Interim results of the ongoing phase 1/2 clinical trial of KVA12123, an engineered IgG1 targeting VISTA, alone and in combination with pembrolizumab in advanced solid tumors.

#CT068

Kineta Inc., Seattle, WA
tguillaudeux@kineta.us
www.kinetabio.com

Evan Y. Yu[1], Jason Henry[2], Manish R. Patel[3], Paul Swiecicki[4], Ida Micaily[5], Benjamin Garmezy[6], Kalyan Banda[1], Marya Chaney[7], Julia Cohen[7], Vinny Hayreh[8], Kurt Lustig[8], Yulia Ovechkina[8], Shawn Iadonato[8], Thierry Guillaudeux[8] and Lee Rosen[9].

[1]Fred Hutchinson Cancer Center, Seattle, WA; [2]Sarah Cannon Research Institute, Denver, