Zacks Small-Cap Research
Sponsored – Impartial – Comprehensive

January 30, 2023
John D. Vandermosten, CFA
312-265-9588 / jvandermosten@zacks.com

scr.zacks.com
10 S. Riverside Plaza, Suite 1600, Chicago, IL 60606

Vyant Bio, Inc. (VYNT: NASDAQ)

Predicting Drug Discovery

Based on our discounted cash flow (DCF) model and a 15% discount rate, Vyant Bio is valued at approximately $2.00 per share. Our methodology applies a 10% probability of success to Vyant's new chemical entities in Rett Syndrome and CDKL5 deficiency disorder.

Current Price (1/27/2023)	$0.92
Valuation	**$2.00**

INITIATION

Vyant Bio's drug discovery platform uses human-derived organoid models of brain disease guided by artificial intelligence and machine learning. It screens thousands of candidates seeking prospective compounds that rescue the diseased organoid phenotype to a healthy, non-disease state, which Vyant believes is a biomarker for clinical efficacy.

Vyant features several programs in late preclinical development in Rett Syndrome (RTT) and CDKL5 Deficiency Disorder (CDD). The most advanced candidate is donepezil, a generic drug for Alzheimer's disease. It has rescued the RTT phenotype & with further work, expected to validate the platform. The RTT program is a new chemical entity identified in collaboration with partner Atomwise. The CDD program is a joint effort with Cyclica to identify a candidate using *in silico* screening and organoids.

Both RTT and CDD are rare diseases and attractive indications for proving the company's discovery platform. Rett affects every 1:10-15,000 while CDD appears in every 1:40-60,000. Both disorders are substantially more common in girls.

If Vyant is successful in validating the platform with successful advances in Rett and CDD, it will pursue additional indications such as Parkinson's disease and partner with others seeking to advance their own platforms.

SUMMARY DATA

52-Week High	**9.85**
52-Week Low	**0.66**
One-Year Return (%)	**-83.1**
Beta	**1.8**
Average Daily Volume (sh)	**408,987**
Shares Outstanding (mil)	**5.91**
Market Capitalization ($mil)	**5.5**
Short Interest Ratio (days)	**0.8**
Institutional Ownership (%)	**6.4**
Insider Ownership (%)	**24.8**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2022 Estimate	**N/A**
P/E using 2023 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Biomedical/Genetics**

ZACKS ESTIMATES

Revenue

(In millions of USD)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2021					$1.1 A
2022	$0.3 A	$0.2 A	$0.2 A	$0.0 E	$0.7 E
2023					$0.0 E
2024					$0.0 E

Earnings per Share

	Q1	Q2	Q3	Q4	Year
2021					-$4.11 A
2022	-$0.76 A	-$0.74 A	-$0.62 A	-$0.61 E	-$2.72 E
2023					-$2.38 E
2024					-$2.19 E

INITIATING COVERAGE

We are initiating coverage of Vyant Bio, Inc. (NASDAQ: VYNT) assigning a valuation of $2.00 per share. Vyant is a drug discovery and development technology company that is focusing on neurodevelopmental and neurodegenerative brain disorders. The company's strategy for developing new therapies combines the application of human-derived organoid models of brain disease, scaled biology and machine learning. The process identifies new drug targets and candidates by screening for efficacy in human induced pluripotent stem cell (iPSC) derived disease models, identifying candidates by their ability to rescue diseased phenotypes to the normal phenotype in the desired neurological disease. This model improves the likelihood of identifying successful candidates by selecting the appropriate genetically-defined patient population and establishing efficacy in an *in vitro* human disease model avoiding reliance on animal models which lack important features necessary to predict human drug response.

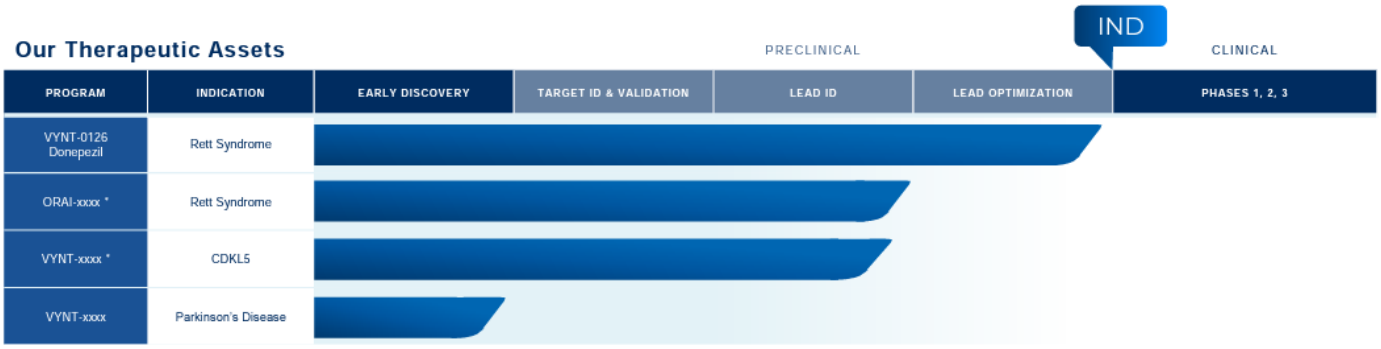
Vyant is distinguished from other drug discovery organizations by its Brain Organoid Screening Platform, which we will refer to as the BOSP. BOSP combines the human organoid platform with software analytics and machine learning to identify drug candidates. The process employs standardized, high-throughput screening of candidates to establish human efficacy in an *in vitro* human disease model prior to expensive clinical studies, reducing the risk of unforeseen toxicity or side effects. The approach is expected to accelerate preclinical drug discovery and development in brain diseases, which can reduce the risk of clinical failure and lower the cost of identifying new agents.

The BOSP platform avoids reliance on imperfect animal models which in many cases do not accurately reflect human pharmacodynamics. BOSP can guide the construction of smaller trials that select only the best drug candidates among thousands that will work in human patients and generate a higher likelihood of success. This can be either a repurposed drug in a new indication or a new chemical entity (NCE).

The process for evaluating a candidate begins with reprogrammed iPSCs which are differentiated into 3-D brain organoids. Functional measures of synaptic network activity in patient-derived brain organoids are then compared to healthy, non-diseased organoids with respect to their electrophysiological signature using high throughput screening and the Fluorometric Imaging Plate Reader, otherwise known as FLIPR. Patient-derived mutant brain organoids are treated with prospective drug candidates, then observed for a change in functional phenotype. Candidates that rescue the diseased phenotype to a healthy, non-diseased state are scored and ranked, providing several promising candidates for further study in other validated assays and ultimately the clinic.

Vyant offers a pipeline of four candidates in three indications. The most advanced is VYNT-0126 in Rett Syndrome (RTT), a rare disease that is caused by a genetic mutation affecting brain development in girls. If funding is received, we anticipate that Australian clinical trials will begin in 2023 followed by US enrollment for a RTT pediatric study. A second therapeutic candidate, in partnership with Atomwise, is also targeting RTT. This candidate, employing the "ORAI-" prefix, has not yet been disclosed and is expected to be the subject of an investigational new drug (IND) application depending on availability of capital. The second indication in the pipeline is cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD), a rare developmental epileptic brain disease caused by mutations in the CDKL5 gene. Additional details will be provided on this candidate after Vyant has strengthened its intellectual property protections. In collaboration with OrganoTherapeutics, Vyant has developed an *in vitro* human Parkinson's disease (PD) drug discovery platform that captures patient pathology and enables high-throughput screening to drive the discovery of disease modifying therapies for PD, the second most common neurodegenerative disorder after Alzheimer's disease.

Exhibit I – Vyant Bio's Drug Candidate Pipeline[1]



[1] Source: Vyant 3Q:22 Corporate Presentation, January 2023.

Vyant plans to begin clinical work on VYNT-0126 for Rett Syndrome in early 2023, launching a Phase II proof of concept study in adult RETT patients in Australia. The trial is expected to enroll up to 48 subjects using a double-blind placebo-control design. A pediatric trial is being considered later in 2023 which would require IND clearance by the FDA and would be conducted in the United States. Vyant may also consider enrolling adult patients in the US if patient recruitment is slow in Australia. Eventually, all development assets will be passed on to a partner that can complete pivotal trials and submit to the FDA using the 505(b)(2) pathway; however, the primary goal for VYNT-0126 is to validate the platform.

Vyant's candidates are a particularly relevant first swing in RTT given the hurdles that gene therapy and X chromosome reactivation face in this indication. While gene therapy or X reactivation may seem to be a natural solution to a genetic disease, in the case of RTT, these approaches can be problematic. Success relies on the precise balance of the proportion of MECP2 protein generated, otherwise another condition known as MECP2 duplication syndrome can occur also causing severe disability.[2]

The drug development industry faces many hurdles in the modern era including declining returns, increasing costs, fewer blockbuster indications and long timelines to generate data needed to obtain regulatory approval. According to a 2016 report, the principal reasons that drugs fail is due to lack of efficacy (57%) or safety (17%).[3] For clinical trials that can cost up to and in excess of a billion dollars to run, tools that help improve efficiency, anticipate in-human toxicity issues and increase the likelihood of success are extremely valuable. Vyant's BOSP platform is one of the tools that can help usher in a more streamlined and better vetted candidate identification process.

Vyant held $9.4 million in cash as of September 30, 2022 and expects to receive additional financial support from the Australian government to fund its Phase II trial. Net cash of $4.4 million from the vivoPharm asset sale in 4Q:22 will also contribute to cash balances. Other rare disease foundation and grant funding may be available. We anticipate that existing cash is sufficient to support operations until the end of calendar year 2023.

Key reasons to own Vyant Bio shares:

- **Candidates vetted using brain organoids prior to costly and time-consuming clinical trials**
  - **Donepezil and undisclosed new chemical entities in Rett's Syndrome**
  - **Undisclosed repurposing and NCE candidates in CDKL5 Deficiency Disorder**
- **Reduces reliance on animal models to identify safe and efficacious candidates**
- **Provides platform technology offering broader applications if validated**
  - **Parkinson's disease**
  - **Alzheimer's disease**
- **Brain Organoid Screening Platform**
- **Complementary partners**
  - **Atomwise - AI/ML screening in RTT**
  - **Cyclica - AI/ML screening in CDD**

Vyant has identified its lead candidate, donepezil, which is an approved product for Alzheimer's disease. As safety and toxicity profiles are already understood by the FDA, the product will enjoy a streamlined pathway through the regulatory process assuming it can show efficacy in pivotal trials. The identity of Vyant's other assets have not yet been disclosed; however, they are new chemical entities (NCE) and will therefore enjoy additional intellectual property protections compared to donepezil. One of the goals of advancing the lead programs in rare disease is to validate the BOSP platform so that diseases with larger populations can be addressed.

In this report we provide a description of the competitive environment in drug discovery, which has been accelerating its use of AI and ML. This is followed by an in-depth description of the primary indications in RTT and CDD. Further sections summarize the details of the recently identified lead candidate, donepezil, and the pathway expected in the pursuit of approval. Intellectual property and patents are addressed as are the risks faced by biotech companies. The research report summarizes the main peers and competitors in the RTT, CDD and brain organoid space and introduces the executives managing the company. Our closing sections provide a summary of key milestones over the recent past and Vyant's valuation. Assumptions behind our discounted cash flow (DCF) model are provided that value the undisclosed NCEs for RTT and CDD and generates a target price. Based on this work we generate a valuation of $2.00 per share.

[2] Clarke, A.J., Sheikh, A.P.A. A perspective on "cure" for Rett syndrome. Orphanet Journal of Rare Disease. April 2018.
[3] Hwang, TJ, *et al.* Failure of investigational drugs in late-stage clinical development and publication of trial results. JAMA Internal Med, 176 (12) (2016), pp. 1826-1833

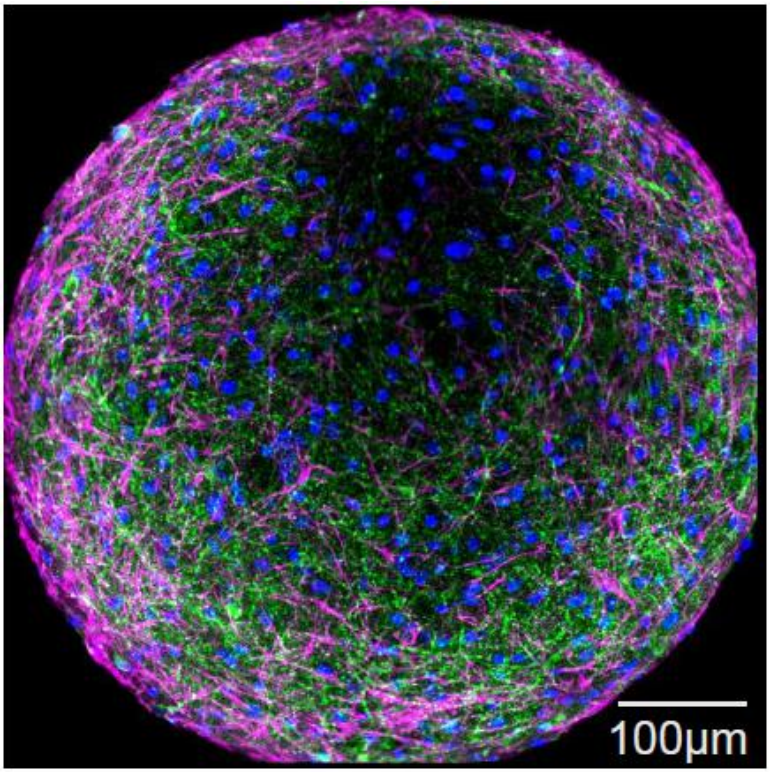
Drug Discovery Platform

Brain Organoids[4]

Brain organoids are created from induced pluripotent stem cells (iPSCs) and artificially grown, *in vitro*, into a mass of cells that provides a reductionist model of the human brain. The three-dimensional (3-D) cell structures grown *in vitro* from stem cells recapitulate key features of the development and performance of the organ. The organoid provides a human-derived model for studying central nervous system (CNS), developmental and neurodegenerative disorders providing a deep understanding of human disease biology. It is the functional interactions between neurons, glial cells and other brain cells in the 3-D physiological network that provides the basis for the ability to predict human efficacy. In preclinical work, brain organoids are screened using high throughput methods evaluating thousands of compounds to rapidly evaluate efficacy and toxicity profiles in the same organoids.

In 2006, it was shown that somatic cells could be converted to pluripotent stem cells using transcription factors, thereby dramatically simplifying the process for obtaining this versatile seed that can be differentiated into any cell in the same species.[5] Somatic cells can be sourced from just about anywhere in the body, frequently from skin or blood. After the cells are sourced, pluripotency-related transcription factors are applied to de-differentiate the cells to their primitive state. The pluripotent cells are then reprogrammed and cultured to produce the desired cell type. During culture, small molecules and growth factors are usually supplemented and promote iPSCs to form specific structures of the different brain regions. Due to the lack of vasculature, the brain organoids are very small, measuring less than 1,000 micrometers (µm) in diameter. In addition to the brain, other types of organoids, such as lung, kidney and prostate organoids have been widely generated and cultured for use in scientific investigation. Brain organoid technology can model human neurological disease, such as tumors and neurological disorders, to explore the pathogenic mechanism and identify effective treatments.

Exhibit II – Brain Organoid[6]



[4] Benito-Kwiecinski, S., Lancaster, M.A. Brain Organoids: Human Neurodevelopment in a Dish. Cold Spring Harbor Perspectives in Biology. 2020.
[5] See this excellent summary on Shinya Yamanaka who discovered that mature cells could be reprogrammed to become pluripotent.
[6] Source: Vyant Presentation, Multiparametric analysis of coordinated network activity reveals target specific functional rescue in a human iPSC derived organoid model of Rett syndrome. November 16, 2022.

The earliest reported creation of a brain organoid was described in a 2013 publication[7] and since then the space has evolved substantially. New engineering techniques have improved the repeatability and uniformity of brain organoid cultures. Future areas of organoid exploration may include vascularization, which will allow for larger and more complex structures. This advance may help even further characterize the safety and efficacy of new agents in humans at the *in vivo* stage of development.

Organoids contain multiple organ-specific cell types which recapitulate the desired function and spatial organization similar to that found in human brains. They confer several benefits relative to other disease models in common use. Below, we list some factors supporting their use.[8] The use of iPSC derived brain organoids:

- Offers insight into neurological and psychiatric disorders that arise during neurodevelopment;
- Overcomes biopsy shortcomings, which provide limited insights into the cause of the disease;
- Bridges the large evolutionary distance between human and mammalian models;
- Avoids expense and ethical considerations related to primate studies;
- Allows researchers to investigate phenotypes specific to humans related to the human genome and the associated human developmental timeline;
- Compensates for other approaches that fail to capture the development of the human brain which prevents temporal phenotypes from being accurately replicated.

Artificial Intelligence and Machine Learning

Vyant's platform is designed to clarify disease pathophysiology and narrow down a collection of potential compounds into a handful of candidates that provide disease-specific rescue. Artificial Intelligence (AI) and Machine Learning (ML) use *in silico* screening to identify discovery prospects. *In silico* methods include databases, quantitative structure-activity relationships, pharmacophores, homology models and other molecular modeling approaches, machine learning, data mining, network analysis tools and data analysis tools that use a computer. Furthermore, computational chemistry can identify binding sites on targets and match them to an existing theoretical library that can extend into the billions of compounds.[9] When high-likelihood hits are identified, the results are then synthesized and screened in spheroids to identify lead scaffolds which can rescue the phenotype.

Exhibit III – High-Throughput Screening Using Cortical Organoids[10]

[7] Sun, N. *et al*. Applications of brain organoids in neurodevelopment and neurological diseases. Journal of Biomedical Science. April 2021.
[8] Sidhaye, J., Knoblich, J.A. Brain organoids: an ensemble of bioassays to investigate human neurodevelopment and disease. Cell Death & Differentiation. January 2021.
[9] Vyant's partner Enamine estimates that it can synthesize 31 billion molecules in its virtual database.
[10] Source: Vyant Presentation: High throughput functional screening to develop novel therapies for CDKL5 deficiency disorder using human iPSC derived cortical organoids. November 2022.

Organoid Advantages

Primates and rodents have historically been used for preclinical *in vivo* work to isolate efficacy, safety and toxicity parameters prior to the start of clinical trials. However, animal models are evolutionarily distant from humans in terms of brain size and complexity. Several factors, including cytoarchitecture complexity, formation of protein aggregates such as tau and amyloid beta and susceptibility to pathogens are barriers that limit the utility of these imperfect representations.

Furthermore, animal models do not necessarily replicate the behavior of a disease in a human and are difficult to scale up during the discovery phase. Enter the iPSC, which can be reprogrammed to form into any cell in the human body including complex brain structures. The human brain organoids bridge the translational chasm that appears between animal models and human testing. The organoids allow the most biologically relevant pre-clinical model and *in vitro* system to validate and screen targets.

Studies using patient-derived brain organoids have revealed novel insights into molecular and genetic mechanisms of complex human neurological disorders such as microcephaly, autism, and Alzheimer's disease. Human iPSCs combined with high throughput screening, have opened new doors to drug discovery.[11] iPSC-derived 3-D organoid models offer an inexpensive and practical approach for drug screening, with the further benefit of patient-specific, genetically-relevant drug efficacy and toxicity data.[12]

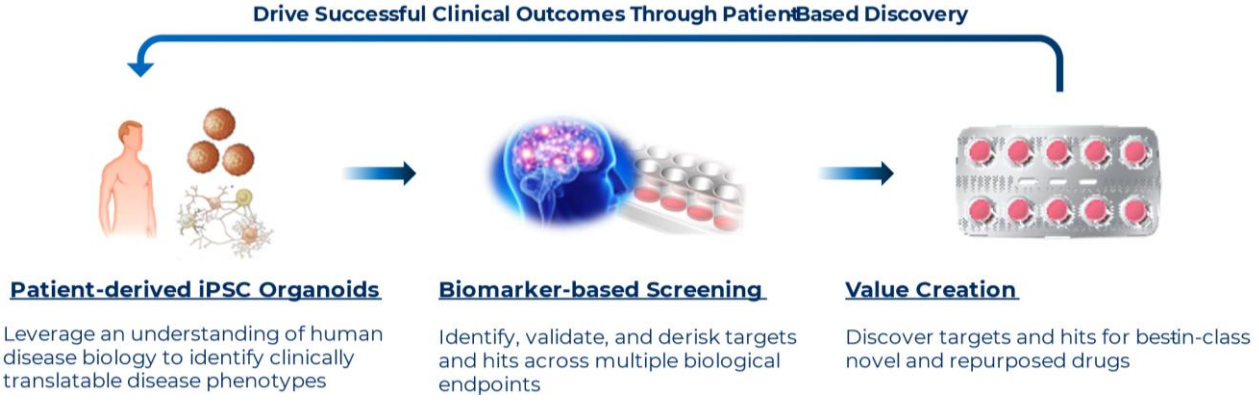
Even though the studies are performed on *in-vivo* type tissue, brain organoids do present limitations as the testing remains *in-vitro* analysis. Brain organoids have a broad transcriptomic signature with poor sub-type specific features and co-expression of markers present on differentiated cells. The organoid cells also exhibit greater expression of stress-related genes which can impair cell type specificity.[13] While imperfect, brain organoids remain important tools for drug screening and addressing problematic features of animal models.

Next Generation of Drug Development

Drug development is expensive, time consuming and suffers from a low success rate. It can cost from several hundred million to over a billion dollars to develop a drug over the one-to-two-decade period from inception to approval. The pathway forward is even more difficult for candidates addressing central nervous system (CNS) disorders, which have suffered from numerous failures due to our lack of understanding about the brain's physiology.[14] Only a small proportion of oncology drugs that enter the clinic are eventually commercialized and many fall by the wayside.

The sunk cost of these failed drugs is an economic burden; however, there is valuable safety and efficacy data embedded in the completed studies. A drug may not have demonstrated efficacy in a certain population; however, that does not mean it cannot be useful elsewhere. Two prominent examples of initial failures that went on to be blockbusters include azidothymidine for HIV and Viagra for erectile dysfunction. Vyant's platform is particularly well suited for repurposing, providing a second chance for compounds that may have activity in new indications.

Exhibit IV – Vyant's Drug Discovery Platform[15]



[11] Lee, C.T., *et al.* 3D brain Organoids derived from pluripotent stem cells: promising experimental models for brain development and neurodegenerative disorders. Journal of Biomedical Science, August 20, 2017.
[12] Lee, C.T., *et al.* 3D brain Organoids derived from pluripotent stem cells: promising experimental models for brain development and neurodegenerative disorders. Journal of Biomedical Science, August 20, 2017.
[13] Bhaduri, A., *et al*. Cell Stress in Cortical Organoids Impairs Molecular Subtype Specification. Nature, February 2020.
[14] See the long list of failed drugs in development for Alzheimer's Disease for reference.
[15] Source: Vyant slide deck, January 2023.

The normal pathway for drug development is a 10 to 15 year journey that requires 10,000 candidates to be identified in basic research to generate one FDA approved medicine. Preclinical efforts focus on basic research, drug discovery and pre-clinical *in vivo* and *in vitro* studies. Pharmacokinetic and pharmacodynamic studies are conducted in preparation for an investigational new drug (IND) application. If successful screening can eliminate candidates that have a low probability of success in human subjects due to limited efficacy or negative side effects, the remaining candidates will be more likely to produce supportive data and eventually be approved.

Countless studies have been conducted to determine the cost of advancing a drug to the finish line. Numbers can range from a few hundred million for a relatively simple indication with a strong signal, to billions for trials that have large populations such as the FOURIER trial.[16] With fewer blockbuster opportunities and costs for trials increasing dramatically, new methods must be found to successfully identify safe and effective medicines.

While drug development has generally succeeded in capturing the low hanging fruit by identifying monotherapies that apply to the broadest segments of disease, the effort becomes more difficult and expensive as remaining afflicted populations are smaller and diseases more complex. Despite this shrinking addressable market, drug development costs have not trended in the same direction, nor have other factors that affect returns such as development time and success rate.

With the advent of sophisticated computational tools, it is now possible to analyze vast quantities of data to identify drug candidates and their companion indications that can advance faster, at lower cost and with a higher degree of confidence in their ultimate success than what has come before.

The Advancement of Artificial Intelligence

The growth in personalized, high-resolution medical data is a function of both the decreasing cost of genetic sequencing and the decreasing cost of data storage and analysis. Increases in computational power and the continued development of AI algorithms allow us to capitalize on this new wealth of medical information. The decline in cost to sequence a genome has exceeded expectations suggested by Moore's Law.[17] In 2001, the cost to sequence one person's genome was approximately $100 million. Two decades later, the cost is below $1,000.[18]

Often AI and ML are used interchangeably, but ML is a subset of AI. ML pioneer Tom Mitchell defines it as "the study of computer algorithms that improve automatically through experience."[19] In general, these terms refer to computer programs that are designed to find trends and relationships across vast amounts of many types of data, and are equipped to do so in an automated, iterative fashion. The system employs the algorithm it has developed to make predictions from novel, real-world inputs. In this way, AI/ML goes beyond a conventional computer program or conventional statistics to be arbitrarily and near-infinitely tunable. The technology can adapt to learn highly complex systems and the power is in using the tuned algorithm to then solve real-world problems. Medicine, and specifically early-stage drug development is rapidly evolving in this direction.

[16] The Phase III FOURIER trial enrolled 27,564 patients to test Evolocumab against placebo for cardiovascular disease. At an estimated cost of $70,000 per patient, just this one Phase III trial could have cost as much as $2 billion for its sponsor Amgen.
[17] Moore's Law states that the number of transistors on a microchip doubles every two years while the cost of computers is halved.
[18] https://www.wired.com/story/the-era-of-fast-cheap-genome-sequencing-is-here/
[19] http://www.cs.cmu.edu/~tom/mlbook.html

Indications

Vyant Bio is primarily targeting two rare central nervous system (CNS) genetic neurodevelopmental disorders, Rett Syndrome (RTT) and CDKL5 deficiency disorder (CDD). RTT is a rare genetic disease with onset shortly after birth, usually from six to 18 months of age. Most patients appear to develop normally for the first six months and begin to lose their previously developed skills such the ability to crawl, walk or communicate as they approach their first year. The condition results in progressive loss of motor skills and language, and affects a child's ability to eat, walk and speak. He, or most commonly, she can display severe cognitive dysfunction, seizures, and autistic-type behavioral symptoms. RTT is caused by mutations in the methyl-CpG binding protein 2 (MECP2) gene located on the X chromosome, and thus primarily affects females. CDKL5 Deficiency Disorder (CDD) is a developmental epileptic encephalopathy, originally classified as an atypical form of RTT with which it shares many similarities. Differentiating factors with RTT include an earlier onset of seizures, which fail to respond to anti-seizure medication, as well as severe motor, cognitive and visual impairment. The cause of CDD comes from a variant in the CDKL5 gene which encodes for a serine threonine kinase designated CDKL5. The protein regulates axon outgrowth, dendritic morphogenesis and synapse formation. Hundreds of variants contribute to the mutation, creating difficulties in assessing genotype and phenotype relationships.

Rett Syndrome

Rett Syndrome (RTT) is a rare genetic, neurodevelopmental disorder. The condition causes developmental challenges throughout childhood, progressively worsening as the child ages. Patients face physical and communication impairments throughout their lives and can live up to middle age. RTT is characterized by normal early development followed by gradual loss of motor functions such as the use of the hands, problems with walking, seizures, and impaired brain development.

Rett syndrome was identified in 1966 by an Austrian pediatrician Dr. Andreas Rett. The age of onset for the disorder and the severity of impairment may vary among affected children although subtle indications may sometimes be evident. Gradually, the loss of purposeful use of hands (apraxia) along with compulsive jerkiness can be particularly disabling, along with cognitive impairments, seizures and autistic-like behavior.

RTT is commonly described in four stages, although not everyone passes through each. In Stage 1, the early onset stage begins near the six-month mark of infant development. Symptoms can be subtle and may manifest as lack of interest in toys, delayed ability to crawl or sit. This period can last up to 18 months. Stage 2, the rapid destructive stage, occurs between one and four years of age. The child may exhibit severe loss of motor and communication skills, sometimes accompanied by breathing irregularities, hyperventilation, loss of social interaction along with slowing head growth. In Stage 3, the plateau stage between the ages two and 10, seizures and apraxia are prominent with slight improvements in behaviors and communication skills. The plateau stage can last for many years and many girls remain in this stage for much of their lives. Stage 4, the late motor deterioration stage, is marked by reduced mobility, muscle weakness and scoliosis, while communication, intellectual and motor skills may be stable or show slight improvement.

Prevalence

Rett Syndrome almost exclusively affects females. The disease occurs in all racial and ethnic groups with similar incidence. Prevalence of Rett Syndrome is estimated to be about one in 22,800 females ages 2-18 years, or about 0.44 per 10,000 in the United States (Texas), 0.56 in France, 0.65 in Sweden and Scotland, and 0.72 in Australia. The genetic abnormalities that cause the disorder occur spontaneously, and thus the risk of a second child in a family developing the disorder is less than one percent. Prenatal genetic testing is available. Because male children have only one copy of the X chromosome, they do not benefit from the back-up copy of MECP2 gene, and develop severe problems and die shortly after birth.

Causes

RTT is a genetic disorder primarily caused by spontaneous mutations in the *MECP2* gene and is not usually inherited. Because the disorder is caused by a random mutation, prevention is not possible. The MECP2 gene is located on the X chromosome (Xq28) and codes for MECP2. About 75-95% of Rett Syndrome cases are caused by mutations in MECP2 while a minority of cases is characterized by mutations in CDKL5 and FOXG1 genes. Human females have two copies of the X chromosome, one of them usually inactivated in any given cell, resulting in varying amounts of defective gene product (MECP2 protein) in various brain tissues, which in turn determines the severity of the symptoms in the affected individual. MECP2 protein plays a critical regulatory role during early development.

Differential gene expression patterns and varying protein levels in various brain tissues during early neuronal development interferes with normal maturation resulting in Rett syndrome symptoms.

Symptoms

Typical symptoms of Rett syndrome include constant repetitive hand movements, usually recognized in children between 6 to 18 months. Other symptoms include a wide variety of mild to severe symptoms involving motor, communication and cognitive skills. The severity of symptoms is a function of the nature of the mutations in MECP2 gene, of which more than 900 are known, and its expression in brain cells. RTT symptoms comprise three broad categories – motor skills, language skills and behavioral development. The most conspicuous symptoms are listed below:

- Hand-wringing, constant and repetitive hand movements;
- Swallowing or chewing problems, poor nutrition;
- Poor language skills, inability to say correct words; loss of speech;
- Breathing difficulties, apnea, hyperventilation; sleep disturbances;
- Autistic-type behaviors – lack of social interaction, eye contact;
- Seizures, balance and coordination issues, gait issues;
- Apraxia, muscle weakness, scoliosis;
- Slower development of head, feet and hands.

Other complications that can arise include sleep disruption to the affected individual and family members, eating difficulties leading to poor nutrition, gastrointestinal problems, muscle, bone and joint problems, and shortened life span.

Diagnosis

Rett syndrome is typically diagnosed by observing signs and symptoms during early development of a child. Parents may first notice some symptoms, doctors may conduct ongoing evaluations, and healthcare providers may administer a genetic test to identify mutations in the MECP2 gene. Diagnosis may be confirmed upon consultation with a pediatric neurologist or a clinical geneticist who may use a set of confirmatory, supportive and exclusion diagnostic criteria.

Approved Treatment

There is no known cure for Rett syndrome. Approved approaches usually focus on management of symptoms by treating seizures, improving movement and communication and providing supportive guidance for affected families. Treatments usually involve prescribing anti-seizure medications, providing physical and speech therapies and applying a multi-disciplinary approach. Other medications may include drugs needed to address breathing irregularities, anticonvulsant drugs needed to control seizures, scoliosis and possible heart abnormalities. Other strategies may require special tools and aids such as braces and splints to manage scoliosis and hand movements, and custom-designed nutritional, social and academic programs.

Trofinetide is a drug that has been developed by Neuren Pharmaceuticals to treat RTT. It acts as an analogue of the neuropeptide IGF-1 and has successfully completed a Phase III clinical trial for RTT. Since then, it has been submitted to the FDA in a new drug application (NDA). The NDA has been accepted for review by the FDA with a projected PDUFA date in March 2023.

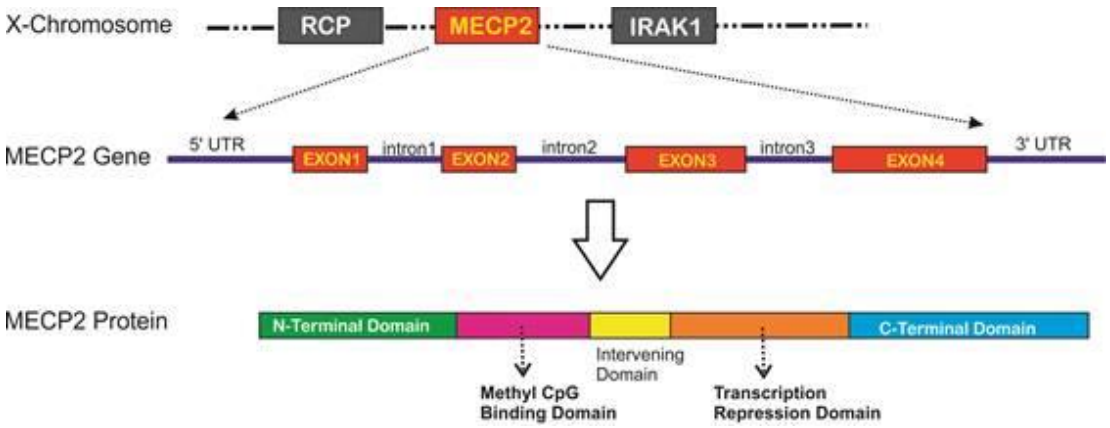
Prognosis

Despite debilitating symptoms, many RTT patients live well into middle age with an adequate quality of life. Because the condition is rare, progress on long term prognosis has been slow and difficult, and understanding the cause of the disorder is required for developing new treatment options. The discovery of MECP2 gene mutation, transgenic mice with knock-out mutations, have accelerated the pace of our understanding of the molecular pathways underlying the syndrome. The lack of a fully functional MECP2 protein interferes with the function of mature brain cells, although understanding the underlying mechanisms is in its infancy. The discovery of the MECP2 protein function and its role in effecting genetic switches in brain cells should help devise therapies that can compensate for the dysfunction. Other approaches may include manipulating biochemical pathways to substitute for the defective MECP2 gene and regulating the expression of a normal MECP2 gene.

MECP2 Gene

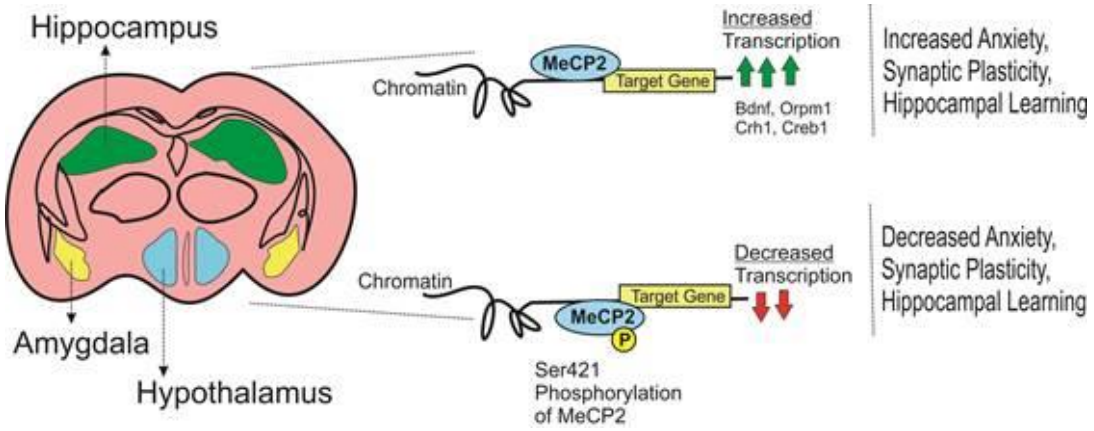
Rett syndrome is caused primarily by a mutation in MECP2 gene encoding the methyl cytosine binding protein 2 (*MECP2*), a critical factor needed for brain development. MECP2 functions as a biochemical switch that can modulate the expression of other genes involved in early development. Because of the mutations in the MECP2 *g*ene, the associated protein does not function properly or is produced in insufficient quantities in RTT individuals. The MECP2 protein is expressed in all cells but is most abundant in brain cells. Deficiency of the protein is believed to result in the failure of synaptic maturation and cortex maintenance and contribute to inflammation.[20] MECP2 acts as a high-level genome-wide transcriptional regulator in neurons and is thought to be an activator, repressor and modulator of various genes, and its deficiency is believed to be responsible for aberrant expression of target genes in brain development.[21]

Exhibit V - The Structure of the MECP2 Gene and MECP2 Protein[22]



MECP2 has been implicated in several aspects of gene regulation while the precise role it plays in transcriptional regulation may depend on other interacting proteins. When interacting with repressor complexes containing SIN3a and histone deacetylases, MECP2 may repress genes while interacting with activator complexes containing cAMP response element binding protein (CREB). Evidence suggests that MECP2 may be a genome-wide epigenetic modulator.[23]

Exhibit VI – Transcriptional Regulation by MECP2 Protein[24]



MECP2 is involved in controlling chromatin structure by regulating long range interactions among chromatin architecture and DNA bridges as a chromatin architectural protein. Importantly, mutations in MECP2 causing Rett syndrome have been shown to disrupt higher order chromatin architecture. As a multifunctional epigenetic modulator, MECP2 assumes critical roles in many biological functions in neuronal differentiation and maturation in RTT patients. Reduced gene expression and protein synthesis in MECP2 deficient cells may lead to RTT in affected patients.

---

[20] Zalosnik, M.I., *et al*. MeCP2 deficiency exacerbates the neuroinflammatory setting and autoreactive response during an autoimmune challenge. Scientific Reports, May 2021.

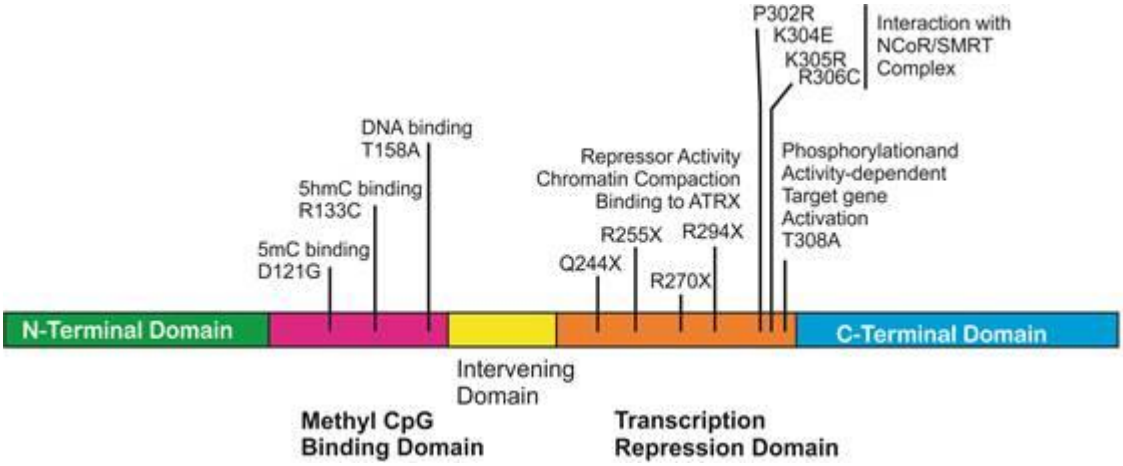
[21] Vichithra R. B. Liyanage and Mojgan Rastegar, Neuromolecular Med. 2014 Jun; 16(2): 231–264.

[22] Analyst work, CorelDraw Software, Corel Corporation, Ottawa, Canada.

[23] Ragione, F.D., *et al*. MeCP2 as a genome-wide modulator: the renewal of an old story. Frontiers in Genetics. September 2012.

[24] Analyst work, CorelDraw Software, Corel Corporation, Ottawa, Canada.

