and 5 holders of record of our warrants to purchase shares of our Class A common stock.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

Recent Sales of Unregistered Securities

On February 10, 2021, in connection with the closing of the Merger, a number of purchasers purchased from us an aggregate of 47,655,000 shares of Class A Common Stock (the "PIPE Shares"), for a purchase price of $10.00 per share and an aggregate purchase price of approximately $476.6 million, pursuant to separate subscription agreements entered into concurrently with the Merger Agreement. The sale was made pursuant to the exemption from registration contained in Section 4(a)(2) of the Securities Act.

Additionally, on February 10, 2021, in connection with the closing of the Merger, certain purchasers purchased 2,500,000 shares of Class A common stock and 833,333 forward purchase warrants (the "Forward Purchase Securities") in a private placement at a price of $10.00 per share for an aggregate purchase price of $25.0 million pursuant to the terms of the forward purchase agreement that Panacea entered into in connection with the Initial Public Offering. Each whole warrant entitles the holder to purchase one share of Class A common stock at an exercise price of $11.50 per share. The sale was made pursuant to the exemption from registration contained in Section 4(a)(2) of the Securities Act. The sales of the PIPE Shares and the Forward Purchase Securities were consummated concurrently with the closing of the Merger.

On March 26, 2021, we issued 368,408 shares of Class A common stock to GiraFpharma, LLC ("GiraF") and Dr. Hung surrendered for cancellation an equal number of shares of Class A common stock. GiraF contributed to Legacy Nuvation Bio all of its intellectual property rights with respect to specified drug development programs to be pursued by Legacy Nuvation Bio in exchange for, among other things, Legacy Nuvation Bio's agreement to issue the above-described shares. This issuance was made pursuant to the exemption from registration contained in Section 4(a)(2) of the Securities Act.

Item 6. Selected Financial Data.

Not applicable.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Exchange Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Forward-looking statements are identified by words such as "believe," "will," "may," "estimate," "continue," "anticipate," "intend," "should," "plan," "expect," "predict," "could," "potentially" or the negative of these terms or similar expressions. You should read these statements carefully because they discuss future expectations, contain projections of future results of operations or financial condition, or state other "forward-looking" information. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements. These forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in this report in Part I, Item 1A — "Risk Factors," and elsewhere in this report. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. These statements, like all statements in this report, speak only as of their date, and we undertake no obligation to update or revise these statements in light of future developments. We caution investors that our business and financial performance are subject to substantial risks and uncertainties. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based on information available to us as of the date of this Annual Report on Form 10-K. While we believe that information provides a reasonable basis for these statements, that information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into or review of, all relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely on these statements.

Overview

We are a clinical-stage biopharmaceutical company tackling some of the greatest unmet needs in oncology by developing differentiated and novel therapeutic candidates. We were founded in 2018 by our chief executive officer, David Hung, M.D., who founded Medivation, Inc. and led its successful development of oncology drugs Xtandi® and talazoparib (now marketed as Talzenna®), leading to its $14.3 billion sale to Pfizer Inc. ("Pfizer") in 2016. We leverage our team's extensive expertise in medicinal chemistry, preclinical development, formulation, and drug development to pursue oncology targets validated by strong clinical or preclinical data and discover novel small molecules that improve the activity and overcome the liabilities of currently marketed drugs. In addition to our focus on development of small molecules for validated targets, we are also developing novel therapeutic candidates based on our proprietary Drug-Drug Conjugate (DDC) platform.

For our lead product candidate, NUV-422, we initiated a Phase 1/2 clinical trial of NUV-422 for the treatment of high-grade gliomas in December 2020. Two additional INDs were cleared by the FDA for NUV-422 for the treatment of advanced breast cancer and for the treatment of prostate cancer in 2021, respectively. Additional trials and trial expansion are planned for NUV-422 in 2022. Our second product is NUV-868, a BD2-selective oral small molecule BET (bromodomain and extra-terminal) inhibitor that inhibits BRD4. An IND has been cleared by the FDA and we intend to initiate a Phase 1 trial of NUV-868 in patients with advanced solid tumors in mid-2022. Our third candidate, NUV-569, is a differentiated oral small molecule selective inhibitor of Wee1 kinase, an important regulator of DNA damage repair. We intend to submit an IND for NUV-569 by year end 2022 and initiate Phase 1 trials in patients with advanced solid tumors following IND clearance. Our adenosine receptor inhibitors are designed to have high affinity for the A_{2A}adenosine receptor, which plays multiple critical roles in human physiology and pathophysiology including anti-cancer immunity. We also designed our adenosine receptor inhibitors to have a reduced affinity for the adenosine A1 receptor, which may potentially improve tolerability. We intend to nominate a clinical development candidate by year end 2022. Lastly, we are also characterizing multiple potential lead product candidates from our DDC platform. We intend to nominate a DDC clinical development candidate by year end 2022.

Merger and Public Company Costs

In October 2020, Legacy Nuvation Bio entered into an Agreement and Plan of Merger with Panacea and Merger Sub pursuant to which Merger Sub was merged with and into Legacy Nuvation Bio, with Legacy Nuvation Bio surviving the merger as a wholly-owned subsidiary of Panacea (the "Merger Agreement"). The transaction provided us with approximately $646 million of gross proceeds, including $476.6 million from a PIPE financing (the "PIPE Investment"). At a special meeting of Panacea stockholders held on February 9, 2021, the Merger was approved and adopted, and the merger and all other transactions contemplated by the Merger were approved. On February 10, 2021,

the Merger was consummated pursuant to the Merger Agreement, Panacea changed its name to Nuvation Bio Inc. and our financial statements became those of Panacea. Following the Closing, Legacy Nuvation Bio was deemed the accounting predecessor and will be the successor registrant for SEC purposes, meaning that Legacy Nuvation Bio's financial statements for previous periods will be disclosed in our future periodic reports filed with the SEC.

While the legal acquirer in the Merger is Panacea, for financial accounting and reporting purposes under U.S. GAAP, Legacy Nuvation Bio was the accounting acquirer and the Merger was accounted for as a "reverse recapitalization." A reverse recapitalization (i.e., a capital transaction involving the issuance of stock by Panacea for Legacy Nuvation Bio's stock) does not result in a new basis of accounting, and the consolidated financial statements of the combined entity represent the continuation of the consolidated financial statements of Legacy Nuvation Bio in many respects. Accordingly, the consolidated assets, liabilities and results of operations of Legacy Nuvation Bio became the historical consolidated financial statements of the combined company, and Panacea's assets, liabilities and results of operations were consolidated with those of Legacy Nuvation Bio beginning on the acquisition date. Operations prior to the Merger will be presented as those of Legacy Nuvation Bio in future reports. The net assets of Panacea were recognized at historical cost (which is expected to be consistent with carrying value), with no goodwill or other intangible assets recorded.

Upon consummation of the Merger and the closing of the PIPE Investment, the most significant change in the post-combination company's future reported financial position is an increase in cash and cash equivalents (as compared to Legacy Nuvation Bio's condensed consolidated balance sheet at December 31, 2020) primarily due to $476.6 million in gross proceeds from the PIPE Investment.

As a consequence of the Merger, we became the successor to an SEC-registered and NYSE-listed company, which has required us to hire additional personnel and implement procedures and processes to address public company regulatory requirements and customary practices. We have incurred and expect to continue to incur additional annual expenses as a public company for, among other things, directors' and officers' liability insurance, director fees and additional internal and external accounting, legal and administrative resources, including increased audit and legal fees.

Our future results of consolidated operations and financial position may not be comparable to historical results as a result of the Merger.

COVID-19 Business Update

The global COVID-19 pandemic continues to rapidly evolve, and we will continue to monitor the COVID-19 situation closely. To date our financial condition and operations have not been significantly impacted by the COVID-19 impact. However, we cannot, at this time, predict the specific extent, duration or full impact that the COVID-19 outbreak will have on our financial condition and operations, including our ongoing and planned preclinical activities and clinical trials. The extent of the impact of the COVID-19 on our business, operations and clinical development timelines and plans remains uncertain and will depend on certain developments, including the duration and spread of the outbreak and its impact on our clinical trial enrollment, trial sites, contract research organizations ("CROs"), third-party manufacturers, and other third parties with which we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. To the extent possible, we are conducting business as usual, with necessary or advisable modifications to employee travel as many of our employees are working remotely. We will continue to actively monitor the rapidly evolving situation related to COVID-19 and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees and other third parties with which we do business. The development of our product candidates could be disrupted and materially adversely affected in the future by the COVID-19 pandemic. Our planned clinical trials also could be delayed due to government orders or site policies on account of the pandemic, and some patients may be unwilling or unable to travel to study sites or enroll in our trials or be unable to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Any of these occurrences could delay our ability to conduct clinical trials or release clinical trial results and delay our ability to obtain regulatory approval and commercialize our product candidates. Furthermore, COVID-19 could affect our employees or the employees of research sites and service providers on which we rely, including CROs, as well as those of companies with which we do business, including our suppliers and contract manufacturing organizations, thereby disrupting our business operations. Quarantines and travel restrictions imposed by governments in the jurisdictions in which we and the companies with which we do business operate could materially impact the ability of employees to access preclinical and clinical sites, laboratories, manufacturing site and office. These and other events resulting from the

COVID-19 pandemic could disrupt, delay, or otherwise adversely impact our business. Further information relating to the risks and uncertainties related to the ongoing COVID-19 pandemic are contained in the section titled "Item 1A. Risk Factors."

Financial Overview

Since our inception in 2018, we have focused substantially all of our resources on conducting research and development activities, including drug discovery, preclinical studies, conducting our Phase 1/2 study of our lead product candidate NUV-422, establishing and maintaining our intellectual property portfolio, developing our manufacturing network and managing the manufacture of clinical and research material, hiring personnel, raising capital and providing general and administrative support for these operations. We have not recorded revenue from product sales or collaboration activities, or any other source. We have funded our operations to date primarily from the issuance and sale of our common and preferred stock, including through the Merger and the PIPE Investment.

We have incurred net losses in each year since inception. As of December 31, 2021, we had an accumulated deficit of $162.8 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses over at least the next several years. We expect our expenses will increase substantially in connection with our ongoing activities, as we:

- advance product candidates through clinical trials;
- pursue regulatory approval of product candidates;
- operate as a public company;
- continue our preclinical programs and clinical development efforts;
- continue research activities for the discovery of new product candidates; and
- manufacture supplies for our preclinical studies and clinical trials.

In addition, we expect to incur additional costs associated with operating as a public company, including significant legal, audit, accounting, regulatory, tax-related, director and officer insurance, investor relations and other expenses that we did not incur as a private company. As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the public or private sale of equity, government or private party grants, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. If we are unable to obtain additional funding, we could be forced to delay, reduce or eliminate some or all of our research and development programs, product portfolio expansion or any commercialization efforts, which could adversely affect our business prospects, or we may be unable to continue operations. If we raise funds through strategic collaborations or other similar arrangements with third parties, we may have to relinquish valuable rights to our platform technology, future revenue streams, research programs or product candidates or may have to grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic or other events. Because of the numerous risks and uncertainties associated with product development, we cannot predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability.

Components of Results of Operations

Research and Development Expenses

Research and development expenses include:

- expenses incurred under agreements with third-party contract organizations, and consultants;
- costs related to production of drug substance, including fees paid to contract manufacturers;
- laboratory and vendor expenses related to the execution of preclinical trials; and

- employee-related expenses, which include salaries, benefits and stock-based compensation.

We expense all research and development costs in the periods in which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks and estimates of services performed using information and data provided to us by our vendors and third-party service providers. Nonrefundable advance payments for goods or services to be received in future periods for use in research and development activities are deferred and capitalized. The capitalized amounts are then expensed as the related goods are delivered and as services are performed. We expense in-process research and development projects acquired as part of asset acquisitions that have no alternative future use.

To date, the majority of these expenses have been incurred to advance our lead product candidate, NUV-422. We expect our research and development expenses to increase substantially for the foreseeable future as we continue to invest in research and development activities related to developing our product candidates, as our product candidates advance into later stages of development, and as we begin to conduct clinical trials. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

General and Administrative Expenses

General and administrative expenses consist of personnel-related costs, facilities costs, depreciation and amortization expenses and professional services expenses, including legal, human resources, audit and accounting services. Personnel-related costs consist of salaries, benefits and stock-based compensation. Facilities costs consist of rent and maintenance of facilities. We expect our general and administrative expenses to increase for the foreseeable future due to anticipated increases in headcount to advance our product candidates and as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the SEC, NYSE, additional insurance expenses, investor relations activities and other administrative and professional services.

Other Income (Expense), Net

Other income (expense) consists of change in fair value of Warrant liabilities, interest earned on our cash equivalents and investments, advisory expense related to our investments and realized gains and losses on marketable securities.

Results of Operations

Years Ended December 31, 2021 and 2020

	Years Ended December 31,		Increase /
	2021	2020	(Decrease)
(In thousands)			
Operating expenses:			
Research and development	$ 69,037	$ 32,603	$ 36,434
General and administrative	24,281	10,948	13,333
Total operating expenses	93,318	43,551	49,767
Loss from operations	(93,318)	(43,551)	(49,767)
Other income (expense), net	6,470	1,892	4,578
Net loss	$ (86,848)	$ (41,659)	$ (45,189)

Research and Development Expenses

Research and development expenses increased by $36.4 million for the years ended December 31, 2021 compared to 2020. The increase was primarily due to a $22.8 million increase in third-party costs related to research services and manufacturing to advance our current preclinical programs and Phase 1/2 clinical trial, $3.8 million related to issuance of common stock as consideration for the purchase of in-process research and development, as well as a $9.8 million increase in personnel-related costs driven by an increase in headcount and stock-based compensation.

General and Administrative Expenses

General and administrative expenses increased by $13.3 million for the years ended December 31, 2021, compared to 2020. The increase was primarily due to a $6.9 million increase in personnel-related costs driven by an increase in headcount and stock-based compensation, a $4.0 million increase in insurance, a $0.4 million increase in taxes, a $1.1 million increase in professional fees and a $1.0 million increase in other miscellaneous expenses.

Other Income (Expense), Net

Other income (expense), net increased by $4.6 million for the years ended December 31, 2021 compared to 2020 primarily related to a $4.2 million decrease in fair value of Warrant liability, increase of $1.0 million in interest income from investments in 2021 primarily because of higher cash balance compared to 2020 offset by an increase of $0.4 million in investment fees and a decrease of $0.3 million in realized gain on marketable securities.

Liquidity, Capital Resources and Plan of Operations

From inception through December 31, 2021, our operations have been financed primarily by the sale and issuance of Series A preferred stock and common stock, including through the Merger and the PIPE Investment. As of December 31, 2021, we had $765.4 million in cash, cash equivalents and marketable securities and an accumulated deficit of $162.8 million.

Our primary use of cash is to fund operating expenses, which consist of research and development expenses related to our lead product candidate, NUV-422, and preclinical programs, and to a lesser extent, general and administrative expenses. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

Based upon our current operating plan, we believe that our existing cash, cash equivalents and marketable securities as of December 31, 2021, will enable us to fund our operating expenses and capital expenditure requirements through at least the next 12 months.

We expect to incur substantial expenses in the foreseeable future for the development and potential commercialization of our product candidates and ongoing internal research and development programs. At this time, we cannot reasonably estimate the nature, timing or aggregate amount of costs for our development, potential commercialization, and internal research and development programs. However, in order to complete our current and future preclinical studies and clinical trials, and to complete the process of obtaining regulatory approval for our product candidates, as well as to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our product candidates, if approved, we may require substantial additional funding in the future.

Cash Flows

The following table summarizes our cash flows for the periods indicated:

	Years Ended December 31,	
	2021	2020
	(In thousands)	
Cash used in operating activities	$ (68,190)	$ (36,529)
Cash used in investing activities	(454,669)	(70,320)
Cash provided by financing activities	625,527	133,135
Net increase in cash and cash equivalents	$ 102,668	$ 26,286

Operating Activities

In 2021, cash used in operating activities of $68.2 million was attributable to a net loss of $86.8 million partially offset by a net change of $4.8 million in our net operating assets and liabilities and non-cash charges of $13.9 million. The change in operating assets and liabilities was due to a $7.4 million increase in accrued expenses, $1.9 million increase in accounts payable offset by $2.4 million increase in prepaid expenses, $1.9 million increase in interest receivable on marketable securities and $0.2 million decrease in deferred rent. The non-cash charges consisted of the issuance of common stock for in-process research and development expense of $3.8 million, stock-based compensation of $9.3 million, amortization of premium on marketable securities of $4.6 million, $0.2 million of

depreciation and amortization expense and $0.2 million of lease expense offset by a change in fair value of Warrant liability of $4.2 million.

In 2020, cash used in operating activities of $36.5 million was attributable to a net loss of $41.6 million partially offset by a net change of $2.1 million in our net operating assets and liabilities and non-cash charges of $3.0 million. The change in operating assets and liabilities was primarily due to a $2.9 million increase in accrued expense and $0.2 million increase in deferred rent offset by $0.7 million increase in prepaid expenses and $0.3 million increase in interest receivable on marketable securities. The non-cash charges consisted primarily of stock-based compensation of $2.2 million and amortization of premium on marketable securities of $0.9 million.

Investing Activities

In 2021, cash used for investing activities of $454.7 million was related to the purchase of marketable securities of $609.3 million, purchases of property and equipment of $0.3 million partially offset by $154.9 million of proceeds from the sale of marketable securities.

In 2020, cash used for investing activities of $70.3 million was related to the $143.3 million purchase of marketable securities and purchases of property and equipment of $0.1 million offset by of $73.1 million of proceeds from the sale of marketable securities and investment held to maturity .

Financing Activities

In 2021, cash provided by financing activities of $625.5 million was related to the $624.8 million net proceeds from the Merger, $0.3 million of proceeds from issuance of common stock under Employee Stock Purchase Plan and $0.4 million of proceeds from exercise of options.

In 2020, cash provided by financing activities of $133.1 million was related to the $135.6 million net proceeds from the Merger offset by $2.5 million of deferred financing costs.

Off-Balance Sheet Financing Arrangements

As of December 31, 2021, we did not have any off-balance sheet arrangements, as defined in Regulation S-K, Item 303(a)(4)(ii).

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of financial condition and results of operations is based upon our consolidated financial statements, which have been prepared in accordance with GAAP. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses. On an on-going basis, we evaluate our critical accounting policies and estimates. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable in the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions and conditions.

While our significant accounting policies are described in the notes to our consolidated financial statements, we believe that the following critical accounting policies are most important to understanding and evaluating our reported financial results.

Research and Development Expenses

We expense all research and development costs in the periods in which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks and estimates of services performed using information and data provided to us by our vendors and third-party service providers. Nonrefundable advance payments for goods or services to be received in future periods for use in research and development activities are deferred and capitalized. The capitalized amounts are then expensed as the related goods are delivered and as services are performed. We expense in-process research and development projects acquired as part of asset acquisitions that have no alternative future use.

Warrant Liability

We account for warrants as either equity-classified or liability-classified instruments based on an assessment of the warrant's specific terms and applicable authoritative guidance in Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") 480, Distinguishing Liabilities from Equity ("ASC 480") and ASC 815, Derivatives and Hedging ("ASC 815"). The assessment considers whether the warrants are freestanding financial instruments pursuant to ASC 480, meet the definition of a liability pursuant to ASC 480, and whether the warrants meet all of the requirements for equity classification under ASC 815, including whether the warrants are indexed to the company's own ordinary shares, among other conditions for equity classification. This assessment, which requires the use of professional judgment, is conducted at the time of warrant issuance and as of each subsequent quarterly period end date while the warrants are outstanding.

For issued or modified warrants that meet all of the criteria for equity classification, the warrants are required to be recorded as a component of additional paid-in capital at the time of issuance. For issued or modified warrants that do not meet all the criteria for equity classification, the warrants are required to be recorded as a liability at their fair value on the date of issuance and each balance sheet date thereafter. Changes in the estimated fair value of the warrants are recognized as a non-cash gain or loss on the statements of operations. The fair value of Public and Forward Purchase Warrants was determined using the closing price of the warrants on the NYSE market. The fair value of the Private Warrants was estimated using the Black-Scholes option pricing formula (see Note 4).

Stock-Based Compensation Expense

We estimate the fair value of our stock-based awards to employees and non-employees that are based on a service condition only using the Black-Scholes option-pricing model, which is impacted by our common stock price as well as other variables including, but not limited to, expected term that options will remain outstanding, expected common stock price volatility over the term of the option awards, risk-free interest rates and expected dividends.

We determine the fair value of stock-based awards that are based on both a service condition and achievement of the first to occur of a market or performance condition using a Monte Carlo simulation.

The fair value of a stock-based award is recognized over the period during which a recipient is required to provide services in exchange for the award, known as the requisite service period (usually the vesting period) on a straight-line basis. Stock-based compensation expense is recognized based on the fair value determined on the date of grant and is reduced for forfeitures as they occur.

Estimating the fair value of stock-based awards as of the grant date using valuation models, such as the Black-Scholes option pricing model, is affected by assumptions regarding a number of variables. Changes in the assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require significant analysis and judgment to develop.

Expected Term—We have opted to use the "simplified method" for estimating the expected term of options whose vesting is based on service condition only, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option (generally 10 years).

Expected Volatility—Due to our limited operating history and a lack of company specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded.

Risk-Free Interest Rate—The risk-free rate assumption is based on the U.S. Treasury instruments with maturities similar to the expected term of our stock options at the time of the grant.

Expected Dividend—We have not issued any dividends in our history and do not expect to issue dividends over the life of the options and therefore have estimated the dividend yield to be zero.

We will continue to use judgment in evaluating the expected volatility, and interest rates utilized for our stock-based compensation expense calculations on a prospective basis.

Recent Accounting Pronouncements

For information about recent accounting pronouncements, see the sections titled "Significant Accounting Policies—Recent Accounting Pronouncements" in Note 2 to our consolidated financial statements for the year ended December 31, 2021 appearing elsewhere in this report.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Interest Rate Risk

We had cash and investments of $765.4 million as of December 31, 2021, consisting of cash, money market funds, municipal bonds, certificate of deposits, exchange traded fund, government securities, commercial paper, and corporate bonds. To date, fluctuations in interest income have not been significant.

We do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate risk exposure. We have not been exposed to, nor do we anticipate being exposed to, material risks due to changes in interest rates.

Foreign Currency Risk

Our expenses are generally denominated in U.S. dollars. A 10% increase or decrease in current exchange rates would not have a material effect on our financial results.

Item 8. Financial Statements and Supplementary Data

This information appears following Item 15 of this report and is included herein by reference.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

Our management carried out an evaluation, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, of the effectiveness of our disclosure controls and procedures, as defined in Rules 13a–15(e) and 15d–15(e) of the Exchange Act, as of December 31, 2021. Based on the evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2021.

We do not expect that our disclosure controls and procedures will prevent all errors and all instances of fraud. Disclosure controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the disclosure controls and procedures are met. Further, the design of disclosure controls and procedures must reflect the fact that there are resource constraints, and the benefits must be considered relative to their costs. Because of the inherent limitations in all disclosure controls and procedures, no evaluation of disclosure controls and procedures can provide absolute assurance that we have detected all our control deficiencies and instances of fraud, if any. The design of disclosure controls and procedures also is based partly on certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions.

Management's Report on Internal Controls Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external reporting purposes in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2021, as required by Rule 13a-15(c) under the Exchange Act. In making this assessment, we used the criteria set forth in the framework in Internal Control—Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on its evaluation, management concluded that our internal control over financial reporting was effective as of December 31, 2021.

The effectiveness of our internal control over financial reporting as of December 31, 2021, has been audited by KPMG LLP, an independent registered public accounting firm, as stated in their report which appears herein.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting (as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions That Prevent Inspections

Not applicable

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K and is incorporated herein by reference to our definitive Proxy Statement for our next Annual Meeting of Stockholders (the "Proxy Statement"), which we intend to file pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended, within 120 days after December 31, 2021.

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item concerning our directors and corporate governance is incorporated by reference to the information set forth in the section titled "Directors and Corporate Governance" in our Proxy Statement. Information required by this Item concerning our executive officers is incorporated by reference to the information set forth in the section entitled "Executive Officers of the Company" in our Proxy Statement. Information required by this Item regarding our Section 16 reporting compliance and code of business conduct and ethics is incorporated by reference to the information set forth in the section entitled "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" in our Proxy Statement.

Item 11. Executive Compensation.

The information required by this Item regarding executive compensation is incorporated by reference to the information set forth in the sections titled "Executive Compensation" and "Compensation for Directors" in our Proxy Statement.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this Item regarding security ownership of certain beneficial owners and management is incorporated by reference to the information set forth in the section titled "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" in our Proxy Statement.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item regarding executive compensation is incorporated by reference to the information set forth in the sections titled "Certain Relationships and Related-Person Transactions," "Corporate Governance," and "Board of Directors and Committees" in our Proxy Statement.

Item 14. Principal Accountant Fees and Services.

The information required by this Item regarding principal accountant fees and services is incorporated by reference to the information set forth in the section titled "Principal Accountant Fees and Services" in our Proxy Statement.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this Annual Report on Form 10-K:

1. Consolidated Financial Statements:

2. Consolidated Financial Statement Schedules

None.

3. Exhibits

We hereby file or incorporate by reference as part of this Annual Report on Form 10-K the exhibits listed in the attached Exhibit Index.

Exhibit Number	Description	Incorporated by Reference			
		Schedule/ Form	File No.	Exhibit	Filing Date
2.1+	Agreement and Plan of Merger, dated October 20, 2020	S-4/A	333-250036	2.1	January 8, 2021
3.1	Amended and Restated Certificate of Incorporation	8-K	001-39351	3.1	February 12, 2021
3.2	Amended and Restated Bylaws	8-K	001-39351	3.2	February 12, 2021
4.1	Specimen Class A Common Stock Certificate	S-4/A	333-250036	4.4	January 8, 2021
4.2	Specimen Warrant Certificate	S-1/A	333-239138	4.4	June 23, 2020
4.3	Warrant Agreement, dated June 30, 2020, between Continental Stock Transfer & Trust Company and the Registrant	S-1/A	333-239138	4.4	June 23, 2020
4.4	Description of Securities	10-K	001-39351	4.4	October 21, 2020
10.1	Form of PIPE Subscription Agreements	8-K	001-39351	10.1	October 21, 2020
10.2	Forward Purchase Agreement, dated June 30, 2020, between Registrant, EcoR1 Panacea Holdings, LLC, EcoR1 Capital Fund, L.P., EcoR1 Capital Fund Qualified, L.P. and EcoR1 Venture Opportunity Fund, L.P.	8-K	000-39315	10.7	July 6, 2020
10.3#	2021 Equity Incentive Plan	8-K	001-39351	10.3	February 12, 2021
10.4#	Forms of Option Grant Notice and Option Agreement under the 2021 Equity Incentive Plan	8-K	001-39351	10.4	February 12, 2021
10.5#	Forms of RSU Award Grant Notice and Agreement under the 2021 Equity Incentive Plan	8-K	001-39351	10.5	February 12, 2021
10.6#	2021 Employee Stock Purchase Plan	8-K	001-39351	10.6	February 12, 2021
10.7#	2019 Equity Incentive Plan, as amended, of Legacy Nuvation Bio	S-4	333-250036	10.13	November 12, 2020
10.8#	Forms of Option Grant Notice and Option Agreement under the 2019 Equity Incentive Plan, as amended, of Legacy Nuvation Bio	S-4	333-250036	10.14	November 12, 2020
10.9#	Form of Indemnification Agreement	S-4/A	333-250036	10.8	January 8, 2021
10.10#	Offer Letter, dated October 6, 2020, by and between Registrant and Jennifer Fox	S-4/A	333-250036	10.11	December 18, 2020
10.11#	Change In Control and Severance Plan	S-4/A	333-250036	10.12	January 8, 2021
10.12	Amended and Restated Registration Rights Agreement, dated February 10, 2021, by and among the Registrant, the EcoR1 Panacea Holdings, LLC, Cowen Investments and certain other stockholders of the Registrant party thereto	8-K	001-39351	10.12	February 12, 2021
10.13	Letter Agreement, dated June 30, 2020, by and among the Registrant, EcoR1 Panacea Holdings, LLC, Cowen Investments, and the Registrant's officers and directors	8-K	001-39351	10.1	July 6, 2020

10.15	Agreement of Lease by and between Zapco 1500 Investment, L.P. and Legacy Nuvation Bio, dated June 30, 2019	S-4/A	333-250036	10.17	December 18, 2020
10.16	Standard Industrial/Commercial Multi-Tenant Lease-Gross by and between 585 Howard Street Partners and the Legacy Nuvation Bio, dated June 7, 2019, as amended	S-4	333-250036	10.19	November 12, 2020
10.17†	Asset Acquisition Agreement by and between RePharmation Inc., GIRAFPHARMA LLC and David Hung, dated January 21, 2019	S-4/A	333-250036	10.19	December 18, 2020
10.18	Stock Restriction Agreement by and between the Legacy Nuvation Bio and David Hung, dated June 17, 2019	S-4	333-250036	10.21	November 12, 2020
10.19	Form of Lock-Up Agreement	8-K	001-39351	10.6	October 21, 2020
14.1	Code of Business Conduct and Ethics	8-K	001-39351	14.1	February 12, 2021
16.1	Letter from Withum	8-K	001-39351	16.1	February 12, 2021
21.1	List of Subsidiaries	8-K	001-39351	21.1	February 12, 2021
23.1*	Consent of KPMG LLP, independent registered public accounting firmEX-23.1				
31.1*	Certification of Chief Executive Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
31.2*	Certification of Chief Financial Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
32.1*	Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.				
101.SCH	Inline XBRL Taxonomy Extension Schema Document				
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document				
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document				
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)				

+ Certain of the exhibits and schedules to this Exhibit have been omitted in accordance with Regulation S-K Item 601. The Registrant agrees to furnish a copy of all omitted exhibits and schedules to the SEC upon its request.

# Indicates a management contract or compensatory plan, contract or arrangement.
† Portions of this exhibit, as marked by asterisks, have been omitted in accordance with Regulation S-K Item 601.
* Filed herewith.

Item 16. Form 10K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

NUVATION BIO INC.

Date: February 28, 2022

By: /s/ David Hung, M.D.

David Hung, M.D.
President and Chief Executive Officer

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints David Hung, M.D. and Jennifer Fox, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Annual Report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his or her substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Signature	Title	Date
/S/ DAVID HUNG, M.D. **David Hung, M.D.**	Chief Executive Officer (*Principal Executive Officer*)	February 28, 2022
/S/ JENNIFER FOX **Jennifer Fox**	Chief Financial Officer (*Principal Financial and Accounting Officer*)	February 28, 2022
/S/ DANIEL G. WELCH **Daniel G. Welch**	Chair of the Board of Directors	February 28, 2022
/S/ ROBERT B. BAZEMORE, JR. **Robert B. Bazemore, Jr.**	Director	February 28, 2022
/S/ KIM BLICKENSTAFF **Kim Blickenstaff**	Director	February 28, 2022
/S/ KATHRYN E. FALBERG **Kathryn E. Falberg**	Director	February 28, 2022
/S/ OLEG NODELMAN **Oleg Nodelman**	Director	February 28, 2022
/S/ W. ANTHONY VERNON **W. Anthony Vernon**	Director	February 28, 2022

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INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of
Nuvation Bio.:

Opinions on the Consolidated Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying consolidated balance sheets of Nuvation Bio Inc. and subsidiaries (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows foreach of the years in the two-year period ended December 31, 2021, and the related notes (collectively, the consolidated financial statements). We also have audited the Company's internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2021 based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Controls Over Financial Reporting. Our responsibility is to express an opinion on the Company's consolidated financial statements and an opinion on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding

prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Measurement of fair value of stock options with service, market and performance conditions

As discussed in Note 11 to the consolidated financial statements, the Company granted stock-based awards that will vest based on various service conditions and achievement of either a market-based or performance-based goal. The Company estimated the fair value of these stock awards using a Monte-Carlo simulation.

We identified the fair value measurement of the Company's stock-based awards based on both a service condition and achievement of either a market-based or performance-based condition as a critical audit matter. Specifically, there was a high degree of subjective auditor judgment due to the complex valuation methodology used and assumption of the expected price volatility of the Company's common stock.

The following are the primary procedures we performed to address this critical audit matter. We evaluated the design and tested the operating effectiveness of certain controls related to the valuation of stock-based awards based on both a service condition and achievement of a market-based or performance-based condition process, including management's method, assumptions and data. We involved valuation professionals with specialized skill and knowledge who assisted in:

- evaluating the appropriateness of the valuation methodology utilized by the Company
- assessing the peer group companies used in the valuation of the stock-based awards by reviewing the business descriptions of the public company peer group and evaluating them to determine that the peer group companies are reasonably comparable in terms of industry and business model of the Company
- developing a range of fair values of the stock-based awards based on both a service condition and achievement of either a market-based or performance-based condition using a separate Monte Carlo simulation and comparing to the Company's estimate for a sample of stock-based awards.

/s/ KPMG LLP

We have served as the Company's auditor since 2019.

Short Hills, New Jersey
February 28, 2022

NUVATION BIO INC. and Subsidiaries
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share data)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 132,423	$ 29,755
Prepaid expenses and other current assets	3,642	914
Marketable securities	632,969	185,997
Interest receivable on marketable securities	3,039	1,092
Deferred financing costs	—	2,925
Total current assets	772,073	220,683
Property and equipment, net	786	688
Lease security deposit	421	421
Operating lease right-of-use assets	2,871	—
Total assets	$ 776,151	$ 221,792
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,925	$ 2,171
Current operating lease liabilities	863	—
Accrued expenses	12,137	4,380
Total current liabilities	16,925	6,551
Warrant liability	11,037	—
Non-current operating lease liabilities	2,192	—
Deferred rent - non current	—	157
Total liabilities	30,154	6,708
Commitments and contingencies (Note 16)		
Stockholders' equity		
Class A and Class B common stock and additional paid in capital, $0.0001 par value per share; 1,060,000,000 (Class A 1,000,000,000, Class B 60,000,000) and 1,174,094,678 (Class A 880,000,000, Class B 294,094,678) shares authorized as of December 31, 2021 and December 31, 2020, respectively, 217,948,568 (Class A 216,948,568, Class B 1,000,000) and 149,042,155 (Class A 91,397,142, Class B 57,645,013) shares issued and outstanding as of December 31, 2021 and December 31, 2020, respectively	909,985	289,482
Accumulated deficit	(162,803)	(75,955)
Accumulated other comprehensive (loss) income	(1,185)	1,557
Total stockholders' equity	745,997	215,084
Total liabilities and stockholders' equity	$ 776,151	$ 221,792

The accompanying notes are an integral part of the consolidated financial statements.

NUVATION BIO INC. and Subsidiaries
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except per share data)

	For the Years Ended December 31,	
	2021	2020
Operating expenses:		
Research and development	$ 69,037	$ 32,603
General and administrative	24,281	10,948
Total operating expenses	93,318	43,551
Loss from operations	(93,318)	(43,551)
Other income (expense):		
Interest income	2,963	1,945
Investment advisory fees	(644)	(271)
Change in fair value of warrant liability	4,231	—
Net (loss) gain on marketable securities	(80)	218
Total other income (expense), net	6,470	1,892
Loss before income taxes	(86,848)	(41,659)
Provision for income taxes	—	—
Net loss	$ (86,848)	$ (41,659)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.44)	$ (0.43)
Weighted average common shares outstanding, basic and diluted	197,887	97,530
Comprehensive loss:		
Net loss	$ (86,848)	$ (41,659)
Other comprehensive income (loss), net of taxes:		
Unrealized (loss) gain on available-for-sale securities, net	(2,742)	1,136
Comprehensive loss	$ (89,590)	$ (40,523)

The accompanying notes are an integral part of the consolidated financial statements.

NUVATION BIO INC. and Subsidiaries
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(In thousands, except share data)

	Redeemable Series A Convertible Preferred Stock		Common Stock and Additional Paid-in Capital			Accumulated Deficit	Accumulated Other Comprehensive (Loss) Income	Total Stockholders' Deficit
	Shares	Amount	Class A Shares	Class B Shares	Amount			
Balance, December 31, 2019	184,501,999	$ 141,864	400,000,000	—	$ 9,759	$ (34,296)	$ 421	$ (24,116)
Retroactive application of the recapitalization due to the Merger (See Note 3)								
Preferred stock	(184,501,999)	(141,864)	36,163,932	—	141,864	—	—	141,864
Common stock	—	—	(321,596,660)	—	—	—	—	—
Balance, December 31, 2019 after effect of the Merger (See Note 3)	—	—	114,567,272	—	151,623	(34,296)	421	117,748
Shares exchanged in recapitalization	—	—	(57,645,013)	57,645,013	—	—	—	—
Issuance of shares (net of $17 in issuance costs) [(a)]	—	—	34,474,883	—	135,657	—	—	135,657
Stock-based compensation	—	—	—	—	2,202	—	—	2,202
Net loss	—	—	—	—	—	(41,659)	—	(41,659)
Other comprehensive income	—	—	—	—	—	—	1,136	1,136
Balance, December 31, 2020	—	—	91,397,142	57,645,013	289,482	(75,955)	1,557	215,084
Issuance and exchange of common stock, net of issuance costs upon the Merger (see Note 3)	—	—	125,252,913	(56,645,013)	606,690	—	—	606,690
Issuance of common stock	—	—	368,408	—	3,787	—	—	3,787
Treasury stock, acquired and retired, at cost	—	—	(368,408)	—	—	—	—	—
Issuance of common stock for purchase under ESPP	—	—	40,118	—	308	—	—	308
Exercise of stock options	—	—	258,395	—	450	—	—	450
Stock-based compensation	—	—	—	—	9,268	—	—	9,268
Net loss	—	—	—	—	—	(86,848)	—	(86,848)
Other comprehensive loss	—	—	—	—	—	—	(2,742)	(2,742)
Balance, December 31, 2021	—	$ —	216,948,568	1,000,000	$ 909,985	$ (162,803)	$ (1,185)	$ 745,997

[(a)] Reflected net of deemed dividend and beneficial conversion feature (see note 8)

The accompanying notes are an integral part of the consolidated financial statements.

NUVATION BIO INC. and Subsidiaries
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

For the Years Ended December 31,	2021	2020
Cash flows from operating activities:		
Net loss	$ (86,848)	$ (41,659)
Adjustments to reconcile net loss to net cash used in operating activities:		
Issuance of common stock for in-process research and development expense	3,787	—
Stock-based compensation	9,268	2,202
Depreciation and amortization	184	103
Non-cash lease expense	184	—
Change in fair value of warrant liability	(4,231)	—
Net amortization on marketable securities	4,593	933
Net loss (gain) on marketable securities	80	(218)
Change in operating assets and liabilities (net of assets and liabilities acquired in the Merger)		
Prepaid expenses and other current assets	(2,416)	(727)
Interest receivable on marketable securities	(1,947)	(264)
Accounts payable	1,861	34
Accrued expenses	7,452	2,921
Deferred rent	(157)	146
Net cash used in operating activities	(68,190)	(36,529)
Cash flow from investing activities:		
Purchases of marketable securities	(609,300)	(143,289)
Proceeds from marketable securities	154,913	70,606
Proceeds from investment held to maturity	—	2,508
Purchases of property and equipment	(282)	(145)
Net cash used in investing activities	(454,669)	(70,320)
Cash flow from financing activities:		
Proceeds from the Merger, net of offering costs paid (see Note 3)	624,769	—
Proceeds from issuance of stock, net of issuance costs	—	135,657
Proceeds from issuance of common stock under ESPP	308	—
Proceeds from exercises of options	450	—
Deferred financing costs	—	(2,522)
Net cash provided by financing activities	625,527	133,135
Net increase in cash and cash equivalents	102,668	26,286
Cash and cash equivalents, beginning of the period	29,755	3,469
Cash and cash equivalents, end of the period	$ 132,423	$ 29,755
Non-cash operating activity:		
Right-of-use asset obtained in exchange for operating lease liability	$ 3,917	$ —
Non-cash investing and financing activity:		
Issuance of common stock for in-process research and development	$ 3,787	$ —
Deferred financing costs in accounts payable and accrued expenses	$ —	$ 403

The accompanying notes are an integral part of the consolidated financial statements.

NOTE 1. DESCRIPTION OF ORGANIZATION AND BUSINESS OPERATIONS

Nuvation Bio Inc. and subsidiaries ("Nuvation Bio"), a Delaware corporation, is a biopharmaceutical company tackling some of the greatest unmet needs in oncology by developing differentiated and novel therapeutic candidates. Nuvation Bio was incorporated on March 20, 2018 (inception date) and has offices in New York and San Francisco.

On February 10, 2021, (the "Closing Date"), Nuvation Bio Inc., a Delaware corporation ("Legacy Nuvation Bio"), Panacea Acquisition Corp. ("Panacea"), and Panacea Merger Subsidiary Corp, a Delaware corporation and a direct, wholly owned subsidiary of Panacea ("Merger Sub") consummated the transactions contemplated by an Agreement and Plan of Merger among them dated October 20, 2020 ("Merger Agreement").

Pursuant to the terms of the Merger Agreement, a business combination of Panacea and Legacy Nuvation Bio was effected through the merger of Merger Sub with and into Legacy Nuvation Bio, with Legacy Nuvation Bio surviving as a wholly owned subsidiary of Panacea (the "Merger") and, collectively with the other transactions described in the Merger Agreement. On the Closing Date, Legacy Nuvation Bio changed its name to Nuvation Bio Operating Company Inc. and Panacea changed its name to Nuvation Bio Inc. (the "Company" or "Nuvation Bio").

NOTE 2. SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position for the periods presented.

Principles of Consolidation

The consolidated financial statements include the balances of the Company and its subsidiaries. All intercompany transactions and balances are eliminated in consolidation.

Liquidity

As of December 31, 2021, the Company has an accumulated deficit of approximately $162.8 million and net cash used in operating activities was approximately $68.2 million for the year ended December 31, 2021. Management expects to continue to incur operating losses and negative cash flows from operations for the foreseeable future.

As of December 31, 2021, the Company had cash, cash equivalents, and marketable securities of $765.4 million. The Company believes that its existing cash, cash equivalents, and marketable securities will be sufficient to meet its cash commitments for at least the next 12 months after the date that these consolidated financial statements are issued. The Company's research and development activities can be costly, and the timing and outcomes are uncertain. The assumptions upon which the Company has based its estimates are routinely evaluated and may be subject to change. The actual amount of the Company's expenditures will vary depending upon a number of factors including but not limited to the progress of the Company's research and development activities and the level of financial resources available.

Significant Risks and Uncertainties

The Company's operations are subject to a number of factors that can affect its operating results and financial condition. Such factors include, but are not limited to: the results of research and development, clinical testing and trial activities of the Company's products, the Company's ability to obtain regulatory approval to market its products, competition from products manufactured and sold or being developed by other companies, the price of, and demand for, Company's products, the Company's ability to negotiate favorable licensing or other manufacturing and marketing agreements for its products, and the Company's ability to raise capital.

The Company currently has no commercially approved products and there can be no assurance that the Company's research and development will be successfully commercialized. Developing and commercializing a product requires significant time and capital and is subject to regulatory review and approval as well as competition

from other biotechnology and pharmaceutical companies. The Company operates in an environment of rapid change and is dependent upon the continued services of its employees and vendors and obtaining and protecting intellectual property.

The COVID-19 pandemic has not had a material adverse impact on the Company's operations to date, however this disruption, if sustained or recurrent, could have a material adverse effect on the Company's operating results and the Company's overall financial condition.

Emerging Growth Company

Upon the completion of the Company's Merger, the Company elected to be an Emerging Growth Company ("EGC"), as defined in the Jumpstart Our Business Startups Act ("JOBS Act"). Effective December 31, 2021, the Company lost its EGC status and is now categorized as a Large Accelerated Filer based upon the current market capitalization of the Company according to Rule 12b-2 of the Exchange Act. The Company is a smaller reporting company but will cease to report as a smaller reporting company commencing with its Quarterly Report on Form 10-Q for the quarter ending March 31, 2022.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amount of revenue and expenses during the year. Accordingly, actual results could differ from those estimates and those differences could be significant. Significant estimates and assumptions reflected in the accompanying consolidated financial statements include, but are not limited to, the fair value of in-process research and development acquired, warrant liabilities, leases, stock options granted and depreciation expense.

Cash and Cash Equivalents

Cash equivalents include short-term, highly liquid instruments, consisting of money market accounts, a money market mutual fund and short-term investments with maturities from the date of purchase of 90 days or less. The majority of cash and cash equivalents are maintained with major financial institutions in North America. Deposits with these financial institutions may exceed the amount of insurance provided on such deposits. These deposits may be redeemed upon demand which reduces counterparty performance risk.

Marketable Securities

Debt securities have been classified as available-for-sale which may be sold before maturity or are not classified as held to maturity or trading. Marketable debt securities classified as available-for-sale are carried at fair value with unrealized gains or losses reported in other comprehensive income (loss). Exchange traded funds are equity securities, which are reported as marketable securities, with readily determinable fair values are also carried at fair value with unrealized gains and losses included in other (expense) income, net. Realized gains and losses on both debt and equity securities are included in other (expense) income, net.

For securities in an unrealized loss positions, management considers the extent and duration of the unrealized loss, and the financial condition and near-term prospects of the issuer. Management also assesses whether it intends to sell, or it is more likely than not that it will be required to sell, a security in an unrealized loss position before recovery of its amortized cost basis. If management determines there is any other than temporary impairment, the entire difference between amortized cost and fair value is recognized as impairment through earnings.

Interest income includes amortization and accretion of purchase premium and discount. Premiums and discounts on debt securities are amortized on the effective-interest method. Gains and losses on sales are recorded on the settlement date and determined using the specific identification method.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk are primarily cash, cash equivalents and marketable securities. The Company maintains its cash and cash equivalent balances in the form of business checking accounts and money market accounts, the balances of which, at times, may exceed federally

insured limits. Exposure to cash and cash equivalents credit risk is reduced by placing such deposits with major financial institutions and monitoring their credit ratings. Marketable securities consist primarily of government and corporate bonds, municipal securities and exchange traded fund with fixed interest rates. Exposure to credit risk of marketable securities is reduced by maintaining a diverse portfolio and monitoring their credit ratings.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Property and equipment are depreciated using the straight-line method over the estimated useful lives of the related assets of generally five years for computers and seven years for furniture and equipment. The cost of leasehold improvements is amortized on the straight-line method over the lesser of the estimated asset life or remaining term of the lease. Maintenance costs are expensed as incurred, while major betterments are capitalized.

Impairment of Long-Lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable and an impairment assessment may be performed on the recoverability or the carrying amounts. If an impairment occurs, the loss is measured by comparing the fair value of the asset to its carrying amount.

Warrants

The Company accounts for warrants as either equity-classified or liability-classified instruments based on an assessment of the warrant's specific terms and applicable authoritative guidance in Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") 480, Distinguishing Liabilities from Equity ("ASC 480") and ASC 815, Derivatives and Hedging ("ASC 815"). The assessment considers whether the warrants are freestanding financial instruments pursuant to ASC 480, meet the definition of a liability pursuant to ASC 480, and whether the warrants meet all of the requirements for equity classification under ASC 815, including whether the warrants are indexed to the Company's own ordinary shares, among other conditions for equity classification. This assessment, which requires the use of professional judgment, is conducted at the time of warrant issuance and as of each subsequent quarterly period end date while the warrants are outstanding.

For issued or modified warrants that meet all of the criteria for equity classification, the warrants are required to be recorded as a component of additional paid-in capital at the time of issuance. For issued or modified warrants that do not meet all the criteria for equity classification, the warrants are required to be recorded as a liability at their fair value on the date of issuance and each balance sheet date thereafter. Changes in the estimated fair value of the warrants are recognized as a non-cash gain or loss on the statements of operations.

Following the Merger, there were 5,787,472 warrants to purchase common stock outstanding, consisting of 4,791,639 Public Warrants, 162,500 Private Placement Warrants and 833,333 Forward Purchase Warrants (as defined below). Each whole warrant entitles the registered holder to purchase one share of our Class A common stock at a price of $11.50 per share. Pursuant to the warrant agreement, a warrant holder may exercise its warrants only for a whole number of shares of our Class A common stock.

The Company evaluated Public Warrants, Private Placement Warrants and Forward Purchase Warrants (the "Warrants") under ASC 815-40, Derivatives and Hedging—Contracts in Entity's Own Equity, and concluded that they do not meet the criteria to be classified in stockholders' equity. Specifically, the settlement value of the Warrants is dependent, in part, on the holder of the Warrants at the time of settlement. Because the holder of an instrument is not an input into the pricing of a fixed-for-fixed option on our common stock, the Warrants fail the indexation guidance in ASC 815-40, which would preclude classification in stockholders' equity. Additionally, the exercise of the Warrants may be settled in cash upon the occurrence of a tender offer or exchange that involves more than 50% of the outstanding shares of the Company's common stock. Because not all of the Company's stockholders need to participate in such tender offer or exchange to trigger the potential cash settlement and the Company does not control the occurrence of such an event, the Company concluded that the Warrants do not meet the conditions to be classified in equity. Since the Warrants meet the definition of a derivative under ASC 815, the Company recorded these Warrants as liabilities on the balance sheet at fair value upon the closing of the Merger, with subsequent changes in their respective fair values recognized in the consolidated statement of operations and comprehensive loss at each reporting date. The fair value of Public and Forward Purchase Warrants was determined using the closing price of the warrants

on the NYSE market. The fair value of the Private Warrants was estimated using a Black-Scholes option pricing formula (see Note 4).

Leases

The Company determines if an arrangement contains a lease at inception. For arrangements where the Company is the lessee, operating leases are included in operating lease right-of-use, or ROU assets; current operating lease liabilities; and non-current operating lease liabilities on its balance sheets. The Company currently does not have any finance leases.

Operating lease ROU assets and operating lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at the commencement date. ROU assets also include any initial direct costs incurred and any lease payments made on or before the lease commencement date, less lease incentives received. The Company uses its incremental borrowing rate based on the information available at the commencement date in determining the lease liabilities as the Company's leases generally do not provide an implicit rate. The incremental borrowing rate is reevaluated upon a lease modification. The operating lease ROU asset also includes any initial direct costs and prepaid lease payments made less any lease incentives. The Company considered information available at the adoption date of Topic 842 to determine the incremental borrowing rate for leases in existence as of this date. The incremental borrowing rate used was the weighted average rate between secured and unsecured lending arrangement. Lease terms may include options to extend or terminate the lease when the Company is reasonably certain that the option will be exercised. Variable payments included in the lease agreement are expensed as incurred. Lease expense is recognized on a straight-line basis over the lease term.

The Company elected to apply each of the practical expedients described in ASC Topic 842-10-65-1(f) which allow companies not to reassess: (i) whether any expired or existing agreements contain leases, (ii) the classification of any expired or existing leases, and (iii) the capitalization of initial direct costs for any existing leases. The Company also elected to apply the short-term lease measurement and recognition exemption in which ROU assets and lease liabilities are not recognized for short-term operating leases. A short-term operating lease is a lease that, at the commencement date, has a lease term of 12 months or less and does not include an option to purchase the underlying asset that the lessee is reasonably certain to exercise. The Company also elected not to separate non-lease components from lease components and instead to account for each separate lease component and the non-lease components associated with that lease component as a single lease component.

Deferred Financing Costs

Costs incurred in advance related to the Merger as described in Note 3 were recorded as deferred financing costs on the condensed balance sheet as of December 31, 2020 and subsequently reclassified to additional paid in capital on the Closing Date of the Merger.

Segment Information

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company's operations are focused on oncology development activities.

Research and Development Costs

Costs incurred in connection with research and development activities are expensed as incurred. These costs include fees paid to consultants, vendors and various entities that perform certain research and testing on behalf of the Company.

Stock-based Compensation

The Company recognizes compensation cost for grants of employee stock options using a fair-value measurement method, that is recognized in operating results as compensation expense based on fair value over the requisite service period of the awards. Forfeitures are recorded as they occur instead of estimating forfeitures that are expected to occur.

The Company determines the fair value of stock-based awards that are based only on a service condition using the Black-Scholes option-pricing model which uses both historical and current market data to estimate fair value. The

method incorporates various assumptions such as the risk-free interest rate, volatility, dividend yield, and expected life of the options.

The Company determines the fair value of stock-based awards that are based on both a service condition and achievement of the first to occur of a market or performance condition using a Monte Carlo simulation.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. The difference between the financial statement and tax basis of assets and liabilities is determined annually. Deferred income tax assets and liabilities are computed for those differences that have future tax consequences using the currently enacted tax laws and rates that apply to the years in which they are expected to affect taxable income. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense.

The Company uses a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken, or expected to be taken, in a tax return. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate. The Company's policy is to record interest and penalties related to income taxes as part of the tax provision. Returns for tax years beginning with those filed for the period ended December 31, 2018 are open to federal and state tax examination.

Recent Accounting Pronouncements

Adopted Standards

In February 2016, the FASB issued Topic 842, which amended prior accounting standards for leases. The Company adopted Topic 842 on January 1, 2021, using the alternative modified retrospective transition method, with no restatement of prior periods or cumulative adjustment to retained earnings. Upon adoption, the Company elected the following package of practical expedients: (i) not to reassess whether any expired or existing contracts as of January 1, 2021, are or contain leases; (ii) not to reassess the lease classification for any expired or existing leases as of January 1, 2021; and (iii) not to reassess initial direct costs for any existing leases as of January 1, 2021. The Company also made an accounting policy election to not recognize any leases with an initial term of 12 months or less within its consolidated balance sheets and to recognize those lease payments on a straight-line basis in its consolidated statements of operations and comprehensive loss over the lease term.

As a lessee, the primary impact of the adoption of Topic 842 was the recognition of operating lease right-of-use assets of $3.9 million, current operating lease liabilities of $1.0 million and non-current operating lease liabilities of $3.1 million on its consolidated balance sheet as of January 1, 2021. The operating lease liability is determined as the present value of future lease payments using its incremental borrowing rate which is based on an estimated rate of interest that the Company would pay to borrow equivalent funds on a collateralized basis. The operating lease right-of use assets is based on the liability adjusted for any prepaid or deferred rent. The lease term is determined by considering whether renewal options and termination options are reasonably assured of exercise. The Company's operating lease agreements may include both lease and non-lease components, which are accounted for as a single lease component when the payments are fixed. Variable payments included in the lease agreement are expensed as incurred. The adoption of the leasing standard did not have an impact on the consolidated statement of operations and comprehensive loss.

Standard Not Yet Effective

In June 2016, the FASB issued Topic 326 on the measurement of credit losses for financial assets measured at amortized cost, which includes accounts receivable, and available-for-sale debt securities. The new guidance replaces the existing incurred loss impairment model with an expected loss methodology, which will result in more timely recognition of credit losses and additional disclosures. As a smaller reporting company, this guidance is effective for fiscal years beginning after December 15, 2022. The Company is a smaller reporting company but will cease to report as a smaller reporting company commencing with its Quarterly Report on Form 10-Q for the quarter ending March

31, 2022. The Company is currently evaluating the potential impact of adopting this guidance on its financial statements.

NOTE 3. Merger

On the Closing Date, Legacy Nuvation Bio, Panacea and Merger Sub consummated the transactions contemplated by a Merger Agreement.

Pursuant to the terms of the Merger Agreement, a combination of Panacea and Legacy Nuvation Bio was effected through the Merger, collectively with the other transactions described in the Merger Agreement. On the Closing Date, Legacy Nuvation Bio changed its name to Nuvation Bio Operating Company Inc. and Panacea changed its name to Nuvation Bio Inc.

In connection with the Merger Agreement, holders of 3,350 shares of Panacea Class A common stock, exercised their right to redeem their shares for cash at a redemption price of approximately $10.00 per share, for an aggregate redemption amount of approximately $0.03 million.

On the Closing Date, a number of purchasers purchased from the Company an aggregate of 47,655,000 shares of Class A Common Stock (the “PIPE Shares”), for a purchase price of $10.00 per share and an aggregate purchase price of approximately $476.6 million.

Additionally, on the Closing Date, certain purchasers purchased 2,500,000 shares of Class A Common Stock (the "Forward Purchase Shares") and 833,333 forward purchase warrants (the “Forward Purchase Warrants”) in a private placement at a price of $10.00 per share for an aggregate purchase price of $25.0 million (the “Forward Purchase”) pursuant to the terms of the forward purchase agreement (the “Forward Purchase Agreement”) that Panacea entered into in connection with Panacea’s initial public offering. The sales of the PIPE Shares, the Forward Purchase Shares and the Forward Purchase Warrants were consummated concurrently with the Merger on the Closing Date.

At the effective time of the merger (the “Effective Time”):

a) each share of Legacy Nuvation Bio Class A common stock and each share of Legacy Nuvation Bio Series A preferred stock issued and outstanding immediately prior to the Effective Time was converted and exchanged for approximately 0.196 shares (the “Exchange Ratio”) of Nuvation Bio Class A common stock. The Nuvation Bio Class A common stock has one vote per share;

b) each share of Legacy Nuvation Bio Class B common stock issued and outstanding immediately prior to the Effective Time (all of which will be owned by the founder (“Founder”) of Legacy Nuvation Bio) was canceled and converted into and exchanged for approximately 0.196 shares of the Nuvation Bio Class B common stock. Immediately following the Effective Time, the Founder voluntarily converted all but 1,000,000 shares of his Nuvation Bio Class B common stock into an equal number of shares of Nuvation Bio Class A common stock: and;

c) each option to purchase Legacy Nuvation Bio Class A common stock (each, a “Company Option”) that was outstanding under Nuvation Bio’s 2019 Equity Incentive Plan immediately prior to the Effective Time, whether vested or unvested, was converted into an option to purchase a number of shares of Nuvation Bio Class A common stock equal to the product (rounded down to the nearest whole number) of (a) the number of shares of Legacy Nuvation Bio Class A common stock subject to such Company Option immediately prior to the Effective Time and (b) the Exchange Ratio, at an exercise price per share (rounded up to the nearest whole cent) equal to (i) the exercise price per share of such Company Option immediately prior to the Effective Time divided by (ii) the Exchange Ratio.

The merger was accounted for as a reverse capitalization, with no goodwill or other intangible assets recorded, in accordance with GAAP. Under this method of accounting, Panacea is treated as the “acquired” company for financial reporting purposes. Accordingly, for accounting purposes, the financial statements of the combined entity represent a continuation of the financial statements of Legacy Nuvation Bio with the Merger being treated as the equivalent of Legacy Nuvation Bio issuing stock for the net assets of Panacea, accompanied by a recapitalization. The net assets of Panacea are stated at fair value, with no goodwill or other intangible assets recorded. Operations prior to the merger are those of Legacy Nuvation Bio.

Summary of Net Proceeds

The following table summarizes the net proceeds from the Merger (in thousands):

Panacea cash at bank and cash held in a trust account	$	144,642
Proceeds from PIPE investment and forward purchase agreement		501,550
Payment of underwriter fees and other offering costs		(23,913)
Payment to Panacea Class A common stockholders who exercised their right to redeem their shares		(32)
Net proceeds		622,247
Assumed assets and liabilities:		
Prepaid expenses		312
Accrued expenses		(601)
Warrant liability		(15,268)
Panacea equity at Effective Time	$	606,690

The underwriter fees and other offering costs in the table above include approximately $2.5 million in connection with the Merger that were paid in 2020 as well as $0.1 million of accrued expenses as of December 31, 2021.

Summary of Shares Issued

The following table summarized the number of shares of common stock outstanding immediately following the consummation of the Merger:

	Class A Common	Class B Common	Total
Panacea shares outstanding prior to the Merger	14,862,500	3,593,750	18,456,250
Less: redemption of Panacea shares prior to the Merger	(3,350)		(3,350)
Conversion of Panacea shares as a result of merger	3,593,750	(3,593,750)	—
Common stock of Panacea	18,452,900	—	18,452,900
Shares issued pursuant to the PIPE financing	47,655,000	—	47,655,000
Shares issued pursuant to the Forward Purchase	2,500,000	—	2,500,000
Issuance of shares upon the Merger	68,607,900	—	68,607,900
Conversion of Old Nuvation Redeemable Series A Convertible Preferred Stock	68,097,805	—	68,097,805
Conversion of Old Nuvation Class A common stock	23,299,337	—	23,299,337
Conversion of Old Nuvation Class B common stock	—	57,645,013	57,645,013
Conversion of Founder shares	56,645,013	(56,645,013)	—
Total shares of Nuvation Bio outstanding immediately following the Merger	216,650,055	1,000,000	217,650,055

NOTE 4. FAIR VALUE MEASUREMENTS AND MARKETABLE SECURITIES

The Company provides disclosure of financial assets and financial liabilities that are carried at fair value based on the price that would be received upon sale of an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Fair value measurements may be classified based on the amount of subjectivity associated with the inputs to fair valuation of these assets and liabilities using the following three levels:

Level 1 — Inputs are unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.

Level 2 — Inputs include quoted prices for similar assets and liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active, inputs other than quoted prices that are observable for the asset or liability (i.e., interest rates, yield curves, etc.) and inputs that are derived principally from or corroborated by observable market data by correlation or other means (market corroborated inputs).

Level 3 — Unobservable inputs that reflect the Company's estimates of the assumptions that market participants would use in pricing the asset or liability. The Company develops these inputs based on the best information available, including its own data.

The following table presents information about the Company's marketable securities as of December 31, 2021 and 2020 and the Warrant liability as of December 31, 2021, measured at fair value on a recurring basis, and indicates the fair value hierarchy of the valuation techniques the Company utilized to determine such fair value. The Company's Warrant liabilities are included within the Level 1 and Level 3 fair value hierarchy. The fair value of the Public and Forward Purchase Warrants is determined using the closing price of the warrants on the NYSE market. The fair value of the Private Placement Warrants is determined using the Black-Scholes option pricing formula. The primary unobservable input utilized in determining the fair value of the Private Warrants is the expected volatility. The expected volatility was estimated considering observable Nuvation public warrant pricing, Nuvation's own historical volatility and the volatility of guideline public companies. There have not been any transfers between the levels during the periods.

	December 31, 2021			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Financial assets:				
Cash equivalents:				
Money market funds	$ 53,292	$ 53,292	$ —	$ —
Commercial paper	30,845	—	30,845	—
Corporate bonds	571	—	571	—
	84,708	53,292	31,416	—
Marketable securities:				
Certificate of deposits	3,000		3,000	—
Commercial paper	16,892		16,892	—
U.S government and government agency securities	267,267		267,267	—
Corporate bonds	320,192		320,192	—
Municipal bonds	10,821		10,821	—
Exchange traded fund	14,797	14,797	—	—
	632,969	14,797	618,172	—
Total financial assets:	$ 717,677	$ 68,089	$ 649,588	$ —
Financial liabilities:				
Warrants	$ 11,037	$ 10,631		$ 406

	December 31, 2020			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents:				
Money market funds	$ 400	$ 400	$ —	$ —
U.S government and government agency securities	9,999	—	9,999	—
	10,399	400	9,999	—
Marketable securities:				
U.S government and government agency securities	98,180	—	98,180	—
Corporate bonds	87,817	—	87,817	—
	185,997	—	185,997	—
Total financial assets	$ 196,396	$ 400	$ 195,996	$ —

Marketable securities consist; U.S. government and government agency, certificate of deposits, commercial paper, corporate bond and municipal securities ("Debt Securities") and an exchange traded fund that primarily owns fixed income securities. Based on the Company's intentions regarding its marketable securities, all Debt Securities are classified as available-for-sale and are carried at fair value based on the price that would be received upon sale of the security. All marketable securities in unrealized loss positions as of December 31, 2021 have been in such position

for less than 12 continuous months. The following table provides the amortized cost, aggregate fair value, and unrealized gains (losses) of marketable securities as of December 31, 2021 and December 31, 2020:

	December 31, 2021			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
	(In thousands)			
Cash equivalents:				
Money market funds	$ 53,292	$ —	$ —	$ 53,292
Commercial paper	30,845	—	—	30,845
Corporate bonds	571	—	—	571
	84,708	—	—	84,708
Marketable securities:				
Certificate of deposits	3,000	—	—	3,000
Commercial paper	16,889	3	—	16,892
U.S government and government agency securities	267,792	213	(738)	267,267
Corporate bonds	320,827	147	(782)	320,192
Municipal bonds	10,849	—	(28)	10,821
Exchange traded fund	14,963	—	(166)	14,797
	634,320	363	(1,714)	632,969
	$ 719,028	$ 363	$ (1,714)	$ 717,677

	December 31, 2020			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
	(In thousands)			
Cash equivalents:				
Money market funds	$ 400	$ —	$ —	$ 400
U.S. government and government agency securities	9,999	—	—	9,999
	10,399	—	—	10,399
Marketable securities:				
U.S. government and government agency securities	97,495	685	—	98,180
Corporate bonds	86,945	872	—	87,817
	184,440	1,557	—	185,997
	$ 194,839	$ 1,557	$ —	$ 196,396

There were no sales of equities securities for the year ended December 31, 2021. For the years ended December 31, 2021 and 2020, the activity related to the net gains (losses) on marketable securities included in other income (expense) on the consolidated statements of operations and comprehensive loss were as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Realized gains (losses) on available-for-sale securities were as follows:		
Realized gains from sales of available-for-sale securities	$ 88	$ 313
Realized losses from sales of available-for-sale securities	(2)	(95)
	86	218
Net gains (losses) on equity securities were as follows:		
Net realized gains on equities sold	—	—
Net unrealized losses on equities	(166)	—
	(166)	—
Total gain (losses) on marketable securities	$ (80)	$ 218

Maturity information based on fair value of the available-for-sale securities is as follows as of December 31, 2021:

	Within one year	After one year through five years	Total
		(In thousands)	
Corporate bonds	$ 172,637	$ 147,555	$ 320,192
U.S. government and government agency securities	137,505	129,762	267,267
Commercial paper	16,892	—	16,892
Municipal bonds	7,791	3,030	10,821
Certificate of deposits	3,000	—	3,000
	$ 337,825	$ 280,347	$ 618,172

NOTE 5. PROPERTY AND EQUIPMENT

Property and equipment, net consisted of the following:

	December 31,	
	2021	2020
	(In thousands)	
Computers	$ 521	$ 248
Furniture and fixtures	312	312
Leasehold improvements	244	244
Total property and equipment	1,077	804
Less accumulated depreciation and amortization	(291)	(116)
Total property and equipment, net	$ 786	$ 688

Depreciation and amortization expense related to property and equipment was $0.2 million and $0.1 million for the years ended December 31, 2021 and 2020, respectively.

NOTE 6. ACCRUED EXPENSES

Accrued expenses consisted of the following:

	December 31,	
	2021	2020
	(In thousands)	
Accrued consultant fees	$ 5,086	$ 278
Accrued employee compensation	6,165	3,231
Accrued professional fees	288	523
Accrued other taxes	402	—
Accrued other	196	348
	$ 12,137	$ 4,380

NOTE 7. LEASES

Our principal executive office is located in New York, New York, where we lease approximately 7,900 square feet of office space under a lease that terminates in 2027, with an option for the Company to extend the lease for an additional five years which is not reasonably assured of exercise. We also occupy approximately 8,200 square feet of office space in San Francisco, California, under a lease that terminates in 2022 with no option to extend.

Operating lease expense was $1.3 million for the years ended December 31, 2021 and 2020. Expense related to variable leases was not significant for the years ended December 31, 2021. Operating cash flows for the year ended December 31, 2021 included $1.2 million for operating leases.

The following table presents the future minimum lease analysis of the Company's operating lease liabilities showing the aggregate lease payments as of December 31, 2021.

	December 31, 2021
	(In thousands)
2022	$ 1,012
2023	552
2024	599
2025	615
2026 and thereafter	711
Total undiscounted lease payments	3,489
Less: imputed interest	(434)
Total operating lease liabilities	$ 3,055

The weighted average incremental borrowing rate used to determine the operating lease liabilities was 6.0%. The Company's weighted average remaining lease term was 4.44 years as of December 31, 2021.

ASC Topic 840 Disclosures

The following table presents the future minimum lease commitments under the Company’s operating leases as of December 31, 2020, as previously disclosed under prior lease accounting standards.

	December 31, 2020
	(In thousands)
2021	$ 1,229
2022	1,013
2023	552
2024	599
2025	615
Thereafter	711
Total future minimum lease payments	$ 4,719

NOTE 8. REDEEMABLE SERIES A CONVERTIBLE PREFERRED STOCK

As of December 31, 2020, one shareholder and certain other shareholders under common management owned approximately 49% of the outstanding preferred stock.

In connection with the Merger, all previously issued and outstanding Redeemable Series A Convertible Preferred Stock were exchanged for the Company's Class A common stock pursuant to the Exchange Ratio established in the Merger Agreement.

The Company had classified the redeemable convertible preferred stock outside of stockholders' deficit because the shares contained certain redemption features that were not solely within the control of the Company.

Beneficial Conversion Feature

In 2020, the Company issued 175,884,898 shares of Redeemable Series A Convertible Preferred Stock ("Series A Preferred Stock") with a beneficial conversion feature as the fair value of the common stock into which the preferred stock is convertible exceeded the purchase price of the preferred stock by $22.6 million on the date of issuance. The Company recognized $22.6 million of the gross proceeds received representing the beneficial conversion amount as an increase to additional paid in-capital and a corresponding $22.6 million reduction to additional paid in-capital for a one-time non-cash deemed dividend to the Series A Preferred Stock on the date of issuance, which is the date the stock first became convertible.

NOTE 9. STOCKHOLDERS' EQUITY

Share Recapitalization prior to the Merger

The consolidated statement of stockholders' equity has been retroactively adjusted for all periods presented to reflect the Merger and reverse capitalization as discussed in Note 3, Merger. In connection with the Merger, all issued and outstanding Redeemable Series A Convertible Preferred Stock (discussed below) were exchanged for the Company's Class A common stock pursuant to the Exchange Ratio in the Merger. The following discussion of share recapitalization occurred in 2020 prior to the Merger.

On November 20, 2020, the Company amended its certificate of incorporation authorizing the issuance of three classes of stock designated as "Class A Common Stock", "Class B Common Stock" and "Series A Preferred Stock", respectively.

As a result of the amended certificate of incorporation, each share of common stock issued and outstanding prior to the amendment was automatically reclassified and became one issued and fully paid share of Class A Common Stock. Immediately following the reclassification, the Company's founder ("Founder") exchanged 281,130,898 shares of the newly classified Class A Common Stock and 12,963,780 shares of Series A Preferred Stock owned into 294,094,678 shares of newly issued Class B Common Stock. The terms of the Stock Restriction Agreement, as discussed below, continues to apply to an equal number of shares Class B Common Stock.

The holder of the Class B Common Stock had the option to convert each share into one fully paid share of Class A Common Stock at any time. Upon the earlier of the date (i) the Founder of the Company owns in aggregate fewer than 220,571,000 shares of Common Stock, (ii) the Founder no longer serves as the Company's Chief Executive Office or (iii) the Founder's death or disability, each share of Common B Common Stock shall automatically convert to one fully paid share of Class A Common Stock and the Company shall not issue any additional shares of Class B Common Stock. Each share of Class B Common Stock shall automatically convert into one paid share of Class A Common Stock upon any sale or disposition of a share of Class B Common Stock.

In the event of liquidation, holders of the Class A and Class B Common Stock are entitled to share ratably in all the Company assets, after liquidation preferences of the preferred stock are satisfied.

As of December 31, 2020, two shareholders owned approximately 95% of the outstanding Class A common stock and the Founder owns 100% of the outstanding Class B common stock.

Common Stock

As discussed in Note 3, Merger, the Company has retroactively adjusted the shares issued and outstanding prior to October 27, 2020 to give effect to the Exchange Ratio established in the Merger Agreement to determine the number

of shares of common stock into which they were converted. As of December 31, 2021, there are 216,948,568 shares of Class A Common Stock and 1,000,000 shares of Class B Common Stock outstanding.

As of December 31, 2021, the Founder owns 100% of the outstanding Class B common stock.

Class A Common Stock Issuance and Cancelation

On March 26, 2021, the Company issued 368,408 fully paid shares of Class A Common Stock to a current common stockholder related to the final settlement of acquired in-process research and development pursuant to a prior asset acquisition agreement and concurrently acquired and retired without consideration the same number of shares of Class A Common Stock held by the Founder. The aggregate fair value for shares issued to current common stockholder is $3.8 million or $10.28 per share and classified as research and development expense on the Consolidated Statements of Operations and Comprehensive Loss, which represents payment of the contingent consideration for acquired in-process research development. The price per share of $10.28 is based on the Company's closing stock price on March 26, 2021.

Common Stock Restriction Agreement

As a result of the Merger, the shares subject to the "Stock Restriction Agreement" between the Company and the Founder was adjusted based on the Exchange Ratio. The number of shares, as adjusted, subject to repurchase per the terms of the Stock Restriction Agreement is reduced each month by 1,101,240 Class A common shares and no common shares will be subject to repurchase by June 2022. As of December 31, 2021, there are 6,061,439 shares of Class A Common Stock subject to the repurchase option.

Voting

Holders of Class A and Class B common stock are entitled to one vote per share on all matters, except that the holders of Class A common stock do not participate in the election of the directors who are elected exclusively by the holders of Class B common stock. Holders of Class A and Class B common stock vote together as a single class on all matters, except that (i) the holders of Class B common stock have the right, voting as a separate class, to elect and remove without cause three directors plus at least 50% of any directors in excess of seven, and (ii) the approval of the holders of a majority of Class B common stock, voting as a separate class, is required for approval by the stockholders of any acquisition (whether by merger, sale of shares or sale of assets) or liquidation. There are no cumulative voting rights.

Conversion

Each share of Class B common stock will automatically convert into one share of Class A common stock upon transfer to a non-authorized holder. In addition, the Class B common stock is subject to a "sunset" provision under which all outstanding shares of Class B common stock will automatically convert into an equal number of shares of Class A common stock if ownership of shares of Class A and Class B common stock held by our President and Chief executive Officer, David Hung, M.D., falls below an aggregate of 43,188,000 shares or if Dr. Hung dies, becomes disabled or ceases to be our Chief Executive Officer, unless he is terminated from such position by us without cause.

NOTE 10. NET LOSS PER SHARE

As a result of the Merger, the Company has retroactively restated the weighted average shares outstanding prior to February 10, 2021 to give effect to the Exchange Ratio.

Basic loss per share is computed by dividing net loss by the weighted-average number of shares of Class A and Class B common stock outstanding, but excluding shares of common stock subject to repurchase for the period. The number of common stock shares subject to repurchase was determined prospectively from the date of the Stock Restriction Agreement described in Note 9. Diluted loss per share reflects the potential dilution that could occur if the stock options to issue common stock were exercised. The Company had a net loss in all periods presented thus the dilutive net loss per common share is the same as the basic net loss per common share as the effect of any options or conversions is anti-dilutive.

The earnings per share amounts are the same for the different classes of common stock because the holders of each class are legally entitled to equal per share distributions whether through dividends or liquidation.

The following securities outstanding at December 31, 2021 and 2020 have been excluded from the calculation of weighted average shares outstanding:

	As of December 31,	
	2021	2020
Class A common shares subject to repurchase	6,061,439	18,184,319
Warrants	5,787,472	—
Class A common stock options	11,216,275	8,490,703

NOTE 11. ACCUMULATED OTHER COMPREHENSIVE (LOSS) INCOME

The following table presents a rollforward of the changes in accumulated other comprehensive (loss) income for the years ended December 31, 2021 and 2020, which is all attributable to unrealized gains (losses) on available-for-sale securities. All amounts are net of tax.

	2021	2020
	(In thousands)	
Balance at beginning of period	$ 1,557	$ 421
Unrealized (loss) gain	(2,656)	1,354
Amount reclassified for realized gains included in gain (loss) on marketable securities	(86)	(218)
Balance at end of period	$ (1,185)	$ 1,557

NOTE 12. STOCK-BASED COMPENSATION

The 2021 Equity Incentive Plan

In March 2019, the Company adopted the 2019 Equity Incentive Plan or ("2019 Plan"), which provided for the grant of options, stock appreciation rights, restricted stock, and other stock awards. In January 2021, our board of directors adopted the 2021 Equity Incentive Plan (the "2021 Plan"). The 2021 Plan was approved by our stockholders in February 2021 and became effective immediately upon the Closing Date of the Merger. Shares available for future issuance under the 2019 Plan were canceled.

Awards. The 2021 Plan provides for the grant of incentive stock options ("ISOs"), within the meaning of Section 422 of the Code to employees, including employees of any parent or subsidiary, and for the grant of nonstatutory stock options ("NSOs"), stock appreciation rights, restricted stock awards, restricted stock unit awards, performance awards and other forms of awards to employees, directors and consultants, including employees and consultants of our affiliates.

Authorized Shares. The maximum number of shares of Class A common stock that may be issued under the 2021 Plan was initially set at 50,684,047 shares of Class A common stock. The number of shares of Class A common stock reserved for issuance under the 2021 Plan will automatically increase on January 1 of each year, starting on January 1, 2022 through January 1, 2031, in an amount equal to (1) 4.0% of the total number of shares of Class A common stock and Class B common stock outstanding or issuable upon conversion or exercise of outstanding instruments on December 31 of the preceding year, or (2) a lesser number of shares of Class A common stock determined by our board of directors prior to the date of the increase. The maximum number of shares of Class A common stock that may be issued on the exercise of ISOs under the 2021 Plan is three times the number of shares available for issuance upon the 2021 Plan becoming effective or 152,052,141 shares.

The Employee Stock Purchase Plan

In January 2021, our board of directors adopted the 2021 Employee Stock Purchase Plan (the "ESPP"). The ESPP was approved by our stockholders in February 2021 and became effective immediately upon the Closing Date of the Merger.

Share Reserve. The maximum number of shares of Class A common stock that may be issued under the 2021 ESPP was initially set at 4,750,354 shares of Class A common stock. The number of shares of Class A common stock reserved for issuance under the 2021 ESPP will automatically increase on January 1st of each year, beginning on January 1, 2022 and continuing through and including January 1, 2031, by 1.0% of the total number of shares of Class

A common stock and Class B common stock outstanding or issuable upon conversion or exercise of outstanding instruments on December 31st of the preceding calendar year or such lesser number of shares of Class A common stock as determined by our board of directors. Shares subject to purchase rights granted under the 2021 ESPP that terminate without having been exercised in full will not reduce the number of shares available for issuance under the 2021 ESPP.

The stock-based compensation expense included in the Company's Consolidated Statements of Operations and Comprehensive Loss for the years ended December 31, 2021 and 2020 is as follows (in thousands):

	Years ended December 31,	
	2021	2020
Research and development	$ 5,020	$ 1,509
General and administrative	4,248	693
	$ 9,268	$ 2,202

Options with Service Conditions

Options granted with only service conditions generally vest over four years and expire after ten years. Stock option activity with service condition only for employees and members of the Company's Board of Directors for the year ended December 31, 2021 is as follows:

	Shares Issuable Pursuant to Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2020	24,425,669			
Conversion adjustment related to the Merger (see Note 3)	(19,638,051)			
Outstanding at December 31, 2020 after adjustment	4,787,618	$ 2.51		
Granted	2,468,443	$ 5.37		
Forfeited	(637,164)	$ 7.63		
Expired	(31,851)	$ 1.74		
Exercised	(258,395)	$ 1.74		$ 2,173
Outstanding at December 31, 2021	6,328,651	$ 5.37	8.69	$ 25,408
Exercisable at December 31, 2021	1,982,052	$ 2.35	8.25	$ 12,309

All unvested options as of December 31 ,2021 are expected to vest. The weighted average grant-date fair value of stock options outstanding on December 31, 2021 and 2020 was $7.54 and $1.67 per share, after effect of the Merger, respectively. Total unrecognized compensation costs related to non-vested stock options at December 31, 2021 was $18.3 million and is expected to be recognized within future operating results over a weighted-average period of 2.39 years.

For stock options granted with only service conditions during the years ended December 31, 2021 and 2020, the inputs in the Black-Scholes option-pricing model to determine the fair value is as follows:

	December 31,	
	2021	2020
Exercise price [(a)]	$8.25 - $14.39	$1.74 - $10.36
Risk-free interest rate	0.51% - 1.39%	0.37% - 1.64%
Expected volatility	90% - 95%	85% - 95%
Expected term in years	5.28 - 6.25	6.08 - 6.25
Dividend	0%	0%

[(a)] After adjustment related to the Merger

For 2020, the Company was a private company and therefore lacked company-specific historical and implied volatility information. As such, the Company estimated its expected stock volatility based on the historical volatility of a publicly traded set of peer companies. For 2021, the Company estimated its expected stock volatility based on the

blended average of its historical volatility and of publicly traded set of peer companies. The expected term of the Company's options has been determined utilizing the "simplified" method. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Dividend yield is based on the expectation that the Company will not pay any cash dividends in the foreseeable future.

Options with Service, Market, and Performance Conditions

Options granted with combined service, market, and performance conditions will vest based on achievement of various service conditions and either a market-based or performance-based goals in three tranches with multiple categories such as the Company's market capitalization, and clinical and regulatory milestones. The market-based and performance-based goals period ends in October 2030. The explicit service periods are three years for tranche 1, four years for tranche 2, and five years for tranche 3. Upon the vesting requirement, 20% of the options will vest for each of tranche 1 and 2, and 60% of the options granted for tranche 3 will vest. The Company recognizes the fair value of the options within each tranche over the longer of their explicit service period or derived service period. The achievement of the performance condition was not deemed probable on the date of grant. As of December 31, 2021, the performance condition was not deemed probable. The expense recognized is based on the fair value of the market condition for the years ended December 31, 2021 and 2020. Stock option activity with combined service, market, and performance conditions for employees for the year ended December 31, 2021 is as follows:

	Shares Issuable Pursuant to Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2020	18,892,549			
Conversion adjustment related to the Merger (see Note 3)	(15,189,464)			
Outstanding at December 31, 2020 after adjustment	3,703,085	$ 4.80		
Granted	1,976,469	$ 11.37		
Forfeited	(791,930)	$ 5.11		
Outstanding at December 31, 2021	4,887,624	$ 7.00	9.52	$ 12,263
Exercisable at December 31, 2021	—	$ —	—	—

The weighted average grant-date fair value of stock options outstanding on December 31, 2021 and 2020 was $6.56 and $3.15 per share, after effect of the Merger, respectively. Total unrecognized compensation costs related to non-vested stock options at December 31, 2021 was $17.1 million and is expected to be recognized within future operating results over a weighted-average period of 4.36 years.

The fair value of the stock options granted with combined service, market, and performance conditions was based on a Monte Carlo simulation with an embedded Black-Sholes pricing model. For the years ended December 31, 2021 and 2020, the fair value was computed using the following assumptions:

	December 31,	
	2021	2020
Exercise price [(a)]	$8.25 - $14.39	$4.60 - $10.36
Risk-free interest rate	0.92% - 1.70%	0.78%
Expected volatility	72% - 74%	71%
Expected term in years	6.23 - 7.50	5.85 - 6.02
Dividend	0%	0%

[(a)] After adjustment related to the Merger

The determination of expected volatility, risk- free rate, and dividend yield was the same approach as used for the above stock options granted with service only conditions. The expected term period represents the time used as an

input in the embedded Black-Sholes pricing model which is based on the midpoint between the vest and expiration dates for each tranche.

NOTE 13. 401(K) PLAN

The Company sponsors a 401(k) plan (the "Plan") covering substantially all employees of the Company. The Plan allows employees to contribute tax deferred salary deductions into the Plan under the provisions of Section 401(k) of the Internal Revenue Code. Matching contributions are made by the Company up to a maximum amount of 3% of employee contributions, subject to certain limitations as defined in the Plan. The Company made matching contributions of $0.4 million and $0.2 million for the years ended December 31, 2021 and 2020, respectively.

NOTE 14. WARRANTS

Following the Merger, there were 5,787,472 warrants to purchase common stock outstanding, consisting of 4,791,639 Public Warrants, 162,500 Private Placement Warrants and 833,333 Forward Purchase Warrants. Each whole warrant entitles the registered holder to purchase one share of our Class A common stock at a price of $11.50 per share. Pursuant to the warrant agreement, a warrant holder may exercise its warrants only for a whole number of shares of our Class A common stock. At December 31, 2021, there were an aggregate of 5,787,472 warrants outstanding.

The Company concluded that the Public Warrants, Private Warrants and Forward Purchase Warrants do not meet the conditions to be classified in equity. The Warrants were recorded at fair value with subsequent changes in fair value reflected in earnings (see Note 4). The change in fair value resulted in a gain of $4.2 million for the year ended December 31, 2021, respectively.

The fair value of Public and Forward Purchase Warrants is determined using the closing price of the warrants on the NYSE market and the related Warrant Liability is included in Level 1 fair value measurements. The Company utilizes the Black-Scholes option pricing formula to determine the fair value of the Private Warrants at each reporting period, with changes in fair value recognized in the statement of operations. The estimated fair value of the Warrant liability for the Private Warrants is determined using Level 3 inputs. Inherent in a binomial options pricing model are assumptions related to expected share-price volatility, expected life, risk-free interest rate and dividend yield. The annualized volatility of the equity was based on a calibration to the publicly traded Warrant price as of the valuation date. The risk-free interest rate was estimated using linear interpolation assuming a term consistent with the time until the Warrants expire, and yield information was based on U.S. Treasury Constant Maturities. The expected life of the Warrants is assumed to be equivalent to their remaining contractual term. The dividend rate is based on the historical rate, which the Company anticipates remaining at zero.

The aforementioned Warrant liabilities are not subject to qualified hedge accounting.

There were no transfers between Levels 1, 2 or 3 during the period ended December 31, 2021.

The following table provides quantitative information regarding Level 3 fair value measurements:

	December 31, 2021	At February 10, 2021 (Closing Date)
Stock price	$ 8.50	$ 10.42
Strike price	$ 11.50	$ 11.50
Term (in years)	4.1	5.0
Volatility	47.8%	35.3%
Risk-free rate	1.1%	0.5%
Dividend yield	0.0%	0.0%
Fair value per Warrants	$ 1.91	$ 2.64

The Company determined the following fair values for the outstanding Warrants (in thousands):

	December 31, 2021
Public Warrants	$ 9,056
Private Warrants	406
Forward Purchase Warrants	1,575
Total	$ 11,037

There were no warrants issued during 2020.

The following presents changes in liabilities classified in Level 3 of the fair value hierarchy for the year ended December 31, 2021 (in thousands):

	Year Ended December 31, 2021
Beginning balance	$ —
Recognition of Private Warrants liability upon Closing Date	475
Change in fair value of Private Warrants liability recognized in earnings	(69)
Ending balance	$ 406

NOTE 15. INCOME TAXES

The provision for income tax expense included on the consolidated statements of operations and comprehensive loss for the years ended December 31, 2021 and 2020 consists of the following:

	December 31,	
	2021	2020
	(In thousands)	
Current tax expense - federal and state	$ 1	$ —
Deferred tax benefit	—	(12,002)
Change in valuation allowance	(1)	12,002
Income tax provision	$ —	$ —

The components of the net deferred tax asset as of December 31, 2021 and 2020 are as follows:

	December 31,	
	2021	2020
	(In thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 13,442	$ 4,427
Research and development tax credits	3,721	698
Capitalized research and development costs	33,435	16,228
Stock-based compensation	1,857	341
Accrued bonus	1,924	—
Lease liability	953	—
Other	26	529
Total deferred tax assets	55,358	22,223
Deferred tax liabilities:		
Unrealized gain on marketable securities	—	(474)
Right of use asset	(896)	—
Other	—	(1)
Total deferred tax liabilities	(896)	(475)
Valuation allowance	(54,462)	(21,748)
Net deferred tax assets	$ —	$ —

A reconciliation between the Company's effective tax rate and the federal statutory rate for the years ended December 31, 2021 and 2020 are as follows:

	December 31,	
	2021	2020
Federal statutory rate	21.00%	21.00%
State income taxes, net of federal tax benefit	10.21%	9.40%
Permanent differences	0.39%	(1.46)%
Tax credits	1.59%	—
True-up	3.87%	—
Change in rate	0.59%	—
Other items	0.01%	0.05%
Valuation allowance	(37.66)%	(28.99)%
Effective tax rate	0.00%	0.00%

As of December 31, 2021, the Company had federal net operating loss carryforwards of approximately $42.7 million and state net operating loss carryforwards of approximately $76.2 million. The federal net operating losses have an unlimited carryover period and state net operating losses expire in years beginning in 2038.

As of December 31, 2021, the Company had federal research and development tax credit carryforwards of approximately $3.7 million and state research and development tax credit carryforwards of approximately $1.6 million. The federal research and development tax credits expire in years beginning in 2039 and state research and development tax credits have an unlimited carryover period.

All of the federal and state net operating losses may be subject to change of ownership limitations provided by the Internal Revenue Code and similar state provisions. An annual loss limitation may result in the expiration or reduced utilization of the net operating losses.

As of December 31, 2021, the Company maintained a full valuation allowance on its net deferred tax assets. The valuation allowance was determined in accordance with the provisions of ASC 740, Accounting for Income Taxes, which requires an assessment of both positive and negative evidence when determining whether it is more likely than not that deferred tax assets are recoverable. Such assessment is required on a jurisdiction by jurisdiction basis. The Company's history of cumulative losses, along with expected future U.S. losses required that a full valuation allowance be recorded against all net deferred tax assets. The Company intends to maintain a full valuation allowance on net deferred tax assets until sufficient positive evidence exists to support reversal of the valuation allowance.

As of December 31, 2021, the Company's total amount of unrecognized tax benefits was $1.6 million, none of which would impact the Company's effective tax rate, if recognized. The Company does not anticipate that the amount of unrecognized tax benefit will significantly increase within the next 12 months.

For the years ended December 31, 2021 and 2020, the activity related to the unrecognized tax benefits were as follows (in thousands):

	Years Ended December 31,	
	2021	2020
Unrecognized tax benefits at beginning of year	$ —	$ —
Gross increases - current year tax positions	893	—
Gross increases - prior year tax positions	702	—
Unrecognized tax benefits at end of year	$ 1,595	$ —

The Company is subject to taxation in the United States and various state jurisdictions. All tax years remain subject to examination for U.S. federal and state purposes. All net operating losses generated to date are subject to adjustment for U.S. federal and state purposes. The Company is not currently under examination in federal or state jurisdictions.

NOTE 16. COMMITMENTS AND CONTINGENCIES

Commitments

The Company leases its office space under non-cancellable operating lease agreements. The leases also require the Company to pay real estate taxes and other operational expenses associated with the leased location and is included in rent expense. The effect of graduating rents, net of the rent credits, is being amortized over the life of the lease so as to result in equal monthly rent expense over the lease term. Deferred rent liability reported in the accompanying consolidated balance sheets represents the cumulative excess of straight-line rental costs over the actual rental payments.

The Company has a standby letter of credit with a bank in the amount of $0.5 million which serves as security for the New York space operating lease. The standby letter of credit automatically renews annually.

Contingencies

From time to time, the Company may be involved in routine litigation that arises in the ordinary course of business. There are no pending significant legal proceedings to which the Company is a party, for which management believes the ultimate outcome would have a material adverse effect on the Company's financial position.