Antibody Engineering & Therapeutics Conference
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Next-generation immunotherapies to address cancer immune resistance

KVA12123 a VISTA Blocking Immunotherapy
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Full Time Employee at Kineta Inc.
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This presentation may be deemed to be solicitation material with respect to the proposed transactions between Yumanity and Kineta and between Yumanity and Janssen. In connection with the proposed transactions, on August 29, 2022, Yumanity filed with the SEC a registration statement on Form S-4 (the “Initial Registration Statement”) as amended by Amendment No. 1 to the Initial Registration Statement filed with the SEC on October 3, 2022 and Amendment No. 2 to the Initial Registration Statement filed with the SEC on October 24, 2022 (together with the Initial Registration Statement, the “Registration Statement”), which contains a preliminary proxy statement and prospectus. The Registration Statement has not yet become effective. Yumanity will mail the definitive proxy statement/prospectus to the Yumanity securityholders, and the securities may not be sold or exchanged until the Registration Statement becomes effective. Investors and securityholders of Yumanity and Kineta are urged to read these materials when they become available because they will contain important information about Yumanity, Kineta and the proposed transactions. This presentation is not a substitute for the Registration Statement, definitive proxy statement/prospectus or any other documents that Yumanity may file with the SEC or send to securityholders in connection with the proposed transactions.

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Immune resistance is a major challenge with current cancer therapy

Next-generation cancer treatments require:

Improving survival for checkpoint inhibitor (CPI) non-responders (70-80%)*

**Reprogramming** the immune system to attack cancer

Integrating *innate and adaptive immune* responses

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*Based on publicly available information*
KVA12123

VISTA blocking immunotherapy

*From bench to bedside*
**KVA12123 - VISTA blocking immunotherapy**

<table>
<thead>
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<th>Drug program</th>
<th>Discovery</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Anticipated Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immuno-suppression: αVISTA mAb</strong></td>
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<td><strong>Indications:</strong> Advanced solid tumors NSCLC, CRC, OC</td>
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- **KVA12123**

- **4Q 2022:** IND Approval & Initiate Phase 1
- **2Q 2023:** Initiate pembrolizumab combo cohort
- **4Q 2023:** Initial Phase 1 data readout
Introduction of the target:
VISTA a B7 family member with close homology to PD-L1

VISTA
- Gene present on chromosome 10q22.1
- Membrane protein of the Ig SF
- 311 AA with 92 AA cytoplasmic domain
- Strongest similarity with PD1-L1 and conserved across species
- Expression is p53 and Hypoxia dependent
- VISTA-R:
  - * VISTA Itself (WO2021527719)
  - * VSIG3/ISGF11 (Wang et al 2018; Mehta et al 2019)
  - * VSIG8 (WO2016050347)
  - * PSGL-1 (Johnston et al 2019)
  - * LRIG1 (WO2015187795)

Source: Li Wang et al. JEM 2011
Introduction of the target:
VISTA expression on human whole blood

- Express on Myeloid cells, Neutrophils, NK cells and Treg
- Highly express on MDSCs, M2 macrophages and Treg in the TME

Source: Kineta on file
Introduction of target: VISTA mediates immunosuppression in the TME

VISTA

- Immunosuppressive molecule controlling T cell activation
- Suppresses T effector functions
- Complementary mechanism with PD1
VISTA is a key driver of immunosuppression in the tumor microenvironment

- Immunosuppressive protein expressed on *myeloid cells*
- Highly expressed in *cold tumors* including lung, colon and ovarian cancers
- Correlates with *poor outcomes* in cancer patients
- Up-regulated after CPI therapy and *associated with treatment failure*

### References:
Blocking VISTA can reverse immunosuppression in the TME

- Inhibits MDSC (myeloid-derived suppressor cells)
- Promotes T\textsubscript{eff} function
- Enhances NK cell activation
- Enhances monocyte activation
Blocking VISTA induces tumor regression
Proof of concept

CT26 mouse model

Source: Kineta on file
Anti-VISTA mAbs: High diversity in both heavy and light chains

107 fully human ScFv antibodies directed against Human VISTA were generated

- 15 $V_H$ diversity groups
- 15 $V_L$ diversity groups
- Highest diversity in CDR3H
Anti-VISTA mAbs are highly potent

ELISA Binding

Octet Kinetic

Flow Cytometry Binding

Source: Kineta on file
Anti-VISTA mAbs are highly specific

Anti-VISTA mAbs bind cyno VISTA-ECD but not mouse VISTA-ECD

Anti-VISTA mAbs bind only to VISTA and not other B7 family proteins

Source: Kineta on file
Lead selection: KVA12123 Fc modification extends serum exposure

KI Mouse PK

Cyno PK

Source: Kineta on file
KVA12123 Fc modification increases binding to FcRn and decreases binding to FcyRI, FcyRIIA, FcyRIIIA

<table>
<thead>
<tr>
<th>Antibody</th>
<th>EC50 FcRn (ug/mL)</th>
<th>EC50 FcRn (nM)</th>
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</thead>
<tbody>
<tr>
<td>KVA12123 (YTE, IgG1)</td>
<td>0.142</td>
<td>0.95</td>
</tr>
<tr>
<td>KVA12104 (WT, IgG1)</td>
<td>0.750</td>
<td>5.0</td>
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</tbody>
</table>