Exhibit VII – Structure and Functional Features of MECP2 Protein[25]



Research has shown that both deficiency and overexpression of MECP2 hold severe neurological implications. Thus, therapeutic strategies to address RTT using MECP2 expression require precision to maintain proper expression levels and thorough appreciation of its role in multiple gene expression pathways. Overexpression can lead to MECP2 duplication syndrome, which is characterized by moderate to severe intellectual disability and other characteristics that are as or more severe than RTT symptoms.[26]

CDKL5 Deficiency Disorder

CDKL5 deficiency disorder (CDD), like RTT, is a rare neurological and developmental disorder. CDD was previously considered an atypical form of Rett syndrome with which it shares many common symptoms including seizures, impaired motor skills, and cognitive disabilities. However, based on the discovery of mutations in the CDKL5 gene, CDD is now known to be a separate condition with its own distinctive causes and symptoms. CDD affects both boys and girls. Its symptoms usually begin in infancy and are characterized by repeated, almost daily seizures within the first few months after birth. Often CDD patients exhibit a special type of epilepsy-type spasms along with difficulties with vision, sitting and walking. Other common symptoms include sleep disturbances, low muscle tone, eating difficulties as well as other gastrointestinal and orthopedic complications.[27]

CDKL5

CDD is caused by mutations in the cyclin-dependent kinase-like protein 5 (CDKL5) gene on the X chromosome, and occurs in three stages, with epileptic encephalopathy and refractory generalized or mixed epilepsy common in later stages. The CDKL5 gene is located on X chromosome (p22.13) and is subject to random inactivation in females. Numerous mutations are known in CDKL5 which result in impaired kinase activity. CDKL5 deficiency leads to altered expression of receptors that affect calcium permeability with significant effects on excitability and synaptic functions. CDKL5 is a serine/threonine protein kinase which regulates several classes of kinases. CDKL5 is critically important for normal brain development as its expression levels increase during neuronal maturation and synaptogenesis, and is most abundant in forebrain structures including cerebral cortex, hippocampus, striatum and olfactory bulb. Knock-out animal models recapitulate the human phenotype, further confirming CDKL5's critical role in normal brain development. CDKL5 likely participates in intracellular signaling pathways by selectively phosphorylating specific kinases and modifying kinase-regulated pathways in the brain.

Prevalence

CDKL5 deficiency disorder is rare with an incidence rate of 1 in 40,000 to 60,000 births.[28,29,30] CDD affects both boys and girls, but is predominant in girls, comprising about 90 percent of those diagnosed. Affected boys tend to exhibit more severe developmental abnormalities with little or no development of intellectual abilities or motor skills.

[25] Analyst work, CorelDraw Software, Corel Corporation, Ottawa, Canada.
[26] National Organization for Rare Disorders. MECP2 Duplication Syndrome.
[27] Wong, K., *et al*. Factors influencing the attainment of major motor milestones in CDKL5 deficiency disorder. European Journal of Human Genetics. August 2022.
[28] National Library of Medicine, CDKL5 Deficiency Disorder.
[29] National Organization for Rare Disorders. CDKL5 Deficiency Disorder.
[30] Jakimiec, M., *et al*. CDKL5 Deficiency Disorder—A Complex Epileptic Encephalopathy. Brain Sciences, February 2020.

Causes
CDD is caused by spontaneous mutations in a gene called the CDKL5 gene and is not inherited. CDKL5 gene encodes the cyclin-dependent kinase-like 5 enzyme and is located on the X chromosome. Its X chromosome locus shifts the incidence of the disorder disproportionately to girls, since the malfunctioning gene can affect levels of the gene product in brain cells. Since boys inherit only one copy of the X chromosome, a defective CDKL5 gene can be fatal in males. Some boys with a CDKL5 variant on their only chromosome may show CDD symptoms. The CDKL5 gene product, the CDKL5 enzyme, is believed to play a critical role in neurons during brain development. Deficiency or malfunctioning variants of the CDKL5 protein in the affected individuals disrupts normal brain development, although the exact mechanism of action is not fully understood.

Symptoms
CDKL5 deficiency disorder can manifest as early as the first week after birth. Common symptoms include:

- Early onset of frequent seizures involving loss of consciousness, muscle rigidity, convulsions, epileptic spasms characterized by muscle jerks, tonic seizures characterized by abnormal muscle contractions, CDD seizures do not improve with treatment;
- Impaired gross motor skills (walking, standing, sitting) and fine motor skills (grasping, purposeful use of hands); repetitive hand movements (clapping, hand licking, hand sucking);
- Delayed development; severe intellectual and speech disability - little or no speech;
- Vision difficulties – cortical visual impairment; poor eye contact, visual fixation;
- Gastro-intestinal abnormalities, difficulty feeding and swallowing, gastrointestinal reflux and/or constipation;
- Sleep abnormalities, teeth grinding (bruxism), irregular breathing.

Other symptoms may include small head size (microcephaly), scoliosis, distinctive facial features in some patients such as high and broad forehead, large deep-set eyes and abnormal spacing between the nose and the upper lip.

Diagnosis
CDD shares many common symptoms with other disorders including RTT. Thus, CDD diagnosis is usually confirmed using a blood test by checking for a genetic change in the CDKL5 gene. Healthcare providers note the common symptoms which include early life seizures for infants, epilepsy and developmental abnormalities for older children, evaluate potential causes and confirm the diagnosis using a genetic test for CDKL5 mutations. Common methods include sequencing of the CDKL5 gene, testing for a panel of known causative genes for epilepsy and developmental abnormalities and other methods to detect large deletions in the X chromosome among others. Since there are known variants of the CDKL5 gene of uncertain significance, the results of a genetic test must be evaluated to determine if the CDKL5 variant is responsible for the disorder.

Treatment
CDD is caused by a random mutation in an X-linked gene and has no cure. Standard of care is designed to improve the quality of life for affected children. Some treatments administer medications to manage seizures, gastrointestinal reflux, sleep, movement issues and breathing difficulties. Feeding issues may be addressed using supplemental input to provide adequate nutrition. Physical, speech and vision therapies are employed to manage motor, communication and behavioral problems while braces, splints and surgeries may be used to address scoliosis and other orthopedic complications. CDKL5 seizures are difficult to control using anticonvulsant medications or their combinations, and as anticonvulsant drugs become refractory, other treatments using steroids and/or intravenous immunoglobulin may be used to manage CDD seizures. In some cases, other options using ketogenic diets, implantation of vagus nerve stimulators (delivering small electrical pulses to the vagus nerve), or corpus callosotomy (disconnecting the nerve fibers connecting two hemispheres of the brain) may be used.

Ganaxolone, a positive allosteric modulator of $GABA_A$ receptors, was approved in March 2022 by the FDA to treat seizures associated with CDKL5 deficiency disorder.

Prognosis
Although there is no known cure for CDD, new treatment options are being developed based on better understanding of the disease progression and complications.

Partners and Key Suppliers

Atomwise

Atomwise employs artificial intelligence and *in silico* screening to advance drug discovery. The company uses deep learning to understand binding attributes modeled by *in silico* three-dimensional protein structures. Its AtomNet technology identifies potential small molecule targets for undruggable targets. The company is able to provide drug discovery services for major disease areas and is working on two novel targets in Rett syndrome that are designated by the "ORAI-" prefix in Vyant's pipeline. So far, Atomwise has been able to use its 3-D structure models to identify the shape of binding sites and match them with small molecules that may turn on, turn off or alter the response of a normal neurotransmitter.

Enamine

Enamine is a Ukraine-based manufacturer of chemical compounds which is able to pull from a library of approximately 200,000 monomers. This resource is called the REAL compound library. It holds all of the necessary drug precursors in place to synthesize a wide variety of custom organic compounds based on a client's specifications. Other provided services include chemistry support, high-throughput screening, pharmacokinetics and toxicity evaluation among others. Work with Enamine was delayed during the first months of the Russian attack in February 2022; however, work has since restarted and Enamine's critical activities are taking place outside of Ukraine.

Cyclica

Cyclica is another partner that uses artificial intelligence to enhance drug discovery. The company focuses on oncology and CNS diseases with services to perform hit discovery, hit validation, hit to lead and lead optimization. Its AI platform evaluates on and off target interactions simultaneously to accelerate the drug discovery process. Cyclica and Vyant are working together in a collaboration offering shared economics for candidates in CDKL5 deficiency disorder. The partner will use its proprietary machine learning platforms to find novel targets, identify repurposing candidates and design new molecules. Efforts will identify, validate and advance new targets and new and existing compounds for streamlined and de-risked discovery of CDD candidates.

OrganoTherapeutics

At the end of the first quarter 2022, Vyant announced a strategic collaboration with OrganoTherapeutics (OT). OT is a developer of proprietary patient-specific organoids that mimic Parkinson's disease (PD) pathology. The collaboration will seek to discover drugs for the treatment of PD using human-derived cells, high-throughput biology and chemistry, and machine learning-based therapeutic design. OT has developed PD-specific midbrain organoids from multiple PD patients, providing the ability to more fully understand drug response based on genetic differences. Vyant Bio and OT recently submitted an application for a Small Business Innovation Research (SBIR) grant to the National Institute of Neurological Disorders (NINDS) to develop a high throughput screening assay to identify clinical candidates for a rare familial PD disease gene. This work recently generated a midbrain organoid model of familial PD that exhibits dopamine neuron degeneration caused by a mutation in the GBA1 gene. Further work will identify novel disease modifying drug targets and therapeutic candidates for Parkinson's disease.

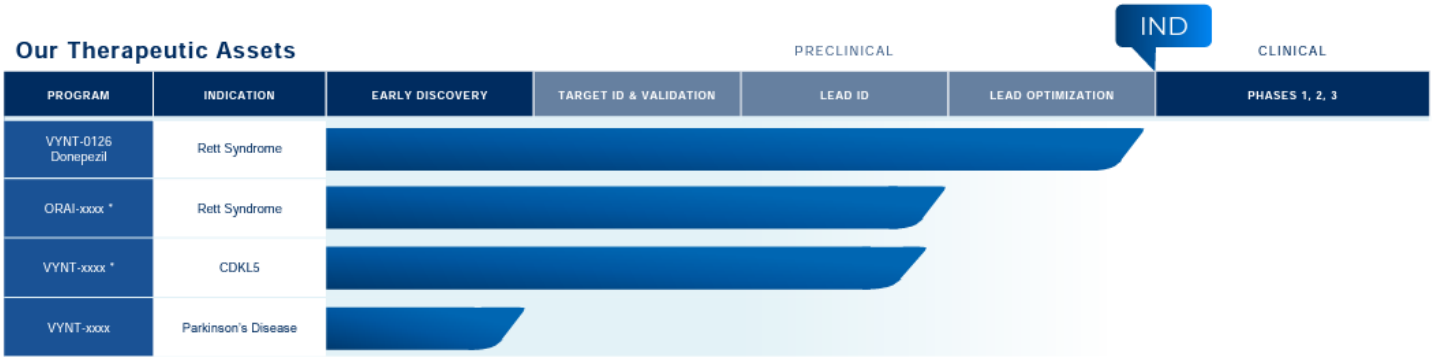
vivoPharm

vivoPharm offers proprietary preclinical test systems supporting clinical diagnostic offerings at early stages for companies in the pharmaceutical, biotechnology and academic spaces. *vivo*Pharm is focused on precision and translational medicine to drive drug discovery and novel therapies. It specializes in conducting studies tailored to guide drug development, starting from compound libraries, and ending with a comprehensive set of *in vitro* and *in vivo* data and reports in support of Investigational New Drug (IND) filings. *vivo*Pharm has locations in Hershey, Pennsylvania and Australia. On November 2nd, 2022, Vyant sold its US *vivo*Pharm subsidiary to Reaction Biology for $5.5 million in cash. After adjustments, tax and expenses, net proceeds of $4.4 million are expected. *vivo*Pharm is now a key supplier to Vyant of contract research organization (CRO) services.

Pharmaceutical Assets

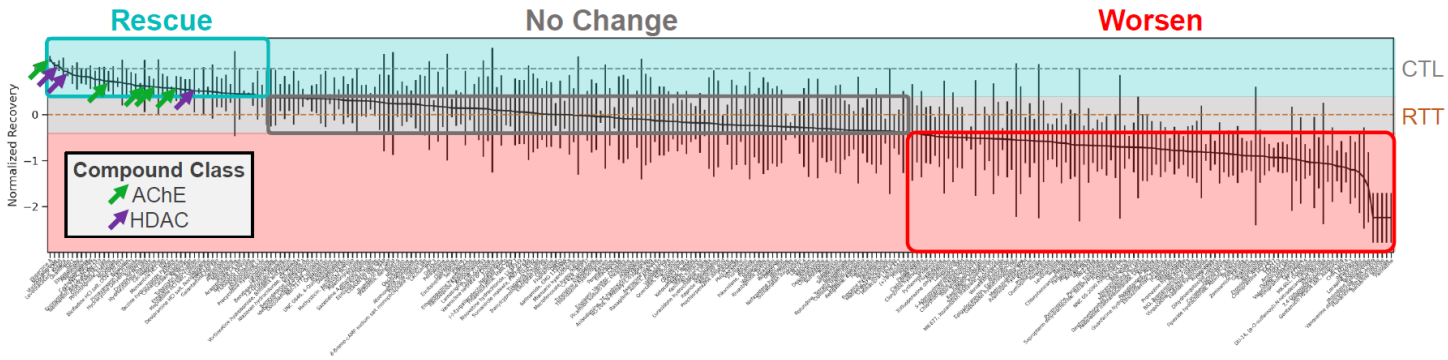
Products and Pipeline

Exhibit VIII – Vyant Bio's Drug Candidate Pipeline[31]



Acetylcholinesterase (AChE) and histone deacetylase (HDAC) inhibitors have been identified as potential therapeutic candidates for Rett Syndrome (RTT) through screening SMART Library[32] compounds. Vyant runs screens of all of its prospective candidates using organoid models. It compares the profile of the waveform produced by the Rett organoid that is treated with the target compound against a healthy control seeking the result that reverts the waveform back to its normal configuration.

Exhibit IX – SMART Library Compounds Ranked by Normalized Recovery[33]

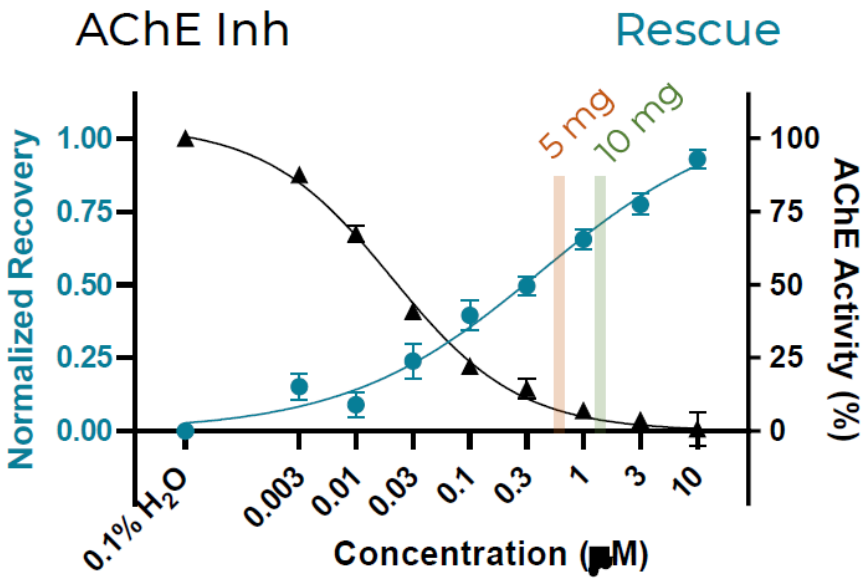


One of the problems in identifying potentially successful RTT compounds is the lack of a screening system that recapitulates the underlying human disease pathophysiology. In response, Vyant has developed an *in vitro* human Rett cortical organoid that exhibits abnormal functional neuronal network activity that can be recorded using high throughput. The platform provides a stable foundation for drug screening. As an index of synaptic dysfunction, the Fluorometric Imaging Plate Reader, or FLIPR tool, is used to evaluate the organoids. Using high throughput screening, it measures calcium transients, which generate an index of the synaptic network activity in the organoids. By measuring the calcium transients, FLIPR can identify the network abnormalities of synaptic signaling. The process provides the biologic endpoint that can be resolved by testing therapeutic agents.

The Rett cortical organoid work has produced results that rescue the functional Rett disease phenotype which are predominantly represented by two drug classes. The acetylcholinesterase inhibitor (AChEI) and histone deacetylase (HDAC) inhibitor classes produced several candidates each. After an intense review of the characteristics of each compound, Vyant selected AChEI donepezil as the most promising compound for treating Rett's foregoing the HDAC inhibitors which presented a less attractive safety profile. The new candidate appears on Vyant's pipeline as VYNT-0126. The primary goal for VYNT-0126 is to validate the brain organoid screening platform. Donepezil's favorable profile is shown in the following exhibit which shows the drugs ability to rescue the Rett phenotype administering doses above 5 mg/kg.

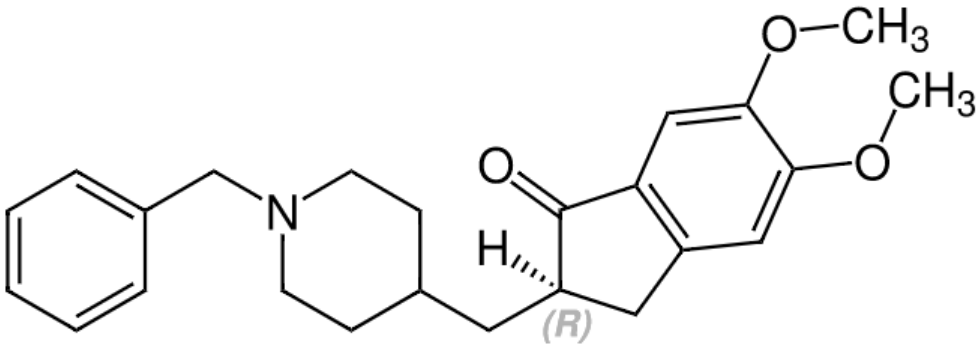
[31] Source: Vyant Presentation January 2023.
[32] This is the International Rett Syndrome Foundation targeted compound library
[33] Source: Vyant Presentation November 16, 2022. Multiparametric analysis of coordinated network activity reveals target specific functional rescue in a human iPSC derived organoid model of Rett syndrome.

Exhibit X – Donepezil Rescue Correlates with AChE Inhibition[34]



AChEI donepezil selectively and reversibly inhibits the acetylcholinesterase enzyme, which normally breaks down acetylcholine. It is commonly used for Alzheimer's disease (AD) and reduces behavioral symptoms, but does not alter the progression of the disease. Off label, it is used for several other dementias and traumatic brain injury (TBI). Application of the drug leads to increased cholinergic neurotransmission in the brain. It blocks the break-down of acetylcholine in the synaptic cleft, thereby preserving it for purposes of neurotransmission.[35]

Exhibit XI – Chemical Structure of Donepezil[36]



Side effects of donepezil are frequently gastrointestinal in nature. This includes nausea, diarrhea, insomnia, vomiting, muscle cramps, fatigue and anorexia.

On November 14, 2022, Vyant submitted an application to conduct a Phase II proof-of-concept clinical trial in adult Rett Syndrome patients in Australia.

ORAI-xxxx

Vyant's second RTT candidate is being developed with partner Atomwise and is a new chemical entity (NCE). Hit to lead optimization efforts are expected to be completed in 2022 and IND-enabling studies will begin in 1H:23. Atomwise employed its AI technology to analyze billions of compounds *in silico* in order to identify potent and selective binders for RTT-effective proteins. The results were further analyzed using 3-D brain organoids to determine biological activity.

Atomwise employed a 3-D structure image of the target protein to identify binding sites that might be accessible to small molecules. The next step determined the function of the small molecules and whether the candidate would

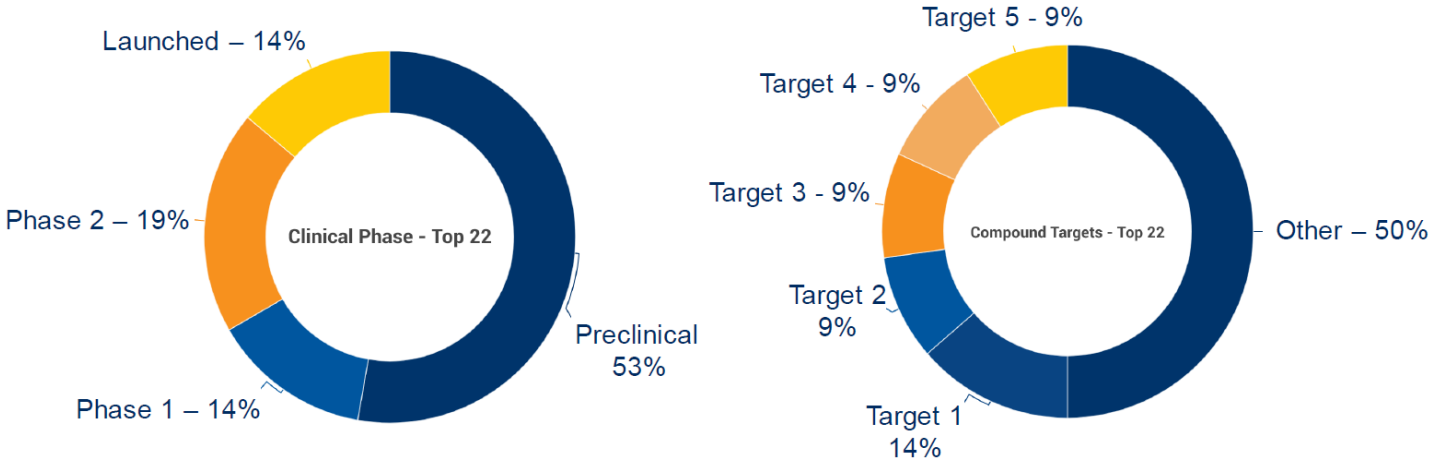
[34] Source: Vyant Presentation November 16, 2022. Identification of a therapeutic candidate for Rett syndrome with a differentiated mechanism of action using a patient derived cortical organoid screening platform.
[35] Aricept (donepezil hydrochloride) FDA Label.
[36] By Denwet - Own work, Public Domain, https://commons.wikimedia.org/w/index.php?curid=63597896.

turn the protein on, off or alter its function in the context of a normal neurotransmitter. Vyant is seeking an allosteric agonist among its candidates that will rescue the RTT disease phenotype. Vyant, in collaboration with Atomwise, has identified small molecules directed against two novel biological targets which have the potential to rescue the Rett phenotype, providing additional opportunities to identify new chemical entities (NCEs) in its drug discovery research for Rett Syndrome.

Vyant CDKL5 Deficiency Disorder (CDD) Candidates

Vyant has screened approximately 5,200 compounds for a signal in CDKL5 Deficiency Disorder or CDD. The screened molecules fall into three categories: FDA approved assets, compounds that have passed Phase I clinical trials or a panel of phenotypic screening compounds. The efforts uncovered 288 repurposing candidates and NCEs that have demonstrated some degree of rescue of the CDD hyperexcitability phenotype. Further confirmatory screening identified 40 assets that produced a full dose response in CDD and control generating 22 top hits. Partner Cyclica is applying machine learning to identify *in silico* molecules for screening of three novel CDD targets. To drive hit-to-lead optimization Vyant is establishing *in vitro* binding and cell-based functional assays for these targets to examine the relationship between target potency and degree of phenotypic rescue. It is validating new isogenic CDKL5-KO (knock out) compared with control cell lines as well as generating new CRISPR-corrected patient lines.

Exhibit XII – Characteristics of Vyant's 22 Top Hits for CDD[37]



[37] Source: Vyant Presentation: High throughput functional screening to develop novel therapies for CDKL5 deficiency disorder using human iPSC derived cortical organoids. November 2022.

Intellectual Property (IP)

As of 2022, Vyant Bio held a portfolio of 12 issued patents in various countries around the globe including the United States, Japan, Singapore and Europe. Vyant's patent strategy is to develop a portfolio that will protect lead products and processes and anticipate workarounds others may pursue for the intellectual property.

The granted patents that are both owned and licensed relate to stem cells, manufacturing processes, product packaging, digital cellular electronics, cell micro-environments and structure, and cell networks. Each patent application includes its own strategy, which may involve the use of provisional patent application filings and related domestic and foreign patent applications that claim the benefits of the provisional applications and that are intended to provide protection in key geographical markets.

Vyant licenses multiple patents and protocols from the University of California, San Diego and Academia Japan for technology required to create and sell induced pluripotent stem cells (iPSCs). Other arrangements are with ID Pharma for the Sendai virus vector technology, and with Max Planck Innovation for mid-brain organoid production.

As the company's new chemical entities (NCEs) are developed, we anticipate additional intellectual property will be generated to support their potential approval and commercialization. At least one NCE for RTT and CDD are expected to be advanced into the clinic following the development of sufficiently supportive IP in the next few years.

Vyant's preeminent patent is titled High Throughput Optical Assay of Human Mixed Cell Population Spheroids. The claim provides a method of performing a functional assay on human spheroids using a fluorometric imaging plate reader. The design addresses the need for automating assays for high throughput systems, using the Fluorometric Imaging Plate Reader, or FLIPR system. FLIPR is able to perform fluorometric analyses on multiple well plates providing a sensitive fluorescence detector. Using the approach as described in the patent, FLIPR allows for the identification of a potential drug hit within seconds of its addition to an assay.

Below we list the key patents behind Vyant's technology:

Exhibit XIII – Selection of Vyant Patents[38]

Title	Patent #	Region	Grant	Priority
Method Of Fabricating Cell Arrays And Uses Thereof	6,510,649	Japan	4/12/19	8/28/14
Method Of Fabricating Cell Arrays And Uses Thereof	11201701540P	Singapore	5/22/20	8/28/14
Method Of Fabricating Cell Arrays And Uses Thereof	10,625,234	US	4/21/20	8/28/14
Surface Energy Directed Cell Self Assembly	11,248,212	US	2/15/22	6/30/15
Method Of Manufacturing Or Differentiating Mammalian Pluripotent Stem Cells Or Progenitor Cells Using A Hollow Fiber Bioreactor	10,760,053	US	9/1/20	10/15/15
Cell Medium Formulation For Cell Stabilization	3,402,330	Switzerland	12/29/21	1/12/16
Cell Medium Formulation For Cell Stabilization	602017051503.5	Germany	12/29/21	1/12/16
Cell Medium Formulation For Cell Stabilization	3,402,330	EU	12/29/21	1/12/16
Cell Medium Formulation For Cell Stabilization	3,402,330	France	12/29/21	1/12/16
Cell Medium Formulation For Cell Stabilization	3,402,330	UK	12/29/21	1/12/16
Projected Capacitive Multi Electrode Eukaryotic Cell Array	11,054,408	US	7/6/21	5/6/16
High Throughput Optical Assay Of Human Mixed Cell Population Spheroids	11,193,159	US	12/7/21	7/14/17

[38] Source: Analyst compiled from RVL Pharma public filings and public information from patent websites

Risks

All investments contain an element of risk which reflects the uncertainty of a business and what it will ultimately achieve. Some investments exhibit higher predictability, with current cash flows and established sales. These enterprises will have a lower level of perceived risk while other companies that are developing an undefined, new technology have a much higher level of perceived risk.

The biotechnology space includes companies at both ends of the spectrum, from mega-cap pharmaceutical powerhouses that have multiple products currently generating revenues, to small operations with a handful of employees conducting pre-clinical studies. Many of the risks faced by the large pharmaceutical companies and smaller biotechnology-focused firms are similar; however, there are some hazards that are particular to smaller companies that have not yet established themselves or their products. The typical risks faced by companies operating in the biotechnology space include those related to liquidity, financing & trading, clinical trials, manufacturing, partnerships, regulatory, personnel, intellectual property, commercialization and geopolitics.

Liquidity, Financing & Trading

Any company may find that securing funding may depend on its position in the economic cycle. During periods of improving confidence, capital may be easy to obtain; however, during a liquidity crisis or a period of heightened risk perception, even companies with bright prospects may be in trouble if they are dependent on the financial markets to fund their work. Early-stage biotech firms rely primarily on equity issuance to fund their operations. The duration of early commercialization efforts can be considerable, requiring substantial capital and personnel to execute. Funds can be sourced through debt or equity issuances; however, these sources may reduce the flexibility of the company and can create difficulties if debt is unable to be repaid.

If capital is required to sustain operations and it is not readily available, a company may be forced to suspend aggressive commercialization efforts, sell equity at a substantial discount to previous valuations and dilute earlier shareholders. A lack of funding may leave potentially promising products without a viable route forward or force a company to accept onerous terms. The pandemic has disrupted capital markets, and related economic effects may last well into the future.

Trading volumes are lower for smaller biotech firms, creating liquidity risk for the investor and large transactions may have a material impact on share price. In periods of crisis or heightened risk perception, share price may be volatile. Companies with smaller capitalizations are typically considered riskier and changes in sentiment may adversely affect their trading prices and volumes. Smaller firms may also have less visibility, compete for investor dollars in a shallow market and be excluded from market indices.

Vyant Bio has endured operational losses since becoming public and expects to continue to do so into the future. The company may fail to monetize its discovery programs and may never become profitable. Vyant passed through a number of transitions over the last two years and holds $9.4 million in cash as of September 30, 2022. Following the end of the quarter, additional funds from the sale of the US portion of *vivo*Pharm has also contributed approximately $4.4 million in cash to the balance sheet. In a January 4th, 2023 press release, Vyant announced the engagement of LifeSci Capital to assist in exploring strategic alternatives to enhance the value of the company. In our experience, these efforts can lead to merger and acquisition activity, a sale of the company and capital raises.

Clinical Trials

For smaller early-stage companies, investing in drug development is a lengthy process. The timeframe for conducting pre-clinical research to eventually commercializing a drug can take from 12 to 15 years or even longer given market and company-specific conditions. And with, on average, only one in one thousand compounds eventually making it to the market from the preclinical stage, the risks are substantial.

Exhibit XIV – Success of Phased Trials and Regulatory Approval[39]

Phase	I - II	II - III	III - NDA/BLA	NDA/BLA - Approval	I - Approval
Probability	**52.0%**	**28.9%**	**57.8%**	**90.6%**	**7.9%**

[39] Summarized from Clinical Development Success Rates 2011-2020. Compiled by Zacks Analysts.

Vyant Bio holds several preclinical assets in its pipeline and expects to begin its clinical program early next year with a Phase I trial in Rett Syndrome which will be conducted in Australia. An investigational new drug (IND) application is planned to be filed in the United States to begin a pediatric Rett Syndrome trial in parallel with the Australian study, the start of which is dependent on successful access to capital.

Manufacturing

Medical product companies can either produce medicines in house or rely on third parties to manufacture them. While there are many benefits to owning manufacturing facilities and exercising direct control over them, in most cases small and medium size pharmaceutical and biotechnology companies work with partners through supply agreements to produce their products. Working with a partner confers a number of benefits including economies of scale, a management team dedicated to compliance with regulatory requirements and the flexibility of engaging other manufacturers based on changing circumstances. The use of a partner also limits the capital burden of a single product company and more closely aligns volume, costs and their respective timing. While there are a number of flexibility benefits to outsourcing manufacturing, a sponsor can also be exposed to several risks. Partner manufacturers may not prioritize its clients' projects and may run afoul of regulatory requirements. The manufacturer may experience quality control or volume constraints that could disrupt client demand. Take or pay contracts may force the client to accept more product than can be sold in a reasonable time, negatively impacting cash flow and producing excessive inventory which could expire before sale. There are offsets to these risks in Vyant's case. The company's lead compound, donepezil, is a generic small molecule drug that is available from many suppliers. The undisclosed new chemical entities that it is developing are also small molecules that can be produced by multiple manufacturers.

Vyant has a close working relationship with Enamine, which is able to synthesize a broad variety of compounds that are needed. A risk specifically relevant to Enamine is related to the location of its headquarters in Kyiv, Ukraine. Continued conflict between Russia and Ukraine may cause additional disruptions to the company's activities. To address this risk, Enamine has relocated its critical activities outside of Ukraine.

Partnerships

Many smaller pharmaceutical and biotechnology companies lack the financial depth and capital availability to commercialize a product globally. While a US-based company may be able to successfully commercialize in the United States, engaging in this activity on a global basis is more difficult, especially in jurisdictions where regulation, culture and language are substantially different than what is common in the United States. While working with a partner reduces the effort and funds required to commercialize globally and can provide an in-place sales team with active relationships, it reduces the amount of control that the license holder can exercise over the process. Partners may change priorities or fail to invest properly to develop the sublicensed product, resulting in lower sales than expected. Partners may also suffer financial setbacks which prevent them from properly commercializing or meeting milestone obligations. We anticipate that Vyant will pass off its candidates to larger partners after the proof-of-concept stage.

Vyant has created partnerships in the drug discovery and compound synthesis spaces that help it identify promising candidates and develop its early-stage pipeline. Partners extend from AI and ML experts that can narrow the portfolio of candidates, to others that have specific disease domain knowledge, such as OrganoTherapeutics which can augment the capabilities of Vyant's Brain Organoid Screening Platform (BOSP), computer and organoid modeling program. We expand on partner and supplier relationships in a previous section.

Regulatory

Regulatory risk centers on clinical trial requirements, marketing approval of the candidate, expedited pathways and associated oversight. Regulations extend to post-marketing surveillance and pricing dynamics. Furthermore, pharmaceutical and biotechnology firms typically maintain a global presence and must navigate the regulatory approval process, clinical trial requirements and marketing regulations in the jurisdiction where they seek to commercialize. Substantial expense is undertaken to bring a molecule or compound through clinical trials and address all of the regulatory agencies' concerns. Companies that have a long history of research success in drug development, with opinion leaders and experts advocating for the product in the field will have an advantage. Previous success with the FDA or other regulatory agencies is another attractive attribute for a sponsor. Vyant's interactions with the FDA will be largely centered on pre-IND meetings and IND submissions. We anticipate that later stage interaction with the FDA, including a new drug application (NDA) submission, will likely be handled by partners.

Vyant's lead candidates are all rare disease assets. Compounds with this classification are granted special benefits and incentives including tax credits, grants, product exclusivity and other favorable exemptions. Rare disease can-

didates frequently enjoy accelerated movement through clinical trials and regulatory review as an incentive for sponsors to fund them.

Personnel

Biotechnology startups rely on the expertise and leadership of management to make decisions and investments on their behalf. Competition for talented and experienced management is intense and matching the optimal skill set with the right company is difficult. Change in management can be disruptive if leaders or scientists are lured away by other firms. Additionally, early-stage biotech companies are often virtual and have a small team which can put them at a disadvantage when compared to larger firms, with full-time specialized personnel. A smaller company with much of the upside tied to stock price may deter certain talent from joining the firm. Vyant recently divested part of its *vivo*Pharm subsidiary and dramatically reduced its personnel count as a consequence of the sale.

Intellectual Property

Despite the existence of patents and trade secrets, the loss of intellectual property is a risk. Vyant's Brain Organoid Screening Platform is protected by a series of global patents protecting the analysis of spheroids, fabrication of cell arrays and differentiating pluripotent stem cells among other drug discovery methods. While this can limit competing in the specific settings identified in the patents, technology can be worked around and approaches can be copied if they demonstrate success, raising the risk that the platform could be imitated or replicated, especially by a larger firm with more resources. Vyant's lead candidate is an already-approved product whose patents have expired. While Vyant or the successor that continues to develop donepezil may be able to alter the formulation of the molecule and win approval as a rare disease drug, the underlying product is generic and widely available. Vyant's other portfolio assets are new molecular entities and may be eligible for 20 years of patent protection.

Market Risk

Successful marketing of approved drug candidates relies on adoption by patients and providers. An approved drug must have convincing clinical trial data and maintain a favorable reputation among prescribers. Marketing is expensive and requires an experienced sales force and a presence in the marketing area. Marketed products remain under surveillance and any unexpected adverse effects may lead to regulatory authorities revoking marketing authorization. Inclusion of the drug in insurance plan offerings is also important. Rapidly obtaining a preferred position on health plan and payor formularies is critical to achieving target penetration rates. If health plans and payors cannot agree on appropriate pricing for the drug and the compound fails to offer a significant benefit above standard of care, sales may be limited. Vyant's lead indication in Rett is a rare disease and does not have other approved products available. These two factors are supportive of high penetration into the addressable market given the limited and attentive audience and the lack of alternatives. Commercialization and marketing will likely be performed by partners.

Geopolitical

Recent trade tensions between the US and China threaten the world economy, and have been exacerbated by the recent pandemic. There had been a cross-pollination of capital and drug development between China and the United States which has slowed as a result of the trade and political dispute between the countries. This conflict may reduce the availability of capital, partnerships and future development and commercialization deals between companies in the two nations. The UK withdrew from the European Union on January 31, 2020. Previously, a drug approved under the centralized procedure in the European Union would be approved in all member states. However, with the withdrawal of the UK, additional efforts and expense may be required to obtain marketing approval in this top five European market. Conflict between Ukraine and Russia has led to disruptions in clinical trials, business operations and movement of products across the borders in these countries. Sanctions have also been placed on Russia and many of the businesses that reside inside its borders which may lead to shortages of certain products. Refugees fleeing the war in Ukraine may also impact nearby countries and their productivity. Due to the war, Vyant's partner Enamine, which is headquartered in Ukraine has suffered disruptions in service to its clients. In an effort to minimize further disruptions, the partner has moved critical activities outside of the country.

Peers and Competitors

Vyant's business touches on several axes including the indications of Rett Syndrome and CDKL5 deficiency disorder. The company also features a discovery platform that uses iPSC-derived brain organoids to identify new therapies that will work in CNS diseases. Others working in the Rett space include Acadia Pharma with its recently submitted NDA for trofinetide, Anavex Life Sciences with its Phase III candidate 2-73, Taysha Gene Therapies with its Phase I/II TSHA102 and Stridebio advancing gene therapy STRX230 in partnership with Sarrepta. CDD receives less focus than Rett, in part due to its more recent emergence as a separate disorder. There are no approved treatments that address the root cause of the disease. However, Marinus' ganaxolone has been approved for seizures in CDKL5 patients while fenfluramine is also being studied in Phase III as a treatment for CDKL5-related seizures by Zogenix which was recently acquired by UCB. Ultragenyx is developing a gene therapy that would be a cure if successful and deliver a functional copy of the CDKL5 gene to cells in the brain.

Drug discovery is the other area of interest and is dominated by internal programs at the large pharmaceutical and biotechnology companies. Other smaller companies have emerged that provide services in support of the industry and Vyant, until recently, was part of this ecosystem. The company's new strategy calls for using the platform to develop candidates internally. Other notable drug discovery enterprises include Herophilus, which uses brain organoids to identify clinical candidates, the Germany-based Evotec, which is collaborating with Bristol Myers on an iPSC-based screening platform and OrganoTherapeutics which uses mini-brains for finding drug candidates in Parkinson's Disease. Other related discovery platforms are offered by Unravel Bio, Dewpoint Therapeutics and Q-State Bio.

CNS disease and drug discovery are some of the fastest growing areas in life sciences given the relatively high proportion of the population that suffers from these maladies, unmet need in neurodegenerative disease and the tremendous cost that may be able to be avoided using new discovery models.

