Zacks Small-Cap Research
*Sponsored – Impartial – Comprehensive*

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# Kineta, Inc. (KA: NASDAQ)

## *KA: A VISTA to a Cure*

Kineta's valuation relies on a DCF model and a 15% discount rate applied to our cash flow estimates. Additionally, we apply a success probability of 15% for KVA12123 in solid tumor cancers which recognizes regulatory and commercialization risks. The model includes contributions from the United States and rest of world.

| | |
|---|---|
| Current Price (6/16/2023) | $2.87 |
| **Valuation** | **$13.50** |

## INITIATION

Kineta is a clinical-stage, oncology-focused biotechnology company targeting innate immune checkpoints in solid tumors. It's pipeline features two assets. Lead candidate KVA12123 is a Ph1/2 anti-VISTA mAb undergoing dose escalation and expansion studies. Asset two is an anti-CD27 mAb that is expected to begin clinical trials in late 2024.

Discovery efforts have produced KVA12123 and demonstrated its specificity to VISTA (V-domain Ig Suppressor of T cell Activation). Preclinical work shows activation of the immune system and anti-tumor response to the molecule as both mono- and combination therapy.

KVA12123 is expected to complete Ph2 trials in 2025, after which pivotal Ph3 trials will begin. BLA submission is expected in 2028 and commercialization in 2029. Ex-US sales are expected one year later. Grant of Fast Track may allow the use of surrogate endpoints and open eligibility for Accelerated Approval which could advance the timeline by two years.

While VISTA is not as prominent as other immune checkpoints, research has shown anti-VISTA's ability to limit tumor growth, especially in combination with other checkpoint inhibitors targeting PD-1 or CTLA-4. While initial clinical studies are broadly focused on solid tumors, OC, CRC and NSCLC are likely end targets for KVA12123.

## SUMMARY DATA

| | |
|---|---|
| **52-Week High** | **15.54** |
| **52-Week Low** | **2.80** |
| **One-Year Return (%)** | **-73.9** |
| **Beta** | **0.6** |
| **Average Daily Volume (sh)** | **20,387** |
| **Shares Outstanding (mil)** | **9.5** |
| **Market Capitalization ($mil)** | **27.3** |
| **Short Interest Ratio (days)** | **1.8** |
| **Institutional Ownership (%)** | **3.4** |
| **Insider Ownership (%)** | **33.1** |
| **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 2023 Estimate** | **N/A** |
| **P/E using 2024 Estimate** | **N/A** |
| **Zacks Rank** | **N/A** |

| | |
|---|---|
| **Risk Level** | **Above Average** |
| **Type of Stock** | **Small-Growth** |
| **Industry** | **Med-Biomed/Gene** |

## ZACKS ESTIMATES

### Revenue

(In millions of USD)

| | Q1 (Mar) | Q2 (Jun) | Q3 (Sep) | Q4 (Dec) | Year (Dec) |
|---|---|---|---|---|---|
| 2022 | $0.4 A | | | | $2.0 A |
| 2023 | $0.3 A | $0.2 E | $0.0 E | $0.0 E | $0.4 E |
| 2024 | | | | | $0.0 E |
| 2025 | | | | | $0.0 E |

### Earnings per Share

| | Q1 | Q2 | Q3 | Q4 | Year |
|---|---|---|---|---|---|
| 2022 | -$1.07 A | | | | -$12.87 A |
| 2023 | -$0.77 A | -$0.52 E | -$0.46 E | -$0.33 E | -$1.93 E |
| 2024 | | | | | -$1.41 E |
| 2025 | | | | | -$1.35 E |

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## INITIATION

We are initiating coverage of Kineta, Inc. (NASDAQ: KA) with a target price of $13.50 per share. This value is based on our estimates for a successful development and commercialization of KVA12123 in advanced solid tumors. The candidate is the subject of a Phase I/II open-label trial. Assuming a standard duration of follow-on pivotal studies, KVA12123 is expected to be submitted to the FDA in 2028 in a biologics license application (BLA) followed by first sales in 2029. We forecast pivotal studies and commercialization to be initiated with a partner in the United States and around the world. There is a possibility of expedited treatment by the FDA and the use of the Fast Track and Accelerated Approval pathways which could advance the timeline by two years.

Kineta has demonstrated preclinical efficacy and safety for its KVA12123 anti-VISTA (anti V-domain immunoglobulin-containing Suppressor of T cell Activation) antibody and is now conducting Phase I/II clinical trials to further characterize safety and identify the proper dose for Phase II studies. Anti-VISTA is differentiated from other immunotherapies in its increased emphasis on the innate immune system and presence in myeloid-lineage cells which have a higher level of VISTA expression compared with other types of cells. VISTA is overexpressed in cancers that have relapsed from previous therapies and contributes to an immunosuppressive environment that allows tumors to grow.

Kineta has begun dosing patients in the Phase I portion of its evaluation of KVA12123 and anticipates providing an update on the initial trial outcomes by year-end. We expect further details regarding the Phase II trial along with the release. The Phase I/II study will determine the safety and efficacy of the anti-VISTA antibody both as monotherapy and in combination with Merck's pembrolizumab (Keytruda) in patients with advanced solid tumors. The four-part effort will look at both dose escalation and dose expansion in the monotherapy and combination approaches. KVA12123 has demonstrated anti-tumor activity and is highly specific to VISTA-expressing cells. Use of the antibody in preclinical work demonstrated enhanced natural killer (NK) cell activation and reversed myeloid-derived suppressor cell (MDSC) suppression of T cells.

Kineta is expected to pursue indications in solid tumors, specifically ovarian cancer (OC), colorectal cancer (CRC) and non-small cell lung cancer (NSCLC) with KVA12123. Together these three cancers affect about 266,000 people in the United States and over 4 million around the globe. We expect to see Kineta follow the data and pursue the indication that initially shows the most promise. Over time, as with other immunotherapies and checkpoint inhibitors, we anticipate KVA12123 to expand into additional indications.

OC and NSCLC have low survival rates, often less than 50% at five years and lower if the cancer has spread. This highlights the unmet need related to these tumors in particular. Furthermore, approved checkpoint inhibitors only work in a minority of patients and require effective combination therapy to achieve higher response rates.

The second candidate listed on the company's pipeline is an anti-CD27 antibody that is undergoing preclinical development for advanced solid tumors. The lead antibody for the program has been selected and its binding potency and reactivity with human CD27 has been confirmed. Efforts have shown that the candidate provides strong agonist proprieties on T cell proliferation and immune system activation. Kineta expects an investigational new drug (IND) application will be filed in 4Q:24 followed shortly after by the start of a Phase I clinical study.

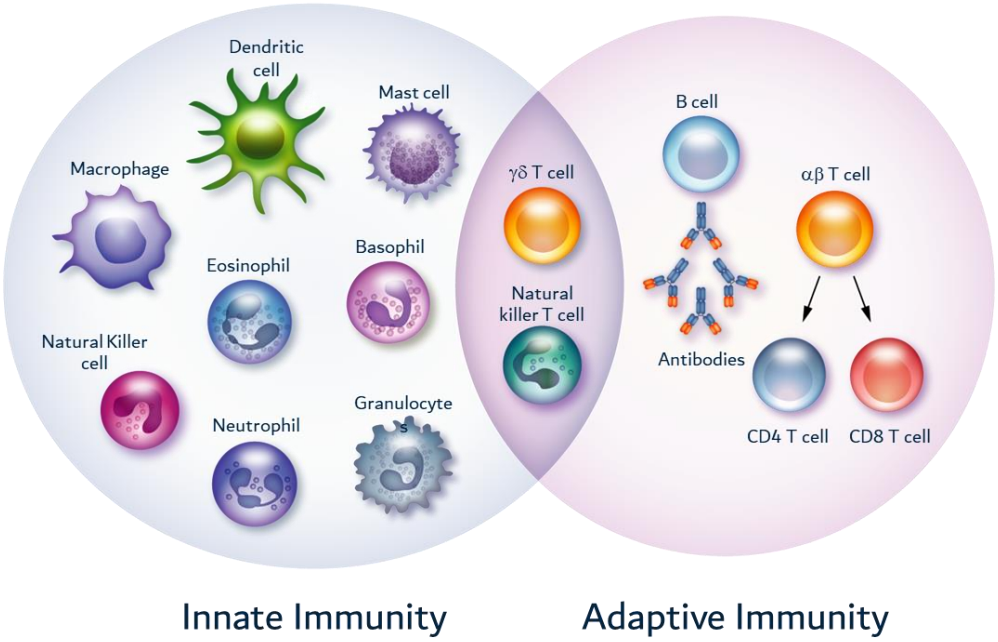
Based on the strong data generated to date, Kineta was able to raise $6 million in funding in April to build on its March 31st cash balance of $9.2 million. Another $22.5 million is expected in July as part of a private placement that will further support the company's development. Based on the expected burn rate of under $5 million per quarter, we anticipate that these funds will be sufficient to support operations into early 2025.

The Phase I trial for KVA12123 is expected to wrap up by year-end 2023 and be followed by a two-year Phase II study. If data from the Phase II are particularly strong in a specific solid tumor indication, Kineta may pursue expedited pathways to obtain earlier approval. Until this is confirmed, we assume a Phase III trial that will complete in 2027, be the subject of a BLA in 2028 and receive approval in 2029. Pricing for approved immunotherapy products is favorable and we anticipate average pricing to be obtained in the United States and in the rest of the world as detailed in our valuation section. We further expect Kineta to work with a larger partner for commercialization around the world, leveraging its in-place global distribution and sales network.

Key reasons to own Kineta shares:

- **Developing KVA12123, a Phase I/II immune checkpoint, to treat solid tumors**
  - **Addresses mechanism of cancer immune resistance**
  - **Integrates innate and adaptive immune responses**
  - **Demonstrates synergies with checkpoint inhibitors (anti-PD-1/PD-L1/CTLA-4)**
- **KVA12123 offers a favorable treatment effect in specific populations**
  - **OC, CRC and NSCLC are high VISTA expressers**
  - **Patients developing resistance to CIs are high VISTA expressers**
- **KVA12123 may augment response rates when combined with existing checkpoint inhibitors**
- **Produces favorable safety profile with no evidence of cytokine release syndrome (CRS)**
  - **Antibody design with engineered Fc region to reduce immunogenicity**
- **Offers additional monoclonal antibody (mAb) assets in early stage development**
  - **Anti-CD27 agonist**
- **Maintains global rights to intellectual property**

**Exhibit I – Innate and Adaptive Immunity[1]**




In the following sections we describe immunotherapy, immuno-oncology (IO), checkpoint inhibitors (CIs) and the related family of targets. We review the composition of the VISTA mAb and discuss the preclinical support for advancing KVA12123 into the clinic. We follow with a description of the ongoing Phase I/II trial, providing timing for expected milestones. An examination of Kineta's other pipeline candidate, an anti-CD27 mAb is followed by a discussion of Kineta's intellectual property efforts. Primary indications being pursued are expected to be ovarian cancer (OC), colorectal cancer (CRC) and non-small cell lung cancer (NSCLC). We discuss other competitors in the immuno-oncology space, including several VISTA-focused peers. The next section reviews recent financial and operational history for the company followed by an introduction to the management team and a summary of risks. Our valuation discussion details the assumptions used to determine our target price. We expect first sales in 2029 for KVA12123 after a favorable trial outcome, successful submission of a BLA and FDA approval. Our work generates a target price of $13.50 per share for Kineta, Inc.

[1] Kineta June 2023 Corporate Presentation

## Immunotherapy

### Immuno-oncology

Immuno-oncology (IO), or cancer immunotherapy, is an approach to fighting cancer that leverages the body's immune system to attack the disease. Normally, the body's immune system can eliminate cancer cells, but in some cases, these mutant cells can adapt to hide by expressing deterrent proteins on their surface among other mechanisms. When IO drugs or biologics are administered, they allow the immune system to recognize harmful cells and destroy them, in many cases with fewer, short-lived side effects compared to surgery, chemotherapy and radiotherapy. Immunotherapy is preferred because it is frequently associated with fewer adverse events, maintains its potency, works well in conjunction with other therapies and is able to better target the disease. Several classes of immunotherapy exist including therapeutic vaccines, checkpoint inhibitors, immune modulators, adoptive cell therapy (CAR-T), oncolytic viruses and antibody drug conjugates to name the most prominent examples. IO can be either active or passive. Active approaches direct the immune system to kill cancer cells by targeting tumor antigens. Passive approaches augment existing tumor responses by the use of a variety of proteins, lymphocytes and cytokines to enhance their activity.

### Checkpoint Inhibitors

Checkpoint inhibitors (CIs) have become one of the most visible immunotherapies in life sciences. Initial work in the early 1980s by industry luminary James Allison tested checkpoint inhibitors in animal models. The first immune checkpoint molecule was discovered in 1987, designated cytotoxic T-lymphocyte antigen number 4 (CTLA-4). Further work led to the start of the first trial for the drug class in 2000 with ipilimumab, a monoclonal antibody that binds and blocks the CTLA-4 receptor. This shift to immunotherapy advanced medicines based on the tumor makeup rather than the site of the disease. After a decade of clinical trials and traversing the regulatory process, ipilimumab was approved in 2011.

While the potential of checkpoint inhibitors was understood in the oncology field, it became more widely known to the general public when Jimmy Carter announced he was cancer free in 2015. The former president's metastatic melanoma was treated with the investigational drug pembrolizumab, which was a different type of checkpoint inhibitor targeting the programmed cell death protein 1 (PD-1). The monoclonal antibody (which is the form of all checkpoint inhibitors) was able to release the brakes on his immune system, thereby allowing it to attack and shrink the tumors. The medicine allowed him to return to health without the need for further treatment. This triumph put checkpoint inhibitors on the front page for not only those in the oncology field but also for the layman.

While CIs were an impressive breakthrough in immuno-oncology, the class does present shortcomings. Complete responses are frequently below 10% and most patients have no response or a partial response. Furthermore, CIs are less effective in more common cancers such as breast cancer, non-small cell lung cancer (NSCLC), prostate cancer and colorectal cancer. One of the reasons why approved therapies in the anti-PD-1, PD-L1 and CTLA-4 classes fail to stimulate clearance of the tumor is the lack of tumor-infiltrating lymphocytes (TILs) in and around the tumor. This condition is known as a cold or immunologically suppressed tumor.

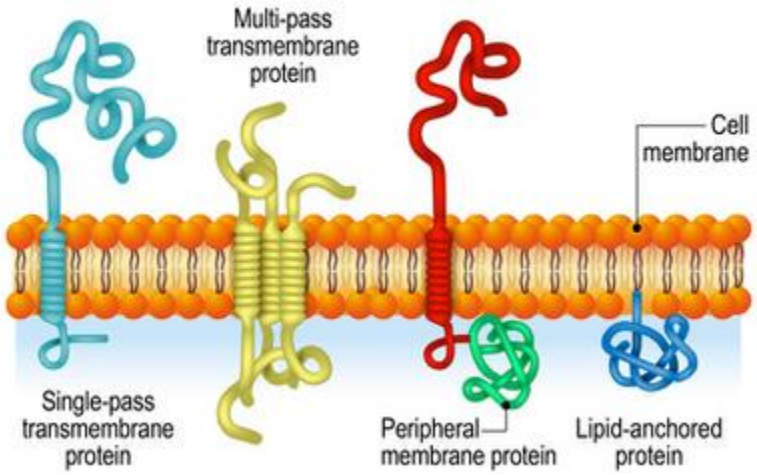
CI's remove the restraints for the immune system's fighters. However, the fighters need to infiltrate the tumor microenvironment for the immunotherapy to work. Other resistance mechanisms may also emerge, where cancer cells may upregulate other immune checkpoints or recruit immunosuppressive cells, such as regulatory T cells or myeloid-derived suppressor cells, to counteract the immune response induced by the checkpoint inhibitors. This has led researchers to identify combination therapies that can activate the immune system in the tumor environment and help overcome resistance mechanisms.

### VISTA

V-domain Ig suppressor of T-cell activation (VISTA) is a novel negative checkpoint that is homologous to PD-1/PD-L1 and suppresses T cell activation. VISTA is an immune checkpoint protein that is expressed on T cells, B cells, natural killer (NK) cells and myeloid cells. VISTA binding to T cells inhibits their activation and the production of cytokines. Under normal conditions, regulatory proteins like VISTA provide benefits to immune regulation, including immune tolerance which prevents the attack of healthy tissues and inflammation control to prevent prolonged immune activation.

VISTA is a type I transmembrane protein consisting of a single N-terminal immunoglobulin (Ig) V-domain, a stalk of approximately 30 amino acids, a transmembrane domain and a 95-amino acid cytoplasmic tail.[2] The IgV domain of VISTA is highly homologous with programmed death ligand 1 (PD-L1). VISTA acts as a ligand on antigen-presenting cells and as a receptor on tumor-infiltrating lymphocytes. A ligand is a molecule that binds to a specific receptor protein, usually on the surface of a cell while a receptor is a protein molecule that recognizes and binds to a specific ligand. Receptors are involved in transmitting signals from the extracellular environment to the interior of the cell, triggering various cellular responses. VISTA suppresses T cell-associated response for immune evasion and survival in several human cancers, such as prostate cancer, non-small cell lung cancer (NSCLC) and colorectal carcinoma. Some of the stimulatory effects of VISTA that have been reported include promotion of activation and proliferation of tumor-specific T cells, leading to improved tumor control and upregulation of autoimmune responses.[3]

**Exhibit II – Transmembrane Proteins[4]**




Unchecked, upregulated VISTA can permit cancer cells to evade immune detection and destruction which may support tumor growth and progression. The anti-VISTA, VISTA blockade or VISTA negative checkpoint regulator blocks the action of the surface protein. The approach uses a monoclonal antibody to bind to VISTA and prevent it from engaging the complementary receptor on other immune cells. This causes a cascade of events which prevents T cell suppression. Blocking VISTA allows T cells to mount an enhanced immune response against cancer cells. The checkpoint inhibitor can be used in combination with other immunotherapies such as PD-1, PD-L1 or CTLA-4 inhibitors which may produce synergistic effects.

VISTA appears more frequently in pancreatic cancer, colorectal cancer, lung cancer, mesothelioma, ovarian cancer prostate cancer and several others. It is also more highly expressed in treated patients, especially those who have relapsed after treatment with other checkpoint inhibitors. Other resources have found that VISTA is overexpressed in certain cancers including cholangiocarcinoma, glioblastoma multiforme, renal clear cell carcinoma, acute myeloid leukemia, lower-grade glioma and pancreatic adenocarcinoma compared to healthy tissue. Other cancers have a *lower* level of VISTA expression and encompass bladder cancer, invasive breast carcinoma, cervical squamous cell carcinoma, endocervical adenocarcinoma, colorectal cancer, diffuse large B cell lymphoma, kidney chromophobe, lung adenocarcinoma, lung squamous cell carcinoma, prostate cancer, melanoma, endometrial carcinoma, and uterine carcinosarcoma.

**Technology and Candidates**

While checkpoint inhibitors and other immunotherapies have improved the survival and side effect profile of cancer treatment and provided a complement and even an alternative to surgery, radiation and chemotherapy, there is still much to do. This unmet need has encouraged new candidates to emerge that seek to precisely stimulate the immune system and work in conjunction with other immunotherapies. The best-known checkpoint molecules include PD-1, PD-L1 and CTLA-4, but others have shown efficacy in tumors such as VISTA and are in early-stage clinical trials under the aegis of several sponsors.

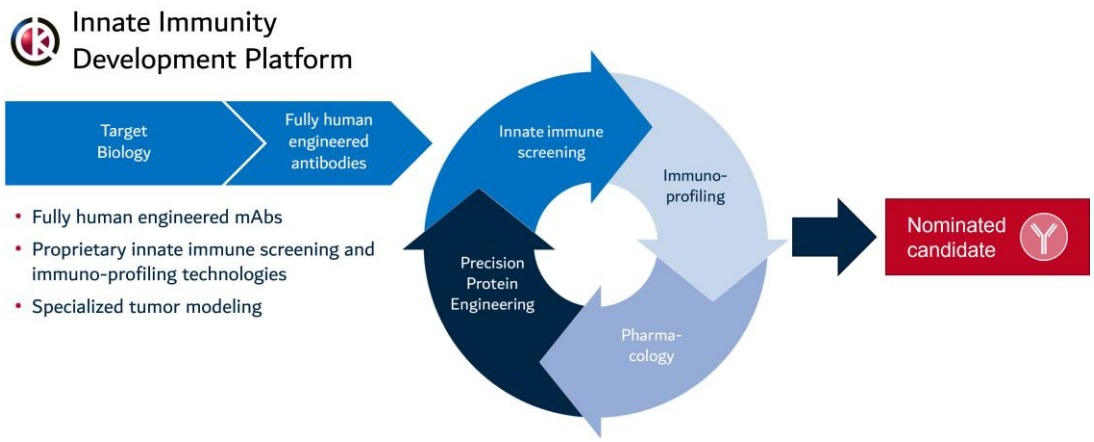
[2] Nowak, E.C., *et al*. Immunoregulatory Functions of VISTA. Immunological Reviews, March 2017.
[3] Hosseinkhani, N, *et al*. The Role of V-Domain Ig Suppressor of T Cell Activation (VISTA) in Cancer Therapy: Lessons Learned and the Road Ahead. Frontiers in Immunology, May 2021.
[4] Shutterstock Image 1362321584

When immune checkpoint inhibitors are used, they release the brakes on the immune system, allowing it to recognize, attack and eradicate cancer cells more effectively. While the most common checkpoints have shown success in several types of cancer, including melanoma, renal cell carcinoma, bladder cancer and others, the class has been less effective in pancreatic ductal adenocarcinoma, ovarian cancer, colorectal cancer and non-small cell lung cancer. Research has shown that combining anti-VISTA therapy with PD-1/PD-L1 inhibitors or CTLA-4 inhibitors can improve the anti-tumor response compared to the use of monotherapy checkpoint inhibition.

**Innate Immunity Development Platform**

Kineta has developed its Innate Immunity Development Platform (IIDP) to identify new candidates that can address cancer resistance. The primary areas of resistance arise from immuno-suppression, exhausted T cells and poor tumor immunogenicity. The company has worked closely with GigaGen, a contract research organization (CRO), to develop highly specific antibody sequences. Kineta has engineered the antibodies so they do not stimulate a systematic inflammatory response such as cytokine release syndrome (CRS). The platform helps develop the antibodies and generate data required for investigational new drug (IND) submission and clearance. The IIDP supported the development of both KVA12123 and the anti-CD27 agonist which appear in the company's pipeline.

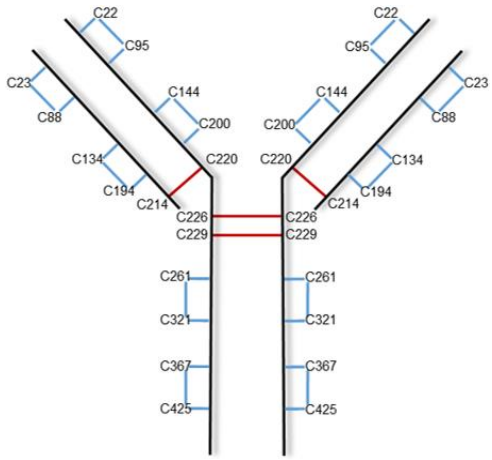
**Exhibit III –The Innate Immunity Development Platform[5]**




**KVA12123: Anti-VISTA Antibody**

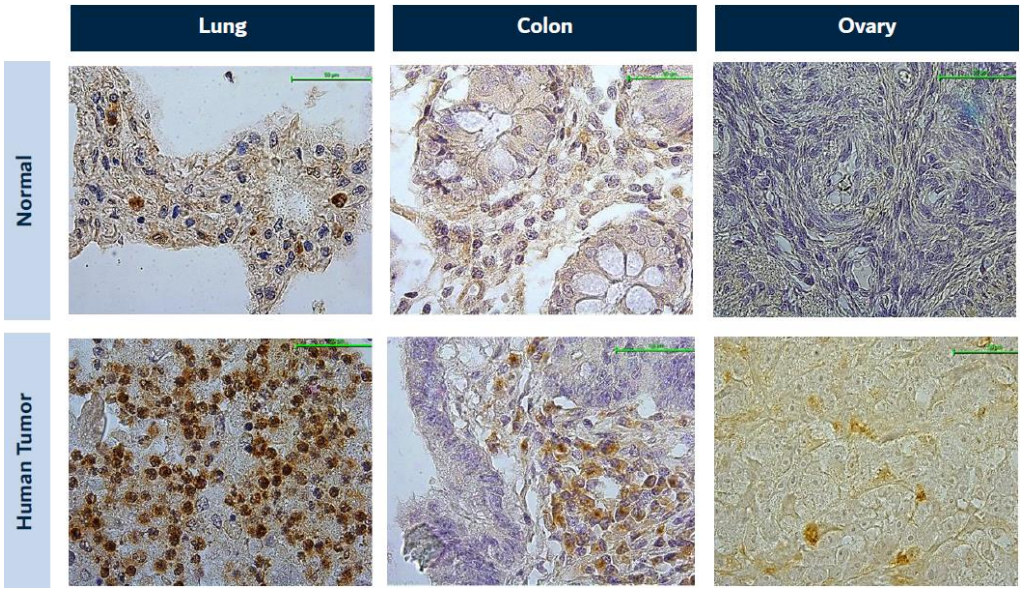
KVA12123 is a VISTA-blocking immunotherapy developed to reverse immunosuppression in the tumor microenvironment (TME). The candidate is a fully-human engineered IgG1 monoclonal antibody that was designed to bind to VISTA through a unique epitope at physiologic and acidic pH levels. The product is being developed as an intravenous infusion. Preclinical work has shown that KVA12123 may be an effective immunotherapy in a broad selection of solid tumors.

**Exhibit IV – KVA12123 Structure[6]**




[5] Kineta 2022 10-K
[6] Source: Kineta management

**Exhibit V – KVA12123 Clinical Oncology Applications in Lung, Colon and Ovary[7]**

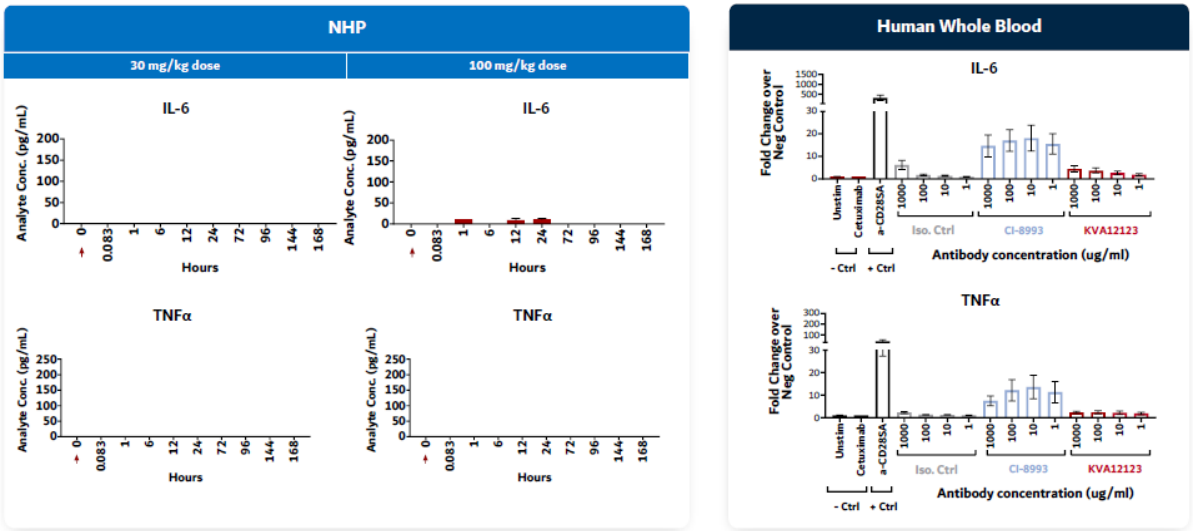



VISTA is upregulated after treatment with other CIs and is associated with poor survival.[8,9] Blocking VISTA has been shown to activate an immune response in cold tumors through both innate and adaptive mechanisms. Blocking high VISTA expression on myeloid cells can drive tumor inflammation, allowing T cell therapies to be more effective. Anti-VISTA can reduce T regs, specifically tumor-specific Foxp3 CD4 regulatory T cells, thereby increasing the effectiveness of cancer immunotherapy. It can enhance the infiltration, proliferation and effector function of tumor-reactive T cells within the tumor microenvironment (TME) and reverse the suppressive environment.[10]

*Cytokine Release Syndrome*

Cytokine release syndrome (CRS) is a systemic inflammatory response that can occur as a result of certain medical treatments, particularly immunotherapies such as CAR-T cell therapy or certain monoclonal antibody treatments. It is caused by the release of large amounts of cytokines into the bloodstream. This activates immune cells that can produce many symptoms similar to that of the flu. When severe, CRS can be life-threatening and cause organ dysfunction or failure.

**Exhibit VI – Absence of CRS-Associated Signal in Multiple Studies[11]**




[7] Kineta corporate presentation, June 2023.
[8] Kuklinski, L.F., *et al*. VISTA expression on tumor-infiltrating inflammatory cells in primary cutaneous melanoma correlates with poor disease-specific survival. Cancer Immunology, Immunotherapy. July 2018.
[9] Kakavand, H., *et al*. Negative immune checkpoint regulation by VISTA: a mechanism of acquired resistance to anti-PD-1 therapy in metastatic melanoma patients. Modern Pathology, December 2017.
[10] LeMercier, I., *et al*. VISTA regulates the development of protective anti-tumor immunity. Cancer Research, April 2014.
[11] Kineta corporate presentation, June 2023.

Kineta has designed KVA12123 to be differentiated as compared to other anti-VISTA products in development that are discussed in the Peer and Competitors section. Other companies sponsoring a VISTA program include Hummingbird, Curis, Sensei, Pierre Fabre and Pharmabcine. KVA12123 has been designed on an immunoglobulin G1 (IgG1) monoclonal antibody backbone which binds to a unique epitope on the VISTA-expressing cells. It can bind to its receptor at both physiologic and acidic pH, which is critical as binding takes place in both the tumor microenvironment and the lymphoid organs. KVA12123 was also designed to avoid CRS. Some of the features that reduce the incidence of CRS when administering KVA12123 include the use of an IgG1 backbone, presence of a mutation that changes the position of the receptor on the cell and reduced binding to Fc γ receptors involved in CRS. Kineta provided support for its assertion of sidestepping CRS with its measure of IL-6 and TNF-α in its preclinical toxicology studies as shown in the preceding exhibit.

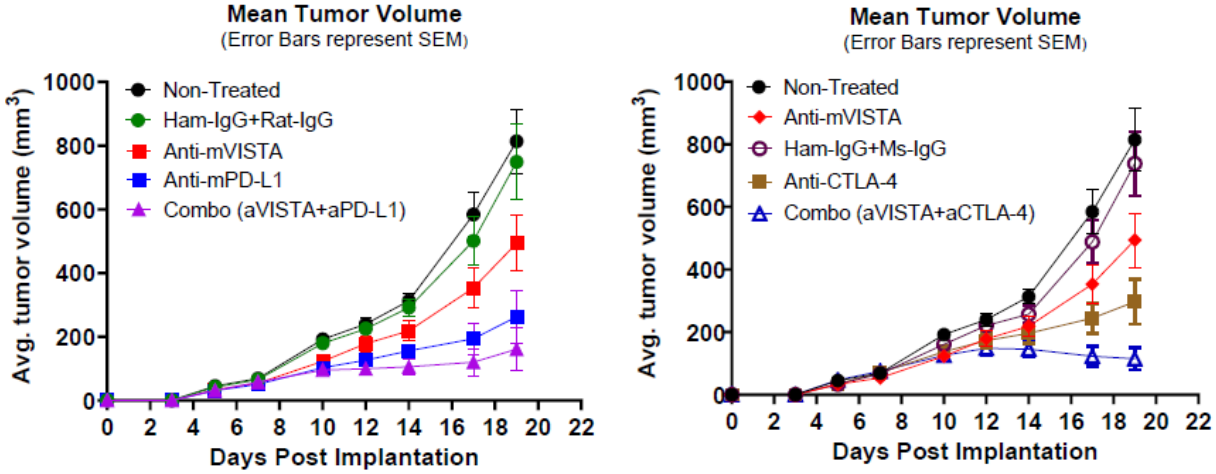
**KVA12123: Preclinical Work**

In preclinical models, KVA12123 demonstrates single-agent tumor growth inhibition in cold tumors and in combination with other checkpoint inhibitors (CIs). It is well-tolerated with no CRS-associated cytokine release (no change in IL6 and TNFα levels) or neurotoxicity. Preclinical work was memorialized in a series of posters presented at scientific conferences beginning in 2020.

*Highly Potent Fully Human anti-VISTA Antibodies*[12]
In its October 2020 American Association for Cancer Research (AACR) poster, Kineta highlighted the background of the VISTA ligand and receptor, showing that it is predominantly expressed in the myeloid lineage within peripheral blood. The goal of the study summarized in the poster was to screen for specific, fully human anti-VISTA antibodies and evaluate them. Kinetic and binding studies were performed which found that Kineta's anti-VISTA antibodies bind to human VISTA but not to mouse VISTA. The poster continued with a study of anti-VISTA tumor response both as monotherapy and in combination with other checkpoint inhibitors. In a mouse model, Kineta demonstrated a reduction in tumor growth for mouse anti-VISTA and an even greater reduction in tumor growth when mouse anti-VISTA was combined with anti-PD-L1 and anti-CTLA-4.

Conclusions from the poster found that Kineta's anti-VISTA antibodies are highly specific and can produce a strong anti-tumor response either by themselves or in combination with other checkpoint inhibitors in a mouse model. The following exhibit shows the effect on tumor volume of mouse anti-VISTA antibody with and without other checkpoint inhibitors compared to non-treated animals.

**Exhibit VII – VISTA Antagonist Antibody Induces Anti-Tumor Response**[13]




*Fully Human Anti-VISTA Antibodies Abrogate the Interaction of VISTA to Its Receptors at Different pH*[14]
This poster, which was presented at the European Society for Medical Oncology (ESMO) conference in December 2020, identified several receptors that may bind with VISTA. The poster further examined how the expression of the receptors appeared in different blood cell populations. The work presented confirmed the binding of VISTA to several receptors; however, the binding was in some cases dependent upon the microenvironment pH.

[12] Poster presentation, AACR, October 2020. Highly Potent Fully Human anti-VISTA Antibodies: A New Target Checkpoint Inhibitor against Immunosuppressive Myeloid Cells.
[13] Kineta poster presentation, October 2020, AACR.
[14] Poster presentation, ESMO, December 2020. Highly Potent Fully Human Anti-VISTA Antibodies Efficiently Abrogate the Interaction of VISTA to Its Putative Receptors at Different pH.

- VISTA binds to VISTA at a pH of 7.4 and 6.0
- VISTA binds to PSGL-1 only at a pH of 6.0
- VISTA binds to LRIG1 at a pH of 7.4
- VISTA binds to VSIG3 at a pH of 7.4
- VISTA binds to VSIG8 at a pH of 7.4

The experiments included in the poster also confirmed that Kineta's VISTA antibodies block VISTA interaction with PSGL-1, VSIG3, VSIG8 and LRIG1. Peripheral blood staining showed that VISTA is highly expressed on myeloid cells, granulocytes, natural killer and natural killer T cells. The receptor/ligand is also expressed on T reg, CD4 and CD8 cells. Of the five putative receptors included in the analysis, binding was confirmed with VISTA at neutral or acidic pH. Most importantly, Kineta's anti-VISTA candidate was able to block the binding of VISTA with these receptors.

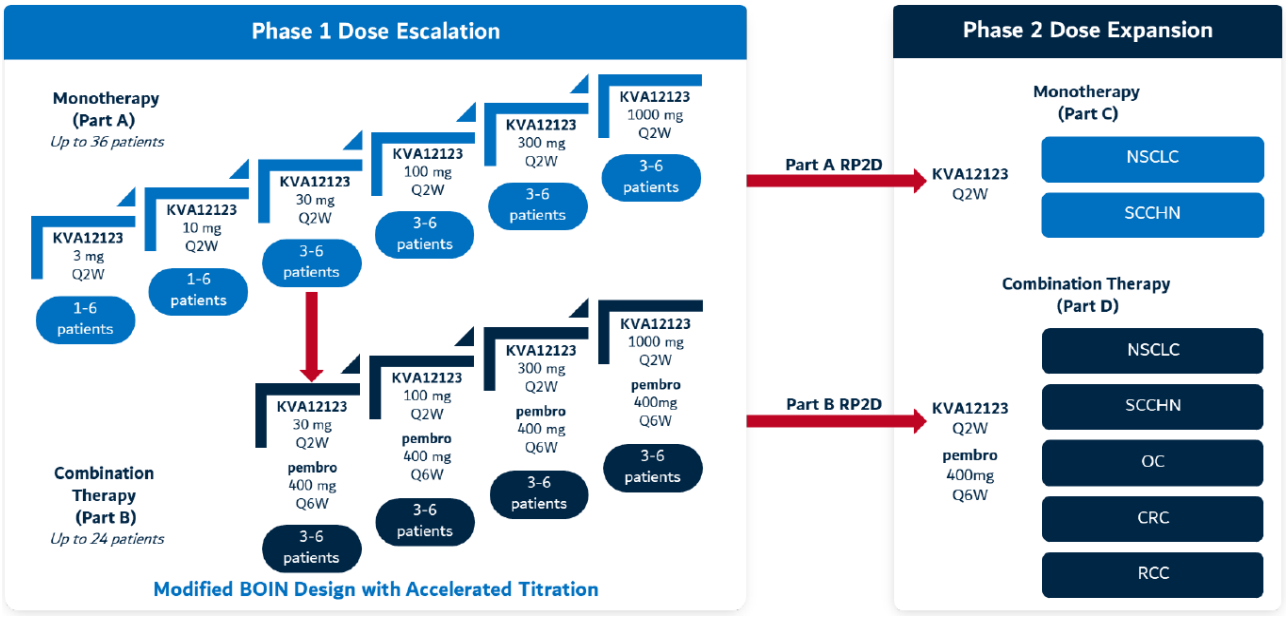
*A Fully Human anti-VISTA Antibody as a Promising Therapy Against Poorly Immunogenic Tumors*[15]
This poster, which was presented in April 2021 at the AACR scientific conference, sought to screen for effective anti-VISTA antibodies, evaluate and select an antagonist anti-VISTA antibody as a clinical candidate and characterize the lead candidate for investigational new drug (IND) submission.

Kineta's anti-VISTA candidates were shown to bind to cell surface human VISTA but not to other B7-family proteins, providing support for its specificity. The antibodies were further shown to enhance T cell, monocyte and natural killer cell activation. The anti-VISTA antibodies were able to reverse myeloid-derived suppressor cell (MDSC) suppression of T cells in PBMC culture.

Kineta developed 107 fully human anti-VISTA antibodies and analyzed them to identify a lead. The resulting candidate is highly specific, allows the activation of numerous components of the immune system and works well in combination with other checkpoint inhibitors. At the time of the poster, the lead candidate was designated KVA 12.1 and is now known as KVA12123.

*VISTA expression in patients with advanced solid tumors*[16]
At the AACR conference in April 2023, Kineta submitted another poster where the underlying work was conducted to better understand the expression level of VISTA in selected human tumor tissues. The poster also outlined the design of the Phase I/II open-label, combination, dose-escalating basket and solid tumor trial for KVA12123.

**Exhibit VIII – KVA12123 Phase I/II Clinical Trial Design**[17]




[15] Poster presentation, AACR, April 2021. A Fully Human anti-VISTA Antibody as a Promising Therapy Against Poorly Immunogenic Tumors
[16] Poster presentation, AACR, April 2023. VISTA expression in patients with advanced solid tumors: A potential biomarker in VISTA-101 clinical trial
[17] Kineta poster presentation, AACR, April 2023.

The authors used immunohistochemistry on tumor-infiltrating immune cells to identify VISTA expression. It was identified on lung, head and neck, ovary, kidney, skin, uterus and liver tumor cells. This indicates the sites where an anti-VISTA antibody may be able to block immune suppression by VISTA. Additional clinical trial details were provided, including plans to collect tissue and serum samples to identify biomarkers that may be significant for measuring KVA12123 efficacy. These samples will also aid in the effort to understand the clinical response to KVA12123 and consider VISTA expression as a potential biomarker for efficacy.

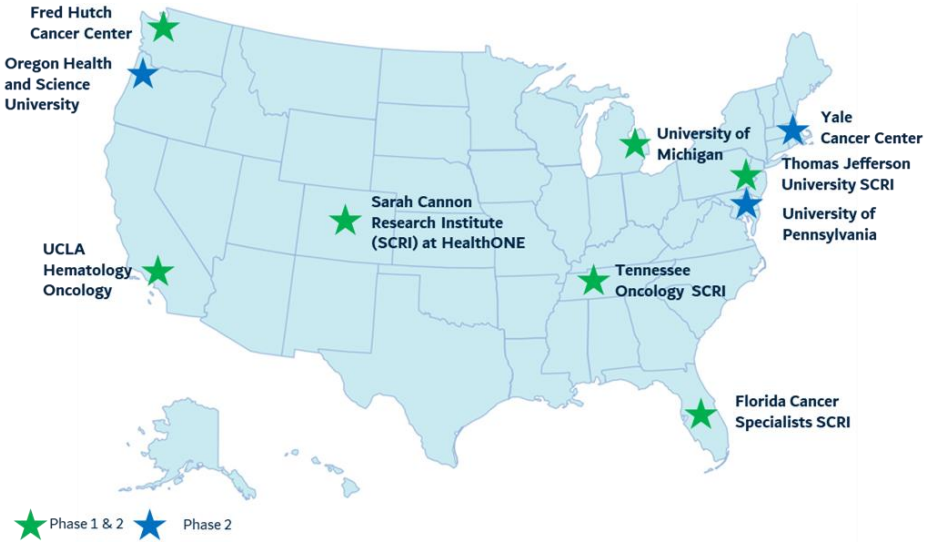
**KVA12123 Phase I/II Clinical Trial in Solid Tumors**

Following the clearance of the investigational new drug (IND) application by the FDA last November, Kineta began preparations for its Phase I/II clinical study evaluating KVA12123 as a single-agent and in combination with pembrolizumab in patients with advanced solid tumors. The initial timeline for the study called for a start to the trial before year-end 2022, which was achieved, and a report of interim results by late 2023. A summary of the trial has been posted on clinicaltrials.gov under NCT05708950.

Kineta is collaborating with Merck through the latter's contribution of pembrolizumab (Keytruda) to the alliance and seeks to determine the safety and efficacy of KVA12123 both alone and in combination with the PD-1 inhibitor. Secondary endpoints include pharmacokinetics, immunogenicity, tumor response as per Immunotherapy Response Evaluation Criteria in Solid Tumors (iRECIST) standards and objective response rate (ORR). The study will be conducted in four parts: The first two will focus on dose escalation (single-agent and in combination), and the second two will focus on dose expansion (single-agent and in combination). Up to 10 dose escalation cohorts will be evaluated in Phase I and results will determine a recommended Phase II dose. Maximum tolerated dose will also be identified. Exploratory endpoints will examine receptor occupancy, chemokine and cytokine levels in blood, immune cell populations in blood and VISTA expression in the tumor pre-and post-treatment.

Adult patients with advanced or metastatic solid tumors that have progressed or have been non-responsive to standard-of-care therapies are eligible to enroll. Up to 60 patients will be enrolled for the Phase I portion. Phase II will narrow the patient population primarily for non-small cell lung cancer (NSCLC), head and neck squamous cell carcinoma (HNSCC), ovarian cancer (OC), colorectal cancer (CRC), renal cell carcinoma (RCC) and potentially other malignancies.

**Exhibit IX – Phase I/II Clinical Research Sites[18]**




On April 12th, the company announced that the first patient had been dosed and confirmed that initial data from the Phase I portion would be provided by the end of 2023. On April 17th, Kineta provided an update on the trial noting that tissue and serum samples would be collected to isolate predictive biomarkers.

Kineta plans to pursue expedited pathways to approval, if available. Several regulatory routes allow for more rapid evaluation and approval of drug candidates. The company has identified Fast Track and Accelerated Approval as possible options. The FDA's Fast Track requires that a drug demonstrate the potential to address an unmet need for a serious condition. It provides several benefits to the sponsor including closer collaboration with the FDA, roll-

[18] Kineta corporate presentation, June 2023.

ing review of the drug's Biologic License Application (BLA), eligibility for Accelerated Approval and Priority Review among other supportive measures. Accelerated Approval is a program intended for serious conditions that qualify as unmet medical needs. The pathway allows for surrogate endpoints to be used, which may greatly accelerate the clinical trial process. As a condition of accelerated approval, the sponsor is required to conduct post-marketing studies to confirm the anticipated clinical benefit.

These programs may allow Phase II data to be used to support a BLA and shorten the length of the trial by using objective response rate (ORR), progression-free survival (PFS) or other intermediate measures to evaluate efficacy. Using these endpoints would reduce the time required to evaluate efficacy as opposed to overall survival (OS), which is considered the most stringent standard for assessing clinical benefit. If a surrogate endpoint is used for provisional approval, OS will likely be required for the primary endpoints in confirmatory trials. To maintain a conservative stance, our estimates assume that Kineta will advance into Phase III trials after Phase II and will not benefit from an expedited pathway. Upon confirmation of either Fast Track or Accelerated Approval, we will adjust the model accordingly.

Our estimates call for the ongoing Phase I study to be completely enrolled by year-end 2023, followed by the start of the Phase II in 3Q 2024. We expect the Phase II to take 24 months to finish, followed by a Phase III in 2026 which would end in late 2027. A BLA is expected to be compiled and submitted to the FDA in 2028 and, if granted, approval and commercialization would come in 2029. For other regions around the world, we anticipate a one-year delay in the submission of a drug application, suggesting that additional regions will grant approval by 2030 and beyond. We discuss the details of our estimates further in the valuation section of this report.

**Anti-CD27 Antibody**

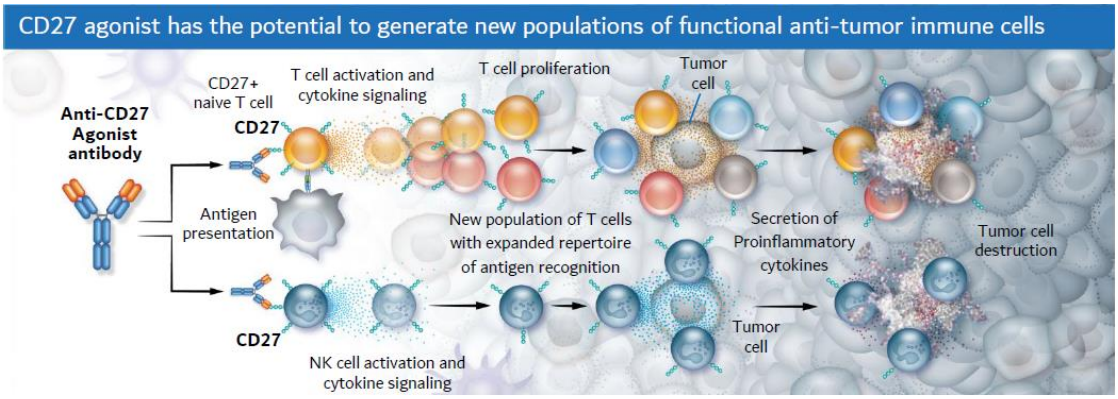
Kineta is developing a novel anti-CD27 agonist monoclonal antibody (mAb) for advanced solid tumors including RCC, OC and CRC. Kineta plans to file an IND and initiate a Phase I clinical trial of its anti-CD27 agonist mAb immunotherapy in the second half of 2024.

CD27 is a member of the tumor necrosis factor (TNF) receptor superfamily that is expressed on CD4 and CD8 T cells. It binds to its ligand CD70 which appears on T and B cells in response to antigen stimulation. The membrane glycoprotein is constitutively expressed and is required for maintenance of T cell immunity. It regulates B-cell activation and immunoglobulin synthesis. When CD27 binds to its ligand, it signals differentiation and clonal expansion in T cells supporting generation and long-term maintenance of T cell immunity.

CD27 has been a cancer drug target for some time and has led to the development of several candidates. Based on our knowledge, Celldex Therapeutics' varlilumab is the most advanced and is being investigated in Phase II studies. Other sponsors for candidates in the class include Merck, Chinook Therapeutics, Ligand Pharmaceuticals and Kineta.

Kineta's candidate is a preclinical asset that will address exhausted T cells. Preclinical work shared to date shows that it has improved survival in colorectal cancer models, and worked well in combination with anti-CD20 and anti-PD-1/L1 candidates. Kineta has identified several features of its product including its ability to activate and induce the maturation and migration of naïve T cells, stimulate the diversification of T cells, enhance natural killer cell activation and activate low-affinity antigens.

**Exhibit X – Mechanism of Action, CD27 Agonist[19]**

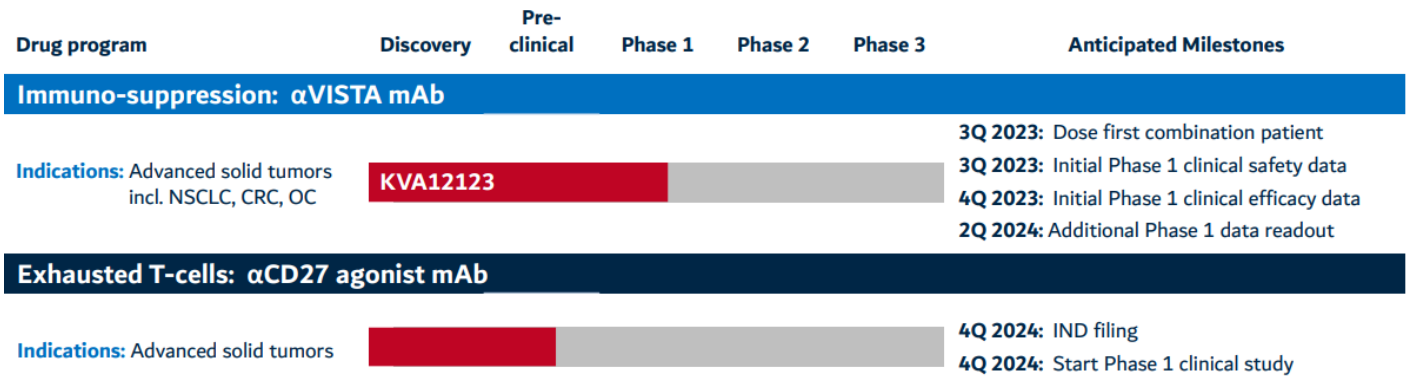



[19] Kineta Corporate Presentation, June 2023.

**Kineta Pipeline**

Kineta features two assets in its pipeline, its Phase I/II anti-VISTA KVA12123 and preclinical stage anti-CD27 agonist. Patients have already been dosed for KVA12123 Phase I dose-ranging study and results are expected before the end of 2023. The anti-CD27 asset, which has not yet been named, is in the process of developing IND-enabling data with a target of IND submission in 4Q:24, followed shortly after by the start of a Phase I study.

**Exhibit XI – Kineta's Immuno-Oncology Pipeline[20]**




**Intellectual Property**

Kineta has filed for intellectual property protection in countries that account for 90% of the revenue generated in the global pharmaceutical market, which includes the US, EU, Japan, Korea, China, India, Singapore, Switzerland, Russia, Canada and Mexico. Kineta is seeking patents that pertain to composition of matter, methods of manufacturing, sequences and structure, indications and other details specific to KVA12123 and its uses.

As a biologic, additional protections are also available to KVA12123, including a period of exclusivity following approval. In the United States, 12 years of exclusivity is available for biologic drugs. The period of exclusivity in the European Union for a biologic is 10 years. Patent term extensions are another tool that Kineta may use and can provide an extension of the patent protection equal to the time a drug is under review by the FDA. However, the extension cannot extend the patent term beyond a total of 14 years from the date the product is approved.

Kineta is applying for a worldwide patent under the Patent Cooperation Treaty (PCT) for Anti-VISTA Antibodies and uses Thereof. The PCT is an international treaty that allows inventors to file a single patent application that can be used to obtain patent protection in multiple countries. The PCT application is assigned the worldwide number WO2022178203A1. The patent application seeks to protect antibodies to V-domain Ig-containing Suppressor of T cell Activation (VISTA) and the compositions of the antibodies. Also provided in the application are methods of using antibodies that specifically bind to VISTA to treat diseases, particularly cancer.

[20] Kineta Corporate Presentation, June 2023.

## Primary Indications

### Ovarian Cancer (OC)

Ovarian Cancer (OC) begins in the female reproductive organ and is the eighth most common cancer in women. The incidence rate of OC has declined since 1990, with the change attributed to increased use of oral contraceptives and a reduction in use of menopausal hormone therapy over the last 20 years. There are several mutations associated with higher rates of OC and a correlation exists with breast cancer, endometriosis and pelvic inflammatory disease. There are several types of OC including epithelial, germ cell, stromal and small cell carcinoma. Epithelial OC is the most common type, comprising 90% of the total. Germ cell and small cell carcinoma are less common in the ovary.

*OC Incidence & Prevalence*
Ovarian cancer is the fifth most common cancer in the United States and is responsible for more deaths than any other type of reproductive system cancer. Half of those diagnosed with OC are over the age of 63 and the disease is more common in white women than black women. According to the American Cancer Society Facts and Figures, about 19,700 women in the United States will be diagnosed with OC in 2023.

In Europe, OC incidence averaged 17.1 per 100,000 in 2018,[21] which, based on today's population is about 128,000 new cases per year. Internationally, OC is the seventh leading cancer diagnosis with about 300,000 diagnosed around the globe in 2021.[22] The World Cancer Research Fund International estimates 314,000 OC cases around the world with an age-adjusted standardized rate of 6.6 per 100,000.

*Symptoms & Diagnosis*
Symptoms for OC are frequently vague in the early stages making detection difficult. The most common are bloating, pelvic or abdominal pain, difficulty in eating and feeling full after small meals, urinary symptoms related to urgency or frequency of urination. Other symptoms may include fatigue, upset stomach, back pain, pain during sex, constipation, period changes and vaginal bleeding.

Diagnosis of ovarian cancer frequently begins when a patient notices the symptoms. A review of medical history and a pelvic exam are conducted and a biopsy is taken. A medical team will review the results and finalize a diagnosis. Blood tests may be taken to identify the presence of a marker called CA-125, which is elevated in patients with OC.

Diagnostic tests may be performed which can include a transvaginal ultrasound or a computed tomography (CT) scan. Genetic testing may also be conducted to identify gene mutations associated with OC such as the BRCA1, BRCA2 and Lynch syndrome genes.

*Current Standard of Care*
Treatment of OC is highly dependent on the type and stage of the disease and patient characteristics. Surgery is frequently appropriate when the cancer has not spread. A hysterectomy may be performed or a bilateral salpingo-oophorectomy, which removes the fallopian tubes and the ovaries. Chemotherapy is also commonly used and includes platinum-based agents combined with a taxane. Targeted therapies are another important approach, used in recurrent or advanced cases such as the poly-ADP ribose polymerase (PARP) inhibitor class. In some situations, radiation therapy may also be appropriate. Some of the targeted immunotherapies that are approved for OC include:

- Bevacizumab (Avastin) targets the VEGF/VEGFR pathway and inhibits tumor blood vessel growth. It is approved for patients with newly diagnosed and relapsed ovarian cancer;
- Dostarlimab (Jemperli) is a checkpoint inhibitor that targets the PD-1/PD-L1 pathway. It is approved for subsets of patients with advanced ovarian cancer that has DNA mismatch repair deficiency (dMMR);
- Pembrolizumab (Keytruda) is a checkpoint inhibitor that also targets the PD-1/PD-L1 pathway. It is approved for subsets of patients with advanced ovarian cancer that has high microsatellite instability (MSI-H), DNA mismatch repair deficiency (dMMR), or high tumor mutational burden (TMB-H).

[21] Ovarian Cancer Statistics, European Federation of Pharmaceutical Industries and Associations.
[22] Ovarian Cancer Landscape in Asia-Pacific, 2012. Novotech.

Cancer can occur as a result of genetic mutations. These mutations can occur spontaneously, through natural errors in cellular management of genetic material, be inherited, or be driven by exposure to carcinogens. When these mutations occur in key genes, such as those responsible for regulating cell growth or angiogenesis, tumors can form and grow in an uncontrolled manner. While these mutations sometimes occur, most often the body is effective in eliminating them. Only those cells with a key combination of mutations that program for growth and evasion of immune response can develop in the body. Tumors may either be benign or malignant. As malignant tumors progress to late stage, they colonize surrounding tissues and can even metastasize if they invade lymph nodes or blood vessels.

Immunotherapy for OC has a low success rate when used as a single-agent. According to a 2021 review article published in the journal Cancer, the overall response rate (ORR) was 9%.[23] This rate increased materially when combination therapies were used, with the ORR rising to 25%.

**Colorectal Cancer (CRC)**

Colorectal cancer or CRC will affect just over 4% of Americans over their lifetime and is characterized by uncontrollable growth of abnormal cells in the colon or rectum. It is also referred to as bowel cancer. CRC frequently begins as a polyp that develops in the mucosal layer of the colon or rectum. If the polyp progresses to cancer, it can then invade nearby tissues such as blood or lymph vessels and metastasize.

There are several types of CRC, including adenocarcinoma, carcinoids, familial and gastrointestinal stromal tumors (GIST). Colon cancer can also be traced to genetic mutations and disease, such as Turcot syndrome. Rectal cancer is another category of CRC that has unique characteristics due to different cell type and location.

*CRC Incidence & Prevalence*
According to the American Cancer Society, 2023 estimated new cases of CRC in the United States are approximately 153,000 with a slightly higher prevalence in men. It is the fourth most common cancer after breast, lung and prostate cancer. In Europe, CRC incidence is approximately 520,000 in 2020[24] and 1.93 million cases[25] globally. The incidence and mortality rate for CRC has declined over time as increased awareness and screening programs have been implemented. Colonoscopies and stool-based tests have helped with preventative action such as polyp removal and detecting the disease when it is easier to treat.

*Symptoms & Diagnosis*
The symptoms of CRC may initially be vague and include fatigue and stomach pain. As the disease progresses, patients notice cramping or burning stomach pain, dark or bloody stool, decreased appetite or weight loss, fatigue and weakness, irregular bowel movements, such as diarrhea, constipation, or narrow stool, yellowing of the skin and eyes (jaundice), rectal bleeding and vomiting. Other indications may include a feeling of being full very quickly when eating and weakness and pain in the abdominal area.

Diagnosis of CRC can come from screening tests which include a digital rectal exam, visual exam using sigmoidoscopy or colonoscopy, imaging using a computed tomography (CT) scan or X-ray with a barium enema. A biopsy may also be taken to be analyzed in the lab and genetic tests may be conducted to identify genes that may be associated with emergence of the disease.

*Current Standard of Care*
The standard-of-care for colorectal cancer (CRC) depends on various factors, including the stage of cancer, the location within the colon or rectum, the patient's overall health and tumor profile. Surgery is often the primary treatment for localized CRC. It involves removing the tumor along with nearby lymph nodes. The extent of surgery can vary depending on the stage and location of the cancer. In some cases, the diseased segment of the large intestine is removed and the healthy portions are rejoined. According to research material from Cedars Sinai, surgery can cure 70% of patients. The hospital further finds that patients with CRC limited to the mucous lining of the colon have a better chance of survival as compared to those where the cancer has spread to the lymph nodes.

Chemotherapy is commonly used in the adjuvant setting after surgery to eliminate any remaining cancer cells and reduce the risk of recurrence. It may also be used in advanced or metastatic CRC to control the growth and spread of the cancer. Radiation therapy may be used in combination with surgery or chemotherapy, particularly for rectal

[23] Goetz, M. T., & Ross, J. S. (2021). Immunotherapy for ovarian cancer: Current status and future directions. Cancer, 127(15), 3238-3252.
[24] Dyba T, Randi G, Bray F, et al. The European cancer burden in 2020: incidence and mortality estimates for 40 countries and 25 major cancers. Eur J Cancer 2021;157:308–47. 10.1016/j.ejca.2021.07.039
[25] World Cancer Research Fund International, Colorectal Cancer Statistics.

cancer. This approach may shrink the tumor before surgery or eliminate any remaining cancer cells after surgery. Targeted therapy drugs, including epidermal growth factor receptor (EGFR) inhibitors and vascular endothelial growth factor (VEGF) inhibitors among other inhibitory molecules specifically target receptors or pathways involved in cancer growth. These treatments are often used in combination with chemotherapy, particularly for advanced CRC with specific genetic mutations. Immunotherapy drugs, such as immune checkpoint inhibitors, help activate the patient's immune system to recognize and attack cancer cells. While immunotherapy has been less effective in CRC compared with other cancer types, its use in CRC is appropriate in specific cases.

Pembrolizumab (Keytruda) and nivolumab (Opdivo), both PD-1 inhibitors, are the two immune checkpoint inhibitors that have been most effective in treating colorectal cancer. They have been approved by the FDA for patients with a subtype of metastatic colorectal cancer called microsatellite instability-high disease. Ipilimumab (Yervoy) is another drug that boosts the immune response for CRC. It blocks another checkpoint protein called CTLA-4. Ipilimumab can be used along with nivolumab to treat colorectal cancer, but it is not used alone. It is given as an intravenous (IV) infusion, usually once every 3 weeks for 4 treatments.

Immunotherapy for CRC provides relatively favorable success when used as monotherapy, generating an overall response rate (ORR) of 36%. When combined with other agents such as chemotherapy or targeted therapy, the ORR rose to 50%.[26]

**Non-Small Cell Lung Cancer (NSCLC)**

Non-Small Cell Lung Cancer, also known as NSCLC, is the most common type of lung cancer, accounting for approximately 85% of all lung cancer cases. NSCLC is characterized by the uncontrolled growth of abnormal cells in the tissues of the lung. NSCLC tends to grow and spread more slowly whereas its counterpart, small cell lung cancer (SCLC) is aggressive and metastasizes rapidly.

There are different subtypes of NSCLC, including adenocarcinoma, squamous cell carcinoma and large cell carcinoma. Adenocarcinoma is the most common subtype and typically originates in the outer parts of the lung. Squamous cell carcinoma develops in the lining of the bronchial tubes and is often linked to smoking. Large cell carcinoma is a less common subtype and can appear in any part of the lung.

The treatment options for NSCLC depend on various factors, including the stage of cancer, the subtype, and the overall health of the patient. Common treatment approaches include surgery, radiation therapy, chemotherapy, targeted therapy and immunotherapy.

*NSCLC Incidence & Prevalence*
Lung cancer is a leading cause of cancer death worldwide. In the US, lung cancer ranks second only after prostate and breast cancer in frequency and leads all other cancers in mortality.[27] NSCLC is the most common type of lung cancer, accounting for nine out of every 10 cases.[28] Of the total NSCLC cases, adenocarcinoma is the most common type, accounting for 40% of NSCLC occurrences. Though prevalence of lung cancer has declined with the decrease in smoking, there exists a subset of the lung cancer population that has never smoked, and NSCLC in never-smokers is metabolically distinct compared to smoking-related NSCLC

According to the American Cancer Society 2023 statistics there are expected to be 238,340 cases of lung and bronchus cancer in the United States. 81%, or ~193,000 cases, are expected to be NSCLC. Applying the 81% proportion to Europe, annually there would be approximately 258,000 new cases in Europe[29] and 1.79 million cases around the globe.[30]

*Symptoms & Diagnosis*
NSCLC typically presents in advanced stages; asymptomatic diagnosis can occur via routine chest x-ray. Advanced NSCLC may cause symptoms such as cough, shortness of breath, joint or bone pain, wheezing, hemoptysis, chest pain, weight loss, hoarseness and fatigue.[31] If the tumor metastasizes, other symptoms will result based

[26] Khaleghi, M., & Shaw, A. (2021). Immunotherapy for non-small cell lung cancer: Current status and future directions. Nature Reviews Clinical Oncology, 18(1), 1-20.
[27] ACS Cancer Facts and Figures 2020
[28] https://www.cancercenter.com/cancer-types/lung-cancer/types
[29] Source: ECIS – European Cancer Information System
[30] Source: cancer.net, Lung Cancer - Non-Small Cell: Statistics
[31] https://www.myamericannurse.com/wp-content/uploads/2016/12/ant2-CE-Lung-Cancer-116a.pdf

on the location. Paraneoplastic syndrome[32] can also occur, resulting in hypercalcemia, confusion, excessive thirst or urination, fatigue, seizures, coma and abnormal antidiuretic hormone secretion.

Diagnosis of NSCLC includes bone scan, imaging tests such as magnetic resonance imaging (MRI), computed tomography (CT) scan and positron emission tomography (PET) scan, analysis of sputum for cancer cell content, and biopsy of the lung.[33]

*Current Standard of Care*

Treatment of NSCLC depends on cancer stage and degree of metastasis. If the tumor remains localized, surgery with (neo) adjuvant chemo- or radiation therapy is recommended. If the tumor has metastasized, chemotherapy, targeted therapy or immunotherapy is used to control the condition. Pembrolizumab can be used as a first-line treatment in cancer cells with 50% or greater programmed cell death ligand 1 (PD-L1) expression. Patients that do not express sufficient levels of checkpoints are prescribed cisplatin or carboplatin in combination with pemetrexed or a taxane, such as paclitaxel or docetaxel. Bevacizumab can also be used, although it is contraindicated in patients with a concern of thrombolysis, hemoptysis, or brain metastasis.[34] Immunotherapy for NSCLC offers a modest success rate when used as a single-agent. A review article found that overall response rate (ORR) for single-agent immunotherapy averaged 22% in 15 studies.[35] This rate increased to 35% when combination approaches were used.

[32] Paraneoplastic syndromes are a group of rare disorders that are triggered by an abnormal immune system response to a cancerous tumor known as a neoplasm. Paraneoplastic syndromes are thought to occur when cancer-fighting antibodies or white blood cells (known as T cells) mistakenly attack normal cells in the nervous system. These disorders typically affect middle-aged to older people and are most common in individuals with lung, ovarian, lymphatic, or breast cancer. Source: NIH, National Institute of Neurological Disorders and Stroke.

[33] https://www.healthline.com/health/lung-cancer-non-small-cell#diagnosis

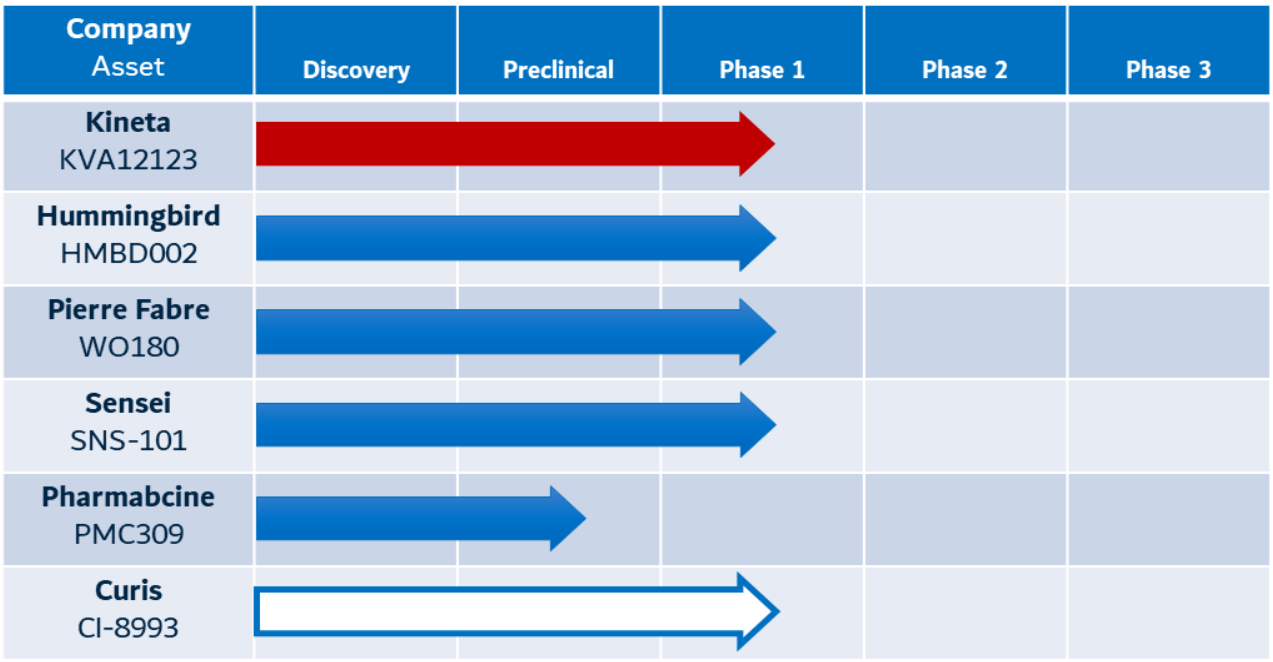
[34] https://www.myamericannurse.com/wp-content/uploads/2016/12/ant2-CE-Lung-Cancer-116a.pdf

[35] Khaleghi, M., & Shaw, A. (2021). Immunotherapy for non-small cell lung cancer: Current status and future directions. Nature Reviews Clinical Oncology, 18(1), 1-20.

## Peers and Competitors

While VISTA has not achieved the name recognition of the best-known checkpoint protein receptors such as PD-1, PD-L1 and CTLA-4, there has been a substantial amount of work conducted to understand its implications. We have identified at least ten different programs advancing anti-VISTA programs ranging from preclinical to clinical stage from a variety of sponsors in the small, mid and large market capitalization ranges. Five companies are evaluating their anti-VISTA antibody drugs in Phase I clinical trials including Kineta, Hummingbird Biosciences, Pierre Fabre and Sensei. Sensei dosed its first patient on June 1, 2023. VISTA has also been used in multiple clinical trials as a biomarker of disease status.

**Exhibit XII – Peers Pursuing Anti-VISTA Programs[36]**




In our summary of peers and competitors, we identify the primary immuno-oncology sponsors and focus on those with checkpoint inhibitor programs. We identified several with active anti-VISTA programs. Many of the checkpoint programs are being evaluated in combination studies, as the synergies between various approaches is being recognized.

VISTA expression is generally associated with worse outcomes in cancer or with progression. It also can increase after anti-PD-1 or anti-CTLA-4 treatment and may be associated with resistance to these immune checkpoint therapies. This strongly suggests that anti-VISTA therapy may be a beneficial complement to checkpoint therapy and increase effectiveness in combination.

Some of the more popular combination approaches that are being used in conjunction with checkpoint inhibitors include chemotherapy, kinase inhibitors, antiangiogenic agents, other checkpoint inhibitors, B-Raf inhibitors and Poly (ADP-ribose) polymerase (PARP) inhibitors among others. These combinations can provide synergistic effects, such as attracting immune cells to the tumor, overcoming resistance and expanding the range of tumors that will respond among other benefits.

[36] Kineta management

**Exhibit XIII – Peers and Competitors[37]**

| Ticker | Company | Price | MktCap (MM) | EV (MM) | Therapeutic Area |
|---|---|---|---|---|---|
| LLY | Eli Lilly | $447.71 | $424,999 | $440,210 | PD-1 Tyvyt |
| MRK | Merck & Co. | $109.32 | $277,392 | $295,079 | Keytruda. TIGIT (MK-7684) & LAG-3 (MK-4280) in development |
| RHHBY | Roche | $39.00 | $266,370 | $278,551 | Broad oncology portfolio: PD-L1 Tecentriq |
| ABBV | AbbVie | $138.64 | $244,601 | $297,171 | Oncology: hematologic malignancies, broad portfolio |
| AZN | AstraZeneca | $75.22 | $233,162 | $253,576 | Imfinzi, PD-L2, Imjudo CTLA-4 |
| PFE | Pfizer | $40.06 | $226,151 | $237,883 | PD-L1 Bavencio, PD-1 sasanlimab |
| NVS | Novartis | $101.83 | $215,839 | $223,975 | Broad oncology portfolio |
| BMY | Bristol-Myers Squibb | $66.16 | $138,992 | $164,801 | Opdivo, Yervoy. Relatlimab, lirilumab in dev. |
| AMGN | Amgen | $229.66 | $122,713 | $151,913 | VISTA asset through acq of "5' Tx"; no evidence pursuing |
| GILD | Gilead Sciences | $78.86 | $98,366 | $115,450 | Checkpoints: MB272, partnership w/ Arcus anti-TIGIT & PD-L1 |
| REGN | Regeneron | $783.05 | $85,607 | $79,349 | PD-1 Libtayo, LAG-3 fianlimab, bispecifics |
| GSK | GlaxoSmithKline | $35.15 | $71,969 | $83,564 | PD-1 Jemperli dMMR endometrial cancer |
| BGNE | BeiGene | $200.21 | $19,193 | $15,567 | PD-1 tilelizumab (China) hepatocellular carcinoma |
| INCY | Incyte Corp | $63.23 | $14,106 | $11,023 | PD-1 retifanlimab & other PD-1 & PD-L1, TIM-3, LAG-3 |
| BEAM | Beam Tx | $33.69 | $2,568 | $1,508 | Precision medicine; oncology & other |
| REPL | Replimune Group | $23.85 | $1,378 | $847 | Oncolytic I-O, encodes checkpoint & expresses costimulatory factors |
| ALLO | Allogene Tx | $4.85 | $707 | $236 | Oncology: CAR-T, liquid & solid tumors |
| BCYC | Bicycle Tx | $27.24 | $818 | $555 | Bicyclic toxin conjugate |
| AGEN | Agenus | $1.77 | $618 | $441 | Checkpoint portfolio: PD-1, CTLA-4, TIM-3, LAG-3, TIGIT |
| CGEM | Cullinan Oncology | $13.05 | $514 | $123 | CLN081 small molecule in NSCLC w/ exon 20 insertion mutations |
| FATE | Fate Therapeutics | $5.58 | $549 | $140 | Multiple targets (CD19/BCMA/HER2) in 5 oncology indications |
| MGNX | MacroGenics | $6.12 | $378 | $137 | PD-1, CTLA-4, LAG-3, HER2, ADC, bispecifics, |
| ALXO | ALX Oncology | $9.43 | $385 | $167 | Checkpoint: CD47 - evorpacept |
| GRCL | Gracell Biotech | $4.91 | $332 | $153 | CAR-T cell therapies |
| IPHA | Innate Pharma | $3.48 | $280 | $215 | Checkpoint: NKG2A target with monalizumab |
| GRTS | Gritstone Bio | $2.19 | $195 | $76 | I-O, cancer vaccines |
| BCAB | BioAtla | $3.78 | $180 | ($13) | Conditionally active biologics: ADCs |
| TCRT | Alaunos Tx | $0.53 | $126 | $89 | TCR-T cell therapy (KRAS, TP53, EGFR) |
| ATOS | Atossa Tx | $0.87 | $110 | $7 | Hormone receptor breast cancer therapy |
| NKTR | Nektar Tx | $0.57 | $108 | ($349) | IL-15 receptor agonists in dev. for liquid and solid tumors |
| ONCY | Oncolytics Biotech | $1.93 | $125 | $103 | Oncolytic virus for BC in combo with IO & targeted therapies |
| KRON | Kronos Bio | $1.64 | $95 | ($132) | I-O for solid & liquid tumors |
| CRIS | Curis | $0.82 | $79 | $7 | CI-8993 for VISTA expressing cancers & other checkpoints |
| SNSE | Sensei Bio | $1.34 | $36 | ($59) | SNS-101: VISTA for solid tumors. Also VSIG4 & CD39 targets |
| MRKR | Marker Tx | $3.14 | $28 | $21 | I-O: multi-tumor antigen approach |
| APGN | Apexigen | $0.49 | $12 | ($1) | Discovery stage VISTA - no evidence pursuing |
| 1801.HK | Innovent Biologics | HK$35.60 | HK$54,625 | HK$49,101 | PD-1 Tyvyt w/ 4 indications approved in China, LAG-3, TIGIT, CTLA-4 |
| 208340.KQ | PharmAbcine | ₩3,580 | ¥24,605 | | VISTA: PMC309. Also anti-angiogenesis VEGF(R2) & TIE2 |
| 600276.SS | Jiangsu Hengrui | ¥46.88 | ¥299,048 | ¥283,160 | PD-1 (camrelizumab), PD-L1 (adebrelimab) |
| RGBP | Regen BioPharma | $1.89 | $6 | $7 | Modulation of checkpoint protein NR2F6. |
| pvt | Hummingbird Bio | | | | Precision oncology, HMBD002-VISTA w/ Keytruda Ph1 |
| pvt | ImmuNext | | | | VISTA collaboration with Curis |
| pvt | Pierre Fabre Labs | | | | anti-VISTA W0180, K01401 |
| KA | Kineta, Inc. | $2.87 | $27.24 | $18.83 | Developing anti-VISTA candidate in Ph1/2 |

[37] Compiled by Zacks' analysts as of June 16, 2023

## Financial & Operational Results

**Milestones**

- CDMO partnership with Samsung Biologics for anti-VISTA antibody development – July 2021
- Pre-IND meeting with FDA for anti-VISTA candidate – July 2021
- Reverse merger with Yumanity Therapeutics announced – June 2022
- Appointment of Thierry Guillaudeux, PhD as Chief Scientific Officer – June 2022
- Appointment of Keith Baker as Chief Financial Officer – October 2022
- Collaboration with Merck to evaluate KVA12123 with Keytruda – October 2022
- IND clearance for KVA12123 for Phase I/II trial in solid tumors – November 2022
- Reverse merger with Yumanity Therapeutics completed – December 2022
- VISTA as I-O target KOL event – March 2023
- First patient dosed in KVA12123 Phase I/II study – April 2023
- $6 million direct offering priced – April 2023
- Addition to Russell Microcap Index – June 26, 2023
- Initial report of clinical safety data – 3Q 2023
- Initial report of clinical efficacy data – 4Q 2023
- IND filing for anti-CD27 agonist – 4Q:24

**1Q:23 Financial Results**

Kineta reported 1Q:23 results in a press release and Form 10-Q filing with the SEC. For the first quarter of 2023 ending March 31, 2023 and versus the prior year's first quarter, revenues fell 35% and consisted entirely of collaboration revenues of $281,000. Loss for the first quarter totaled ($6.5) million or ($0.77) per share. Operational expenses rose 20% as decreases in research and development (R&D) expenses were more than offset by an increase in general and administrative (G&A) expenses.

- Revenues totaled $281,000 and were related to a previous collaboration with Merck rather than the ongoing contribution to the Phase I/II combination trial with Keytruda. This compares to prior year amounts of $433,000 which consisted of licensing and grant revenues.
- Research and development expenses totaled $2.8 million, down 29% from $4.0 million attributable to a decrease in activity related to KVA12123;
- General & Administrative expenses were $3.9 million, up 144% from $1.6 million with the increase arising from the issuance of stock-based compensation and increased public company expenses such as professional service fees and insurance;
- Net loss was ($6.5) million vs. ($5.0) million or ($0.77) and ($1.07) per share, respectively.