Source: Kineta on file
KVA12123 binds at physiologic and acidic pH

Binding studies by ELISA and Octet demonstrate rapid on-rate and slow off-rate from pH 7.4 to pH 6.0.
KVA12123 blocks VISTA interaction with its receptors

### Table: Antibody EC50 (nM)

<table>
<thead>
<tr>
<th>Antibody</th>
<th>VSIG3</th>
<th>PSGL1</th>
<th>VSIG8</th>
<th>LRIG1</th>
<th>VISTA</th>
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<tr>
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<td>IgG1</td>
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<td>&gt;670</td>
<td>&gt;670</td>
<td>&gt;267</td>
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<tr>
<td>KVA12123 Fab</td>
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<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>221</td>
</tr>
</tbody>
</table>

Source: Kineta on file
Blocking VISTA with KVA12123 activates both innate and adaptive immune cells

- **Increases monocyte differentiation and activation**
  - HLA-DR, CD80, CD86, CXCL10

- **Reduces MDSC-mediated T cell suppression**

- **Increases HLA-dependent T cell activation**

**NK dependent mechanism of action**

**Enhances NK cell activation**

Source: Kineta on file
KVA12123 demonstrates single agent tumor growth inhibition in preclinical models

Monotherapy
Bladder Cancer Model MB49

hVISTA KI mice

Mean Tumor Volume

Days Post Implantation

Avg. tumor volume (mm$^3$)

- Control MsIgG2a
- KVA-12.2a WT
- KVA-12.2a LALA

Tumor Growth Inhibition

Anti-VISTA: 75%

Monotherapy
T Cell Lymphoma Model EG7

hVISTA KI mice

Mean Tumor Volume

Days Post Implantation

Avg. tumor volume (mm$^3$)

- Control MsIgG2a
- KVA-12.2a WT
- KVA-12.2a LALA

Tumor Growth Inhibition

Anti-VISTA: 66%

KVA12.2a: mouse isotype equivalent of KVA12123

Source: Kineta on file
KVA12123 demonstrates single agent tumor growth inhibition and in combination with PD-1 in preclinical models

**Combination Therapy**
- Colon Carcinoma Model MC38*  
- *hVISTA KI mice*
- Mean Tumor Volume
  - IgG Control
  - KVA12.2a
  - Anti-mPD1
  - KVA12.2a / Anti-mPD-1

**Tumor Growth Inhibition**
- Anti-VISTA: 35-42%
- Anti-PD1: 42-60%
- Combo: 68%

*Combination therapy studies used sub-optimal doses of each agent

**Combination Therapy**
- Bladder Cancer Model MB49*  
- *hVISTA KI mice*
- Mean Tumor Volume
  - Human IgG1
  - KVA12.2a
  - Anti-mPD1
  - KVA12.2a / Anti-mPD-1

**Tumor Growth Inhibition**
- Anti-VISTA: 40%
- Anti-PD1: 67%
- Combo: 85%

**Immune Cells In the TME**
- DC in Tumor
- M1 TAMs
- G-MDSC in Tumor

**Source:** Kineta on file
KVA12123 was observed to be well-tolerated in NHP toxicology studies

- No mortality
- No change in CRS cytokine levels (IL6 or TNFα)
- No treatment-related findings
- Well tolerated
- No overt clinical signs or weight loss

Kineta has completed multiple, single and repeat-dose toxicology studies in NHP with doses of KVA12123 up to 100 mg/kg

Source: Kineta on file
KVA12123: No CRS-associated in preclinical models in NHP toxicology studies as well as in human whole blood

**KINETA**

Source: Kineta on file
Clinical applications for KVA12123 are primarily focused on solid tumors with high levels of VISTA expression.

Brown staining in human tumors indicates VISTA expression.
Phase 1 dose escalation study monotherapy and in combination with pembrolizumab in advanced solid tumors

**Patient population:** Patients with advanced solid tumors

**Primary objectives:** Safety and tolerability, Recommended Phase 2 dose (RP2D) or maximum tolerated dose (MTD) of KVA12123

**Secondary objectives:** Pharmacokinetics, Immunogenicity, Tumor response in subjects with advanced solid tumors per iRECIST (ORR)

**Exploratory objectives:** Biomarker and receptor occupancy

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**Part A**

Planned dose levels for single-agent KVA12123 dose escalation

monotherapy

IV=intravenous; Q2W=every 2 weeks (KVA12123)

- 3 mg
- 10 mg
- 30 mg
- 100 mg
- 300 mg
- 1000 mg

1-6 subjects in each cohort

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**Part B**

Planned dose levels for KVA12123 dose escalation in combination with pembrolizumab

- 30 mg
- 100 mg
- 300 mg
- 1000 mg

3-6 subjects in each cohort

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The KVA12123 study is a Phase 1/2 clinical trial. Part A and Part B are presented above. Part C and Part D are Phase 2 expansion cohorts and will enroll patients with tumor types defined in Part A and Part B.
Anti-CD27 agonist mAb immunotherapy
Anti-CD27 agonist to address exhausted T cell mechanism of cancer immune resistance

Exhausted T cells

- Activates and induces the maturation and migration of naïve T cells.
- Drives the diversification of the T cell repertoire
- Enhances NK cell activation
- Activates low affinity antigens

CD27 agonist has the potential to generate new populations of functional anti-tumor immune cells

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