Exhibit XV – Public Companies[40]

Ticker	Company	Price	MktCap (MM)	EV (MM)	Therapeutic Area
ABBV	Abbvie	$146.28	$258,693	$311,420	Broad neurodegenerative & rare disease platform
ACAD	Acadia Pharma	$18.57	$3,007	$2,700	Rett; trofinetide NDA submitted; PDUFA 12Mar23
AVXL	Anavex Life Sci	$10.56	$823.3	$671.0	2-73 for Rett in Ph3; fast track
BIIB	Biogen	$290.08	$41,772	$43,760	Broad neurodegenerative disease platform
EVO	Evotec	$10.16	$3,656	$3,030	Discovery platform-iPSC, metabolic CNS indication
GSK	GlaxoSmithKline	$35.30	$72,263	$88,800	Broad neurodegenerative & rare disease platform
JNJ	Johnson & Johnson	$168.23	$439,834	$439,510	Broad neurodegenerative & rare disease platform
LLY	Eli Lilly	$342.10	$325,056	$342,280	Broad neurodegenerative & rare disease platform
MRK	Merck	$105.38	$267,180	$239,710	Broad neurodegenerative & rare disease platform
MRNS	Marinus Pharma	$6.26	$310,607	$191,520	IV & oral ganaxolone for CDKL5
NEU.AX	Neuren Pharma	AU$7.96	AU$1,027	AU$987.7	Licensed trofinetide to Acadia, Rett
NVS	Novartis	$89.49	$193,013	$203,280	Gilenya clinical work in Rett
PFE	Pfizer	$43.79	$245,807	$251,430	Broad neurodegenerative & rare disease platform
RARE	Ultragenyx Pharma	$43.72	$3,065	$2,190	Gene therapy for CDKL5 (UX055)
RHHBY	Roche	$39.29	$257,836	$286,360	Broad neurodegenerative & rare disease platform
TSHA	Taysha Gene	$1.76	$109.9	$76.3	Rett; Gene Therapy: TSHA102-AAV9, Ph1/2
UCBJY	UCB	$40.83	$15,512	$18,000	CDKL5-Acquired Zogenix
Acquired	Zogenix				Bought by UCB-Rare genetic epilepsies
private	Neurogene				RTT gene therapy: NGN-401 IND cleared
private	Cerevance				PD, AD & other CNS. Ph1 in psychiatric disorders
private	Stridebio				Gene therapy for Rett w/ SRPT (STRX230)
private	Herophilus				Discovery platform-organoids, CNS genetic disease
private	Unravel Bio				Target discovery: BioNAV platform. Rett
private	OrganoTherapeutics				Brain organoids for PD
private	Dewpoint Tx				Drug platform targeting biomolecular condensates
private	Q-State Bio				CNS disorders/discovery for Rett, cell models, AI, ML
VYNT	Vyant Bio	$0.92	$5.5	-$2.2	Organoid discovery platform for Rett/CDKL5

[40] Price as of January 27, 2023

Management Profiles

Jay Roberts, President and Chief Executive Officer

Jay Roberts has been the President and Chief Executive Officer of Vyant Bio, Inc. since 2018. Mr. Roberts had previously served as the Chief Operating Officer of Cancer Genetics. Prior to joining Cancer Genetics, Mr. Roberts served as the Chief Financial Officer for VirMedica, Inc., an innovative technology solutions company that provides an end-to-end platform that enables specialty-drug manufacturers and pharmacies to optimize product commercialization and management. Before VirMedica, Mr. Roberts was the Chief Financial and Administrative Officer for AdvantEdge Healthcare Solutions Inc., a global healthcare analytics and services organization. Prior to that, Mr. Roberts also served as the Chief Financial Officer and Treasurer for InfoLogix, Inc., a publicly-traded, healthcare-centric mobile software and solutions provider. He has also held CFO roles at leading public medical device and healthcare services firms including Clarient, Inc., a publicly-traded provider of diagnostic laboratory services, and Daou Systems, Inc., a publicly-traded healthcare IT software development and services firm. In addition, he has held key senior executive roles with MEDecision, Inc., HealthOnline, Inc., and the Center for Health Information. Mr. Roberts earned a Bachelor of Science and a master's degree in Business Administration from the University of Maine. He is a member of the Fellows and a former member of the Board of Directors and Past Chair for the Drug Information Association, a global neutral forum enabling drug developers and regulators access to education and collaboration. Mr. Roberts also serves on the Board of Directors of Cohere-Med Inc., a clinical analytics company.

Robert T. Fremeau, Jr., PhD, Chief Scientific Officer

Dr. Fremeau is an experienced R&D leader with over two decades of drug discovery experience in academia and industry advancing next-generation drug development for severe neurological disorders. He is an accomplished scientist and biotech entrepreneur with an established history of scientific innovation and program leadership at the intersection of target validation, translation, and clinical development. As a Scientific Director at Amgen Inc., he led and contributed to multiple teams that advanced small molecules into clinical trials against innovative targets across neurological indications. Throughout his academic career at Duke University and UCSF, Dr. Fremeau made seminal contributions to the first molecular and functional characterization of the receptors and transporters for the biogenic amine and amino acid neurotransmitters. Dr. Fremeau holds numerous patents and has authored over 65 peer-reviewed publications in high-impact scientific journals including Science, Nature, Neuron, PNAS, Journal of Medicinal Chemistry, and Journal of Neuroscience. Dr. Fremeau served on the editorial board of the journal "Molecular Pharmacology" and was an *ad hoc* member of the MDCN-5 and NLS-2 study sections at the NIH and the Division of Neuronal and Glial Mechanisms study section at the National Science Foundation.

Andrew D.C. LaFrence, CPA, Chief Financial Officer

Andrew D.C. LaFrence joined Vyant's predecessor, StemoniX, as its Chief Financial Officer in August 2019 and, since March 2020, also served as its Chief Operating Officer. Mr. LaFrence has 38 years of accounting and finance experience, including executive management positions at public and private life sciences companies. Previously, he was Senior Vice President and Chief Financial Officer of Biothera Pharmaceuticals, Inc. from May 2018 to August 2019, as well as Vice President Finance, Information Systems and Chief Financial officer at Surmodics, Inc. (NASDAQ: SRDX) for five years. Prior to Surmodics, Mr. LaFrence served as Chief Financial Officer for CNS Therapeutics, a venture-backed intrathecal drug development and delivery company. Prior to his operating company experience, Mr. LaFrence was an audit partner at KPMG LLP where he focused on supporting venture-backed, high-growth medical technology, pharmaceutical, biotech and clean tech private and public companies. Mr. LaFrence is a certified public accountant and has a bachelor's degree in accounting and a minor in business administration from Illinois State University.

Operational Milestones

Recent Milestones

Vyant Bio has undergone a metamorphosis over the last two years, changing from a preclinical test systems company in early 2021 named Cancer Genetics to a near clinical stage drug development company focused on rare neurological disease. The first major change came in early 2021 with the announcement of the StemoniX acquisition. StemoniX brought iPSC cell-derived neural and cardiac screening platforms to the table allowing for predictive, accurate and consistent models for high throughput screening. Dr. Robert Fremeau was added as Chief Scientific Officer in October 2021, bringing his years of experience as scientific director at Amgen leading efforts validating, translating and developing clinical candidates.

Below we list key milestones.

- Merger of Cancer Genetics, StemoniX & CGI – March 2021
- Corporate name change to Vyant Bio – April 2021
- Strategic collaboration with Cyclica – August 2021
- CSO Dr. Robert Fremeau, Jr. added to executive team – October 2021
- Shift in focus neurological developmental and degenerative disease therapeutics – December 2021
- Lincoln Park Purchase Agreement – March 2022
- Strategic collaboration with OrganoTherapeutics – March 2022
- 1:5 reverse stock split – July 2022
- Sale of US *vivo*Pharm Subsidiary – November 2022
- Poster presentation at 2022 CDKL5 Forum (Loulou Foundation) – November 2022
- Rett presentations at Neuroscience 2022 – November 2022
- Sale of Australian *vivo*Pharm Subsidiary – December 2022
- Pre-IND feedback from FDA for clinical trial – January 2023
- Lead optimization for ORAI-xxxx – 2Q:23

At the end of 2021, Vyant announced its shift away from a drug discovery service provider and purveyor of iPSC-derived disease screening models. Moving into 2022, Vyant shored up its financing relationships, signing an at-the-Market agreement with Canaccord Genuity and a purchase agreement with Lincoln Park. The sale of the US portion of *vivo*Pharm in November 2022 added funds to the coffers. In late March 2022, Vyant and OrganoTherapeutics (OT) joined forces to design and identify Parkinson's disease (PD) drugs. The effort will leverage OT's high-throughput biology and chemistry, and machine learning-based strengths with Vyant's organoids. As 2022 progressed, several posters were presented for the advancements made in both Rett syndrome (RTT) and CDKL5 deficiency disorder (CDD). Management entered into a master services agreement with an Australian CRO, which is expected to manage the RTT trial next year with donepezil. Other 2023 events include public identification of the undisclosed assets for RTT and CDD.

On November 15th, 2022, Vyant reported third quarter revenues and filed its 3Q:22 Form 10-Q. A conference call was held in conjunction with the releases where management provided additional information regarding the company's operational and financial progress. For the first nine months of the year ending September 30, 2022 revenues of $620,000 were reported. Operating expense was ($13.0) million yielding a net loss of ($12.4) million or ($3.15) per share.

After the turn of the year, Vyant announced that it would be pursuing strategic alternatives with the help of LifeSci Capital as its financial advisor. Management expects that the effort will identify alternatives that will enhance shareholder value and recognize the progress that has been made in the company's drug discovery platform. During this process, Vyant will continue to execute on its business plan.

For the nine months ending September 30, 2022 and versus the same period ending September 30, 2021:

- Revenues of $620,000 fell 21.3% compared to $788,000. Service revenues experienced a material decline from prior year levels due to a decrease in contribution from the Maple Grove facility while product revenues increased slightly due to increased shipping volumes and higher pricing;
- Product cost of services was $38,000 yielding a gross margin of 40.4% while product cost was $909,000, yielding a negative gross margin as costs exceeded revenues;
- Research & development expense totaled $5.2 million, rising 78% from $2.9 million, driven by costs related to transforming the Maple Grove facility into a research and development facility, higher payroll expenses and the opening of a new facility in California;
- Selling, general & administrative expense was $6.9 million, up 18% from $5.8 million on recognition of severance benefits, higher professional expenses and greater insurance expense;
- Merger related expenses were nil vs. $2.3 million;
- Ignoring discontinued operations, net loss was ($12.4) million vs. ($14.6) million or ($3.15) and ($3.91) per share, respectively.

As of September 30, 2022, cash and equivalents stood at $9.4 million. This amount compares to a $20.6 million balance in cash and equivalents held at the end of 2021. Cash burn in the first nine months of the year was ($11.0) million while financing cash flows were a trivial ($111,000) draw. Following the report of third quarter results, Vyant sold the US-based division of the *vivo*Pharm subsidiary which is expected to contribute a net $4.4 million to its cash balance.

Valuation

Vyant Bio is an early-stage drug development company centered on the screening of new and existing compounds for neurology disease using brain organoids. It recognizes the shortcomings of using animal models for identifying safe and efficacious compounds for brain diseases given the vast differences between human and non-human brains. The company uses an extensively researched approach to measure drug effects on the Rett Syndrome (RTT) and CDKL5 Deficiency Disorder (CDD) phenotype with the objective of its rescue. While Vyant is expected to begin clinical work on donepezil this year in RTT, the effort is primarily to validate the platform and we do not expect this asset to ultimately provide revenues to Vyant as it is an already approved, easily accessible generic. This shifts the value-driving candidates towards the new chemical entities (NCEs) that Vyant is advancing.

We value Vyant's pursuit of two rare disease indications, RTT and CDD. The first, RTT, requires the successful development of an as yet undisclosed small molecule NCE which is expected to begin a Phase I study in 2024 following clearance of an investigational new drug (IND) application. The CDD indication will be advanced also using an as yet undisclosed NCE small molecule.

Only limited treatments are approved for RTT which address the symptoms of the disease. For CDD, anti-seizure medication ganaxolone is approved for CDD. Based on the limited therapeutics options available and the lack of a disease modifying therapy for either RTT or CDD, we anticipate high penetration in both indications.

RTT affects from one in ten to one in fifteen thousand girls around the world. We adopt the midpoint of 1:12,500 to generate our estimate of the RTT population in our forecasted regions. For the addressable market, we assume 20% of the RTT population is at a severity level great enough to seek treatment. This approach is used for both the US population, which generates an addressable market of about 2,700 patients in 2023 and for the developed world population, which generates an addressable market of about 8,000. Population growth estimates are 0.5% for the US and 0.75% for the developed world ex-US.

The timeline for the NCE RTT clinical trials begins in 2025 with a Phase I clinical trial. According to our model, Phase II studies will begin in 2026 and take one year. This will be followed by Phase III efforts in 2027 and 2028 and then a new drug application (NDA). The NDA should be submitted to the FDA in 2029 followed by approval and first sales in 2030. We model a 10% penetration in year one of commercialization rising to 72% by year seven. The relatively high capture rate is a function of limited alternatives and a small RTT community which we anticipate will embrace an effective therapy. Pricing is forecast at $180,000 per year of treatment in 2030, reflecting the environment enjoyed by successful rare disease drugs; inflation is set at 3% per annum. Seven years of exclusivity is expected in the US; however, we expect patent protection will endure until 2043.

We anticipate filings in Europe and other ex-US geographies in 2030. Assuming approval, commercialization will begin in 2031. We model a 10% penetration into the addressable market in year one rising to 72% by year seven, and remaining at this level until patents expire in 2043. Pricing is forecast at ~40% of US levels or $74,000 per annum in 2030. Ten years of exclusivity is granted by the European Medicines Agency for successful rare disease drugs; however, the patent is expected to stave off competition until 2043.

Vyant is focused on drug discovery and early-stage research and development. We anticipate that successful assets will be passed on to partners for ultimate commercialization after proof of concept. In return for granting a license, upfronts, milestones and royalties are forecast. Based on the potential opportunities for the NCE in RTT, we anticipate that 22% of revenues will be paid to Vyant to be spread among upfronts, milestones and royalties.

CDD is less common than RTT and occurs in every one in 40,000 to 60,000 births. Our model uses a 1:50,000 prevalence to estimate the CDD population in the US and developed world. In the United States, this generates a CDD population of 6,600 and with a 20% anticipated addressable market, about 1,300 will be candidates for the product. In the developed world, we anticipate an addressable market of about 4,000.

Vyant is also developing an undisclosed new chemical entity (NCE) for CDD which will be the subject of an IND in 2024 and expected to be in the clinic shortly after. Phase II studies are expected to begin in 2025 and produce actionable data by 2027. Phase III studies are forecasted to start in 2028 and generate pivotal data by the end of 2029. A new drug application is modeled to be submitted in 2030 with US commercialization beginning in 2031. For Europe and the rest of the developed world, we anticipate commercialization will begin in 2032.

For the United States, we estimate a 10% penetration in year one of commercialization, rising to 72% by year seven. Sales as a proportion of addressable market will continue at this level until the anticipated end of patent protection in 2043. The relatively high penetration is a function of limited alternatives and a small CDD community which we expect will embrace the effective therapy. Pricing is forecast at $180,000 per year of treatment in 2031, reflecting the environment enjoyed by successful rare disease drugs; inflation is set at 3% per annum. While seven years of exclusivity will be granted to the product as a rare disease asset, patent protection is expected to extend beyond this until 2043.

We anticipate filings in Europe and other ex-US geographies for the CDD candidate in 2031. Assuming approval, commercialization will begin in 2032. We model a 10% penetration into the addressable market in year one rising to 72% by year seven, and remaining at this level until 2043 when related patents are expected to expire. Pricing is forecast at 40% of US levels or $74,000 per annum in 2032. Ten years of exclusivity is granted by the European Medicines Agency for successful rare disease drugs; however, related patents are expected to extend beyond this period until 2043.

As with the 505(b)(2) asset, we anticipate that the successful CDD asset will be passed on to partners for ultimate commercialization. Vyant's product for CDD will be an NCE, and if successful, we anticipate that a net 22% of revenues will be paid to Vyant divided among upfronts, milestones and royalties.

Probability of success (PoS) is an important component of our valuation model and a number of factors drive its value. Some of the elements considered include whether or not a candidate is first in class, results of previous studies, side effect profile, the benefit of the Brain Organoid Screening Platform and use of brain organoids and other components. Based on our assessment of Vyant's platform, we estimate a 10% likelihood of success for the RTT NCE. The undisclosed asset for CDD will also be assigned a 10% PoS based on its preclinical status. For reference, we assume approximately 10% of average candidates starting Phase I, 15% of those in Phase II and 50% of those in Phase III are ultimately approved. Weighting each of the programs by their NPV generates an overall PoS of 10.0%.

We use a DCF model to value Vyant's cash flows employing a 15% discount rate and a weighted 10.0% probability of ultimate commercialization for the portfolio of assets. Cash taxes are estimated at 26%, which consists of 21% federal and 5% state and local which will be recognized when net operating losses are exhausted. We assume outstanding options and warrants below our target price will be exercised, and add resulting cash to the balance sheet. Capital raises will be required in the near future to support the anticipated clinical trials. We estimate that 3.0 million shares will be issued next year at $1 per share to raise $3.0 million to support near term operations.

The result of our forecasts and estimates generates a valuation and present value of Vyant Bio of $2.00 per share.

Conclusion

Vyant Bio recognizes the importance of using AI, ML and human-derived brain organoids to identify candidates that can address rare CNS, developmental and neurodegenerative disease. Combined with the Fluorometric Imaging Plate Reader (FLIPR) high throughput screening tool, the company is able to rapidly narrow down thousands of candidates to only a few that are able to rescue the disease phenotype. Drug development is expensive, lengthy and offers low success rates. Platforms such as Vyant's will be necessary to more quickly and accurately identify candidates that offer high degrees of efficacy and safety. The use of brain organoids helps avoid many of the pitfalls that result from the use of animal models. In many cases, animal model CNS is too evolutionarily distant from humans and is a poor predictor of results. Running tests using brain organoids can help researchers anticipate the compounds that will perform well in humans.

Vyant's portfolio consists of donepezil and several undisclosed repurposing assets and new chemical entities (NCEs). The lead product, donepezil, is an already-approved generic that will be difficult to commercialize and serves as a tool to validate Vyant's drug discovery platform. Other assets that are NCEs offer more upside as they can secure intellectual property protection and potentially avoid generic competition until the 2040s.

Rett syndrome (RTT) and CDKL5 deficiency disorder (CDD) are both rare diseases. Candidates that pursue them will enjoy several benefits, including financial support, closer relationships with regulatory agencies and smaller, less expensive trials among other advantages. Support from Rett and CDKL5 organizations and governments, such as that of Australia for the upcoming RTT trial, are expected to keep costs low while generating supportive data for the brain organoid screening platform.

Vyant's differentiating characteristic is its brain organoid screening platform that combines artificial intelligence, high throughput screening, and the FLIPR technology to rapidly identify candidates that can rescue the mutant phenotype. As the platform is using human iPSC-derived brain organoids, the approach is able to sidestep several of the shortcomings presented by animal models which lack important features necessary to predict human drug response.

Vyant Bio held $9.3 million on its balance sheet as of September 30, 2022 and received additional net funds of approximately $4.4 million from the sale of its US-based subsidiary. It recently announced its intent to pursue strategic alternatives with an advisor while continuing to execute on its existing business plan. We also see grants and other types of funding coming from private Rett and CDKL5 organizations.

Key reasons to own Vyant Bio shares:

- **Candidates vetted using brain organoids prior to costly and time-consuming clinical trials**
  - **Donepezil and undisclosed new chemical entities in Rett's Syndrome**
  - **Undisclosed repurposing and NCE candidates in CDKL5 Deficiency Disorder**
- **Reduces reliance on animal models to identify safe and efficacious candidates**
- **Provides platform technology offering broader applications if validated**
  - **Parkinson's disease**
  - **Alzheimer's disease**
- **Brain Organoid Screening Platform**
- **Complementary partners**
  - **Atomwise - AI/ML screening in RTT**
  - **Cyclica - AI/ML screening in CDD**

Based on our analysis of Vyant's brain organoid screening platform and portfolio of pipeline assets, we see a pathway forward to the clinic and to future partnering. We initiate on Vyant Bio with a valuation of $2.00 per share.

PROJECTED FINANCIALS

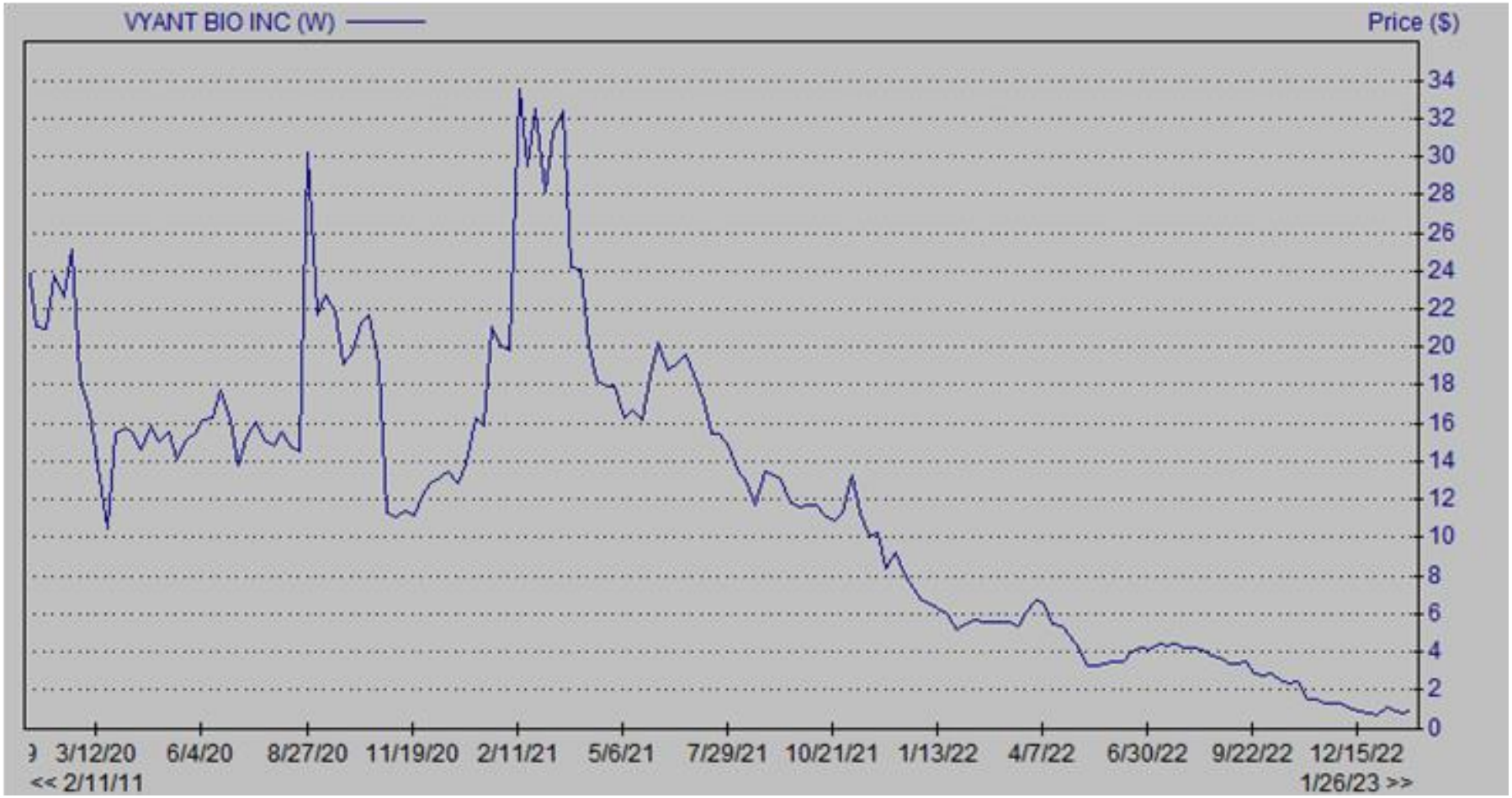
Vyant Bio, Inc. - Income Statement

Vyant Bio, Inc.	2021 A	Q1 A	Q2 A	Q3 A	Q4 E	2022 E	2023 E	2024 E
Total Revenues ($US '000)	**$1,148**	**$303**	**$165**	**$152**	**$48**	**$668**	**$0**	**$0**
YOY Growth	*32%*	*49%*	*-50%*	*-90%*	*-87%*	*-42%*	*-100%*	*# DIV/0!*
Cost of Goods Sold, Service	$408	$38	$0	$0	$0	$38	$0	$0
Gross Margin	39%	60%	0%	0%	0%	60%	0%	0%
Cost of Goods Sold, Product	$1,439	$348	$304	$257	$89	$998	$0	$0
Gross Margin	-198%	-67%	-84%	-69%	-85%	-74%	0%	0%
Research & Development	$4,273	$1,551	$1,688	$1,993	$1,700	$6,932	$9,000	$10,200
Selling, General & Administrative	$8,424	$2,763	$2,509	$1,583	$1,825	$8,680	$6,200	$6,250
Other Costs	$2,310	$0	$0	$0	$0	$0	$0	$0
Income from operations	($15,706)	($4,397)	($4,336)	($3,681)	($3,566)	($15,980)	($15,200)	($16,450)
Operating Margin	*-1368%*	*-1451%*	*-2628%*	*-2422%*	*-7429%*	*-2392%*	*# DIV/0!*	*# DIV/0!*
Other Income	($2,869)	($9)	$11	$34				
Pre-Tax Income	($18,575)	($4,406)	($4,325)	($3,647)	($3,566)	($15,980)	($15,200)	($16,450)
Tax Rate	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Net Income	**($18,575)**	**($4,406)**	**($4,325)**	**($3,647)**	**($3,566)**	**($15,944)**	**($15,200)**	**($16,450)**
Net Margin								
Reported EPS	**($4.11)**	**($0.76)**	**($0.74)**	**($0.62)**	**($0.61)**	**($2.72)**	**($2.38)**	**($2.19)**
YOY Growth								
Basic Shares Outstanding	4,523	5,803	5,883	5,883	5,883	5,863	6,400	7,500

Source: Company Filing // Zacks Investment Research, Inc. Estimates

HISTORICAL STOCK PRICE

Vyant Bio, Inc. – Share Price Chart[41]



[41] Source: Zacks Research System

DISCLOSURES

The following disclosures relate to relationships between Zacks Small-Cap Research ("Zacks SCR"), a division of Zacks Investment Research ("ZIR"), and the issuers covered by the Zacks SCR Analysts in the Small-Cap Universe.

ANALYST DISCLOSURES

I, John Vandermosten, hereby certify that the views expressed in this research report accurately reflects my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the recommendations or views expressed in this research report. I believe the information used for the creation of this report has been obtained from sources I considered to be reliable, but I can neither guarantee nor represent the completeness or accuracy of the information herewith. Such information and the opinions expressed are subject to change without notice.

INVESTMENT BANKING AND FEES FOR SERVICES

Zacks SCR does not provide investment banking services nor has it received compensation for investment banking services from the issuers of the securities covered in this report or article.

Zacks SCR has received compensation from the issuer directly or from an investor relations consulting firm engaged by the issuer for providing non-investment banking services to this issuer and expects to receive additional compensation for such non-investment banking services provided to this issuer. The non-investment banking services provided to the issuer includes the preparation of this report, investor relations services, investment software, financial database analysis, organization of non-deal road shows, and attendance fees for conferences sponsored or co-sponsored by Zacks SCR. The fees for these services vary on a per-client basis and are subject to the number and types of services contracted.

POLICY DISCLOSURES

This report provides an objective valuation of the issuer today and expected valuations of the issuer at various future dates based on applying standard investment valuation methodologies to the revenue and EPS forecasts made by the SCR Analyst of the issuer's business.
SCR Analysts are restricted from holding or trading securities in the issuers that they cover. ZIR and Zacks SCR do not make a market in any security followed by SCR nor do they act as dealers in these securities. Each Zacks SCR Analyst has full discretion over the valuation of the issuer included in this report based on his or her own due diligence. SCR Analysts are paid based on the number of companies they cover.
SCR Analyst compensation is not, was not, nor will be, directly or indirectly, related to the specific valuations or views expressed in any report or article.

ADDITIONAL INFORMATION

Additional information is available upon request. Zacks SCR reports and articles are based on data obtained from sources that it believes to be reliable, but are not guaranteed to be accurate nor do they purport to be complete. Because of individual financial or investment objectives and/or financial circumstances, this report or article should not be construed as advice designed to meet the particular investment needs of any investor. Investing involves risk. Any opinions expressed by Zacks SCR Analysts are subject to change without notice. Reports or articles or tweets are not to be construed as an offer or solicitation of an offer to buy or sell the securities herein mentioned.