As of March 31, 2023, cash totaled $9.2 million. This amount compares to the $13.1 million balance in cash held at the end of 2022. Cash used in operations was ($4.9) million versus ($5.4) million for 1Q:23 and 1Q:22 respectively. Kineta's cash as of March 31, 2023, together with the $5.5 million net proceeds received in April 2023 from the registered direct offering plus the committed proceeds of $22.5 million related to the second closing of the private placement, is expected to fund operating expenses and capital expenditure requirements into early 2025.

## Management and Board of Director Profiles

**Shawn Iadonato, Ph.D., Chief Executive Officer and Board Member**

Dr. Shawn Iadonato serves as Kineta's CEO. He has nearly twenty years of experience leading startup biotech companies and is a co-founder of Kineta and initially served as Chief Scientific Officer. Under his leadership at Kineta, the company established a proprietary screening platform for identifying innate immune modulators and has advanced novel drug programs in immuno-oncology, neuroscience and biodefense. The company also established strategic partnerships with Pfizer, Genentech and the Wellcome Trust.

Prior to founding Kineta, Dr. Iadonato co-founded and served as CSO of Illumigen Biosciences. At Illumigen, he pioneered a patented drug discovery platform that relied upon recruitment and screening of healthy populations to identify shared "wellness" genes. Dr. Iadonato also led the successful discovery and preclinical development of Illumigen's anti-hepatitis C drug, which ultimately led to the sale of the company to Cubist Pharmaceuticals (now part of Merck & Co.) in 2007. Before Illumigen, Dr. Iadonato managed the Human Genome Center at the University of Washington. He is co-inventor on 49 issued U.S. and foreign patents. He is Principal Investigator or co-Investigator on numerous government grants and contracts. Dr. Iadonato received a PhD in Genetics from the University of Washington and is a graduate of the University of Pennsylvania

**Craig Philips, President**

Craig Philips serves as President of Kineta. He has over thirty years of pharmaceutical industry experience at both Fortune 500 pharmaceutical and smaller biotech companies. Mr. Philips has served Kineta since 2013 in a variety of executive management roles. Prior to joining Kineta, Mr. Philips was President at CTI Biopharma a NASDAQ-listed clinical and commercial stage oncology company where he led the commercial and development activities in the US and EU. Additionally, he was responsible for business development activities and transactions of several drug programs. Previously, Mr. Philips spent over 20 years with leading biopharmaceutical companies and held strategic and operational leadership roles in the US, Asia, Australia and Europe. He has spent the majority of his career in the clinical and commercial development of oncology and specialty pharmaceuticals including the launch of four new pharmaceutical products each of which exceeded $1 billion in sales.

Mr. Philips sits on the board of several private biotech companies, Life Science Washington and is a commercial advisor to the Fred Hutchinson Cancer Research Center. He received a BS in Business Administration and an MBA from The Ohio State University.

**Keith Baker, Chief Financial Officer**

Keith Baker serves as Kineta's CFO. He has over 30 years of experience in companies ranging from small to large, privately held to publicly traded and start-ups to established firms with a variety of business models. Mr. Baker has extensive financial expertise in corporate finance, public accounting SEC reporting as well as mergers and acquisitions. Prior to joining Kineta, Mr. Baker served as CFO of several technology companies including Element Data, Inc., a decision intelligence technology firm, and Zemax, LLC, a software company in optical and illumination design. He has served as a fractional, interim or project CFO for several start-up and growth-stage businesses. Previously, Mr. Baker led SEC financial reporting and the Sarbanes-Oxley compliance program at Targeted Genetics Corporation (now Armata Pharmaceuticals), a biotechnology company focused on developing anti-bacterial therapeutics. Mr. Baker started his career in public accounting as an auditor at Deloitte & Touche LLP.

Mr. Baker is a Certified Public Accountant (Inactive). He was a U.S. Army paratrooper prior to earning his Bachelor of Science degree in Accounting from Central Washington University.

**Pauline Kenny, J.D., General Counsel**

Pauline Kenny heads all legal, corporate governance and securities regulatory compliance initiatives at Kineta and its corporate affiliates and subsidiaries. Ms. Kenny brings over twenty years of legal experience working both in-house and as outside counsel and is admitted to practice law in Washington.

Prior to joining Kineta in 2012, Ms. Kenny practiced law at a local boutique corporate and securities law firm where she represented a wide variety of emerging and established companies and advised clients in areas such as debt and equity financings, licensing and commercial matters, intellectual property protection, merger and acquisition transactions and employment issues. Ms. Kenny has also served as in-house counsel at a local venture-backed software startup as well as at a large publicly traded company. Ms. Kenny earned a B.A. in Communications from the University of Washington and a J.D. from Seattle University.

**Thierry Guillaudeux, Ph.D., Chief Scientific Officer**

Dr. Thierry Guillaudeux has over thirty years of experience in immuno-oncology (IO) in France and in the United States. Dr. Guillaudeux has a strong executive background in academia, heading a research laboratory of the French National Institute of Health with more than sixty employees for ten years and serving as a Vice President in Technology Transfer at the University of Rennes where he negotiated and executed numerous contracts and licenses with industry. Dr. Guillaudeux has also served as a board member of two French companies for more than five years.

Dr. Guillaudeux is leading Kineta's IO programs from discovery and pre-clinical to IND filling. This includes all *in vitro* and *in vivo* IO assay developments to evaluate the mechanisms of action of Kineta's drugs as well as conduct toxicology studies for lead antibody selection. He is leading the clinical trial efforts for KVA12123 and the scientific strategy for the selection of new innovative IO programs at Kineta.

His fields of expertise are B cell lymphoma, lung cancer and the tumor microenvironment. He has published more than 50 peer-review publications and is a co-inventor of multiple patents in the field. He was principal investigator or co-investigator on numerous French government and non-profit grants for his laboratory.

Dr. Guillaudeux received his B.S. and M.S. degrees from the University of Rennes and his PhD in Immuno-Oncology from the University of Toulouse. He obtained his post-doctorate at the Fred Hutchinson Cancer Research Center and was responsible for the sequencing of the Human Major Histocompatibility Complex I.

**Jacques Bouchy, EVP Investor Relations and Business Development**

Jacques Bouchy heads investor relations and business development at Kineta. He has over thirty years of pharmaceutical industry experience at Fortune 500 pharmaceutical and smaller biotech companies. Mr. Bouchy led the execution of Kineta's strategic partnerships with Pfizer and Genentech along with other external collaborations.

Prior to joining Kineta in 2014, Mr. Bouchy held leadership roles within the commercial organizations of Fortune 500 pharmaceutical companies. At GSK, he led payer marketing, pricing strategy and contracting of several mid to late-stage respiratory assets. He led a team that planned and executed the successful payer launch of BREO® Ellipta for the U.S. market ($1.5B product in 2020). Mr. Bouchy started his career at Schering-Plough where he held roles of increasing responsibility in the sales and managed markets organizations as well as the Merck/Schering-Plough joint venture. As a Regional Director, he led a team across the western U.S. that was accountable for all managed care payers that generated annual product sales of ~$300M. Mr. Bouchy has successfully launched twelve new pharmaceutical products throughout his career. He serves on the BIO Biodefense Committee and previously served on the board of the ALA's Washington Asthma Initiative. Mr. Bouchy earned a B.S. in Marketing from the University of Colorado.

## RISKS

All investments contain an element of risk that 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 titans that have multiple products 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, some hazards are particular to smaller companies that have not yet established themselves or their products.

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.

Even if a company has a strong, experienced team that is developing a therapy with a high likelihood of success and a large addressable market, securing funding may be difficult. Access to financing comes and goes in cycles. 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. If capital is needed to sustain operations and it is not readily available, the company may be forced to suspend research and development, sell equity at a substantial discount to previous valuations and dilute earlier shareholders. A lack of funding may leave potentially promising therapies without a viable route to progress or force a company to accept onerous terms.

### Regulatory Environment

All drugs must navigate the regulatory approval process in the US, EU, Japan and other countries before commercialization. Success is uncertain and may take years depending upon the needs and desires of the determining authority. Substantial expense is undertaken to bring a molecule or compound through clinical trials and address all of the regulatory agencies' concerns. Isolating companies that have a long history of research success in drug development, with opinion leaders and experts in the field are important factors that can help mitigate this risk. Companies that have achieved previous success with the FDA or other regulatory agencies also are more attractive than those who may be new to the process. Some accelerated pathways to approval have been put forth such as those outlined in the Orphan Drug Act and the Breakthrough Therapy designation; however, changes in sentiment or perceived safety for pharmaceuticals drugs could change the regulatory environment to demand a more thorough process and these pathways may be extended or additional requirements may be put in place. Kineta has highlighted the Fast Track and Accelerated Approval routes as possible expedited pathways for KVA12123.

**Exhibit XIV – Success of Phased Trials and Regulatory Approval[38]**

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

### Competitive Environment

Many firms are participating in the oncology space and products must compete against established treatments that are entrenched in the health care system. In oncology, for example, there are hundreds of approved agents available. According to Evaluate Pharma there are 188 marketed drugs in the immuno-oncology space as of mid-2023. On the development side, there are 38 IO agents filed, 190 in Phase III and 890 in Phase II. To differentiate itself from these other sponsors, Kineta has developed a platform to identify effective monoclonal antibodies with favorable side effect profiles. Its lead candidate is pursuing a broad mandate in solid tumors that do not respond to other therapies. The company plans to start with a basket trial and follow the data to the tumors that respond best to KVA12123.

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

**Partners**

In recent years, contract research organizations (CROs) have taken on a larger role in the development of drug candidates as the complexity and cost of trials has increased. Finding appropriate populations to participate in clinical trials has become increasingly difficult due to the shift to personalized medicine and orphan indications that address only a small group of patients. This shift has increased the dependence on specialized CROs for project management and clinical monitoring services that add additional risks related to third parties. Kineta in particular has relied on its CRO partner, GigaGen to help develop antibody sequences for its programs. The company has granted GigaGen royalties and other monetary benefits for this support.

Kineta has entered into a clinical collaboration with Merck, which provides pembrolizumab for its combination studies with KVA12123. Kineta is responsible for conducting the related research and will share safety, tolerability, pharmacokinetic and anti-tumor activity of KVA12123 and pembrolizumab with its partner. Merck may withdraw its participation in the collaboration or refuse to make pembrolizumab available on favorable terms. Partnering with Merck for its PD-1 inhibitor may displace other potential combination partners that may have candidates with improved safety and efficacy when used with KVA12123.

In January 2023, Kineta entered into an agreement with PPD Development (PPD) to provide services and support for the active Phase I/II clinical trial. PPD will assist in the effort to identify clinical sites, initiate and open clinical sites and monitor and validate research at each site. PPD will also provide support in preparing and developing interim safety data reports for review and analysis by the independent safety monitoring committee. The CRO partner may face competing demands which can adversely affect the work they are managing on behalf of the client. CROs and subcontractors must abide by strict execution and trial parameters that if violated can jeopardize trial execution or data validity. Patient recruitment may be difficult. Subcontractors supervise and execute research as well as conduct biometric and pharmaco- vigilance, which are complex tasks. Clinical investigational centers need sufficient capacity and the candidate drug needs to be manufactured in compliance with current Good Manufacturing Practices (cGMP) and be available to administer. Finally, the data itself needs to achieve statistical significance to justify regulatory approval.

**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, in most cases small and medium size biopharmaceutical companies work with partners through supply agreements to make their products. Working with a partner confers several 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 numerous benefits to outsourcing manufacturing, a sponsor can also be exposed to several risks. Partner manufacturers may not prioritize client projects and may run afoul of regulatory requirements. The manufacturer may experience quality control or volume constraints that could disrupt demand. Take or pay contracts could 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. Kineta has engaged Samsung Biologics to perform biologics development and manufacturing services for the VISTA program. Manufacturing services are performed at Samsung's facilities in South Korea.

**Intellectual Property**

Despite the existence of patents, exclusivity and trade secrets, infringement of intellectual property is a risk. Kineta's intellectual property protection was developed in conjunction with GigaGen which is eligible for licensing fees, milestones and royalties related to the commercialization of KVA12123. Kineta relies on a patent portfolio to protect its biologic assets that address composition of matter, methods of manufacturing, indications pursued and other elements. The company is in the process of obtaining these patents worldwide. While the protective patents can prevent others from using the same technology as used in KVA12123, other anti-VISTA approaches may be successfully pursued that do not violate Kineta's intellectual property. Biologics receive 12 years of exclusivity in the United States and 10 years in the European Union following regulatory approval which may or may not exceed any patent protection. Kineta may also pursue patent term restoration along with the regular life of a patent, which is 20 years. Patent term restoration compensates for the time lost during the regulatory approval process.

**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 amongst prescribers. Marketing is expensive and requires an experienced sales force and a presence in the marketing region. 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.

**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, creating additional trade, transportation and other barriers between the UK and mainland Europe. Conflict between Ukraine and Russia has led to disruptions in clinical trials in these countries. Sanctions have also been placed on Russia and many of its businesses which may lead to product shortages. Refugees fleeing the war in Ukraine may also impact nearby countries and their productivity which could affect clinical trials and commercialization in these areas.

**Inflation**

Drug price inflation has gained attention as it and other health care costs have risen at a materially faster pace than inflation. As new therapies have been approved, drug prices have increased to reflect higher development costs and improved pricing power of pharmaceutical and biotech companies. On the demand side, deductibles have been steadily increasing over the last decades, and in some cases, individuals and families must cover several thousand dollars in costs before the benefits of insurance begin. Cost sharing or co-insurance is another component of insurance plans that directly increases the burden on patients. This has resulted in greater elasticity in demand for drugs than was previously the case. Individuals with high deductibles or no insurance may be very sensitive to price and avoid treatments with high cost.

While we have discussed a broad variety of risks above, we believe that our forecast parameters, discount rates, success probabilities and valuation metrics address these potential outcomes and our target price reflects an assumption of these risks faced by biotechnology companies.

## VALUATION

Kineta's lead candidate, KVA12123, is an anti-VISTA monoclonal antibody that is in Phase I/II trials for solid tumors. It is expected that early results will narrow down the field of tumor targets to OC, CRC and NSCLC. The candidate has shown VISTA specificity, ability to sidestep CRS, anti-tumor activity and synergy with anti-PD-1s, providing a strong argument for KVA12123 to enter the clinic. Most solid tumors with high VISTA expression have a poor prognosis, providing an entrée for KVA12123 to address a severe unmet need. In later stages, five-year survival for the target indications is well below 50%, demonstrating an unmet need that may be able to be met with new combination therapies.

KVA12123 is now in a Phase I/II trial and is undergoing dose escalation and dose expansion studies both as monotherapy and in combination with Merck's pembrolizumab. We anticipate that the Phase I will complete by year-end 2023 and be followed by a 24-month Phase II effort. While it is possible that a strong signal may emerge and superior efficacy may allow for expedited treatment, our forecasts call for a pivotal Phase III trial to be conducted in 2026 and 2027, a BLA submission in 2028 and commercialization in 2029. We forecast sales outside the United States to commence in 2030.

Our addressable market includes the annual incidence of OC, CRC and NSCLC in the United States and ex-US based on our review provided in the Primary Indications section. This produces an addressable population of 266,000 in the US and almost 3.8 million in the rest of the world. Population growth is estimated at 0.5% in the US and 1.0% ex-US. The oncology space is a busy one, with numerous offerings in a variety of drug classes. In this competitive environment, we anticipate a five-basis point penetration in year one growing to a 200-basis point penetration by year eight (2036), where penetration remains steady until new products or biosimilars compete away share in 2044. Outside the US we anticipate a similar start to sales with penetration of 5 basis points in year one (2030) rising to 120 basis points by year six where it remains until 2044 when competitive forces are expected to reduce sales.

Pricing is expected to be $175,000 per course of treatment for the United States in 2029 growing at a rate of 3% per annum. Outside the US, pricing is expected to be at 40% of US levels, or $70,000 per course of treatment growing at 1% per annum. Partnership is the logical decision for an R&D-focused company, and we anticipate that a mid-to-large size biopharma will take the reins either during pivotal trials or after approval to commercialize KVA12123. In return for the rights to a successful asset, we anticipate upfronts, milestones and royalties. Due to the difficulty of estimating timing and mix for this complex arrangement, we model an all-in royalty that represents all of the economic value received by Kineta by its commercializing partner. The amount of economic value received by Kineta will depend on KVA12123's stage when the deal is signed and other factors including the number of bidders for the asset and its perceived value in the marketplace at the time of the negotiation. We estimate Kineta will receive an all-in royalty of 28% of net sales from a partner net of all manufacturing, sales and marketing costs. The royalty amount includes all economic value from the arrangement including upfronts, milestones and royalties paid on revenues.

Estimates for operational costs call for just over $20 million in cash expense for 2023, $23 million in 2024 and $25 million in 2025 after which costs are estimated to grow at a mid-single-digit per annum rate. Following profitability, net operating losses will be consumed. After NOLs are exhausted, we forecast a 25% cash tax rate on earnings. After tax cash flows to the company are discounted at a 15% rate with a terminal growth rate of -10%. We apply an overall 15% likelihood of success.

Option and warrants are assumed to be exercised if below our target price with proceeds added to cash and exercised shares added to shares outstanding. Despite the conservative stance of our assumptions, penetration into addressable markets can potentially be higher for KVA12123 if study results demonstrate strong efficacy, synergy and safety and success in additional indications. We note that the determinant for many of the variables in our model will be the ultimate performance of Kineta's candidates in the clinic and in pivotal studies. We will update our model accordingly as data is made available.

Based on the assumptions identified in our discounted cash flow model, we generate a valuation of $13.50 per share.

## CONCLUSION

Kineta is developing a promising candidate in the checkpoint inhibitor class that will target the VISTA immune checkpoint. Many studies have shown a synergy between anti-VISTA candidates and checkpoint inhibitors, providing a strong rationale for advancing a product in this category.

Kineta has completed its preclinical research which has identified a VISTA-specific candidate that induces a strong anti-tumor response both as monotherapy and with other checkpoint inhibitors. Its asset can reverse MDSC suppression of T cells and sidestep a serious adverse event in immunotherapy, CRS. VISTA is expressed in a wide variety of cancer types, including ovarian cancer, colorectal cancer, non-small cell lung cancer, cervical cancer, melanoma and hepatocellular carcinomas with the first three potentially serving as initial candidates for Kineta's proof of concept trials.

KVA12123 is Kineta's lead candidate and the subject of an ongoing Phase I/II clinical trial that is now conducting dosing studies. The multi-phase trial is expected to be run over the 2023-2025 period and generate data that will confirm the initial indications that will be pursued. We expect that Kineta will continue clinical trial work to add more indications as R&D efforts advance. Although our model does not include any expedited treatment for KVA12123, strong initial data in the Phase II may support the use of the Fast Track and Accelerated Approval pathways, which could advance commercialization by up to two years.

Many cancers are not cured and patients move into second, third and later line therapies to eradicate resistant tumors. This provides a large unmet need that new combination therapies may address. Based on our review, there are about 266,000 new cases in the US and 3.8 million outside the US in the primary indications that Kineta plans to pursue in OC, CRC and NSCLC. Our model anticipates an initial approval in the most promising indication, and later expansion into other indications with penetration into these markets growing over time. Pricing for a course of therapy is expected to be in line with other immunotherapies, which is expected to generate royalty and other related revenues for Kineta through the commercialization activities of a partner.

Kineta has recently raised capital and has a private placement planned for July that will add another $22.5 million to the company's coffers. Cash burn is estimated to be under $5 million per quarter, which suggests sufficient funding to support operations potentially into early 2025. This forecast includes the contribution from the anticipated private placement in July.

Key reasons to own Kineta shares:

- **Developing KVA12123, a Phase I/II immune checkpoint, to treat solid tumors**
  - **Addresses mechanism of cancer immune resistance**
  - **Integrates innate and adaptive immune responses**
  - **Demonstrates synergies with checkpoint inhibitors (anti-PD-1/PD-L1/CTLA-4)**
- **KVA12123 offers a favorable treatment effect in specific populations**
  - **OC, CRC and NSCLC are high VISTA expressers**
  - **Patients developing resistance to CIs are high VISTA expressers**
- **KVA12123 may augment response rates when combined with existing checkpoint inhibitors**
- **Produces favorable safety profile with no evidence of cytokine release syndrome (CRS)**
  - **Antibody design with engineered Fc region to reduce immunogenicity**
- **Offers additional monoclonal antibody (mAb) assets in early stage development**
  - **Anti-CD27 agonist**
- **Maintains global rights to intellectual property**

KVA12123 adds another compelling entry into the immuno-oncology universe and has shown promising activity along with other checkpoint inhibitors in addressing high VISTA-expressing tumors. Our valuation work takes into account commercialization of the asset around the globe, assuming a 15% probability of success. As KVA12123 progresses and generates additional data, we will refine our indications and timeline accordingly. We initiate on Kineta Inc. with a target price of $13.50 per share.

## PROJECTED FINANCIALS

**Kineta Inc. - Income Statement**

| Kineta, Inc. | 2022 A | Q1 A | Q2 E | Q3 E | Q4 E | 2023 E | 2024 E | 2025 E |
|---|---|---|---|---|---|---|---|---|
| **Total Revenues ($USD)** | **$1,953** | **$281** | **$161** | **$0** | **$0** | **$442** | **$0** | **$0** |
| Research & Development | $15,928 | $2,843 | $3,325 | $3,458 | $3,500 | $13,126 | $14,210 | $14,870 |
| General & Administrative | $8,696 | $3,924 | $1,800 | $1,800 | $1,800 | $9,324 | $9,889 | $10,320 |
| In-process R&D | $18,860 | $0 | $0 | $0 | $0 | $0 | $0 | $0 |
| Income from Operations | ($41,531) | ($6,486) | ($4,964) | ($5,258) | ($5,300) | ($22,008) | ($24,099) | ($25,190) |
| Other Items | ($21,922) | $6 | ($19) | ($19) | ($19) | ($50) | ($50) | ($50) |
| Non-controlling Interest | ($45) | ($29) | ($21) | ($22) | ($23) | ($95) | ($105) | ($114) |
| Pre-Tax Income | ($63,408) | ($6,451) | ($4,962) | ($5,255) | ($5,296) | ($21,963) | ($24,044) | ($25,126) |
| Provision for Income Tax | $0 | $0 | $0 | $0 | $0 | $0 | $0 | $0 |
| **Net Income** | **($63,408)** | **($6,451)** | **($4,962)** | **($5,255)** | **($5,296)** | **($21,963)** | **($24,044)** | **($25,126)** |
| **Reported EPS** | **($12.87)** | **($0.77)** | **($0.52)** | **($0.46)** | **($0.33)** | **($1.93)** | **($1.41)** | **($1.35)** |
| Basic Shares Outstanding | 4,926 | 8,361 | 9,500 | 11,522 | 16,250 | 11,408 | 17,100 | 18,550 |

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

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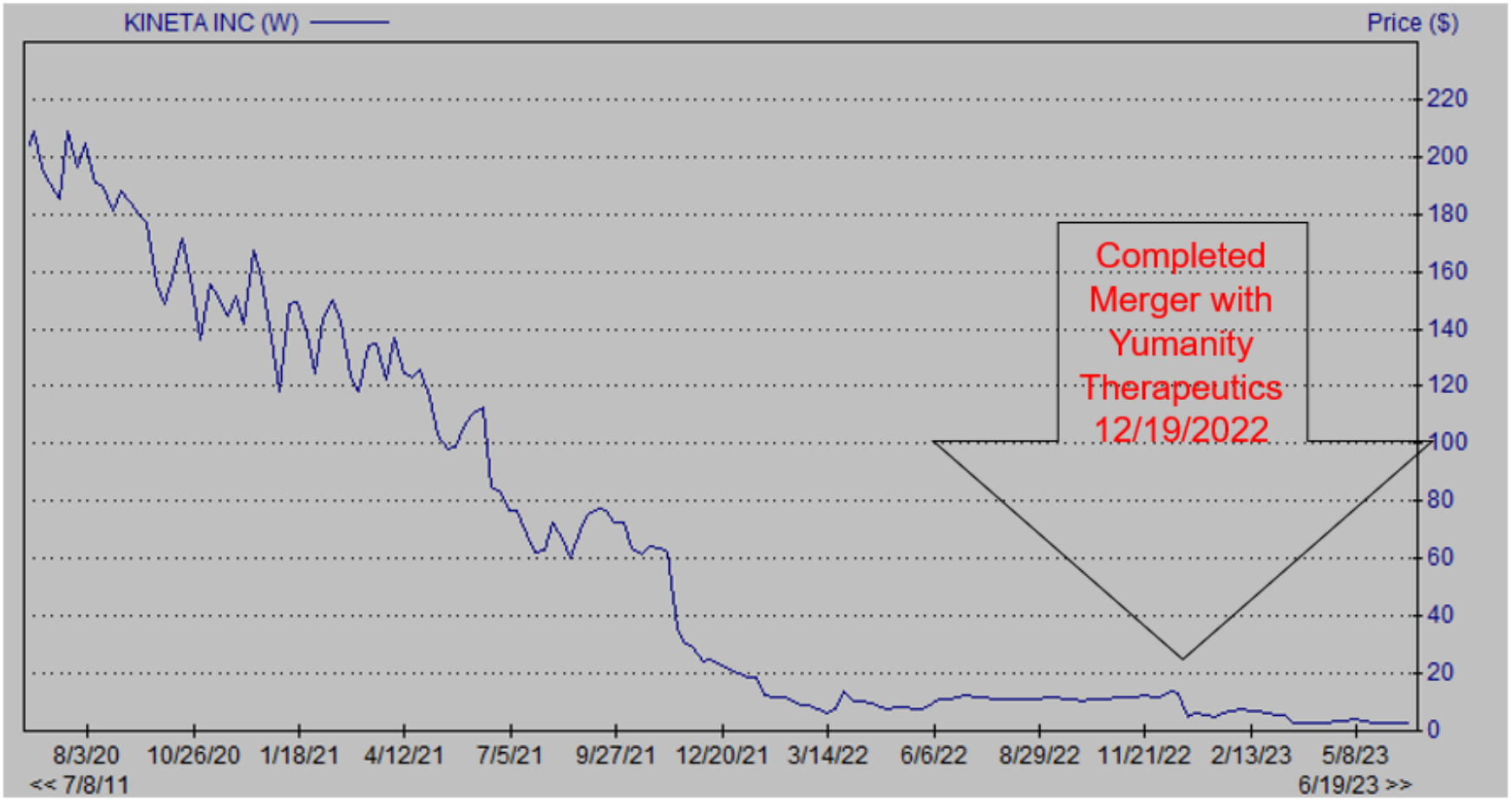
## HISTORICAL STOCK PRICE

**Kineta Inc. – Share Price Chart[39]**




[39] Source: Zacks Research System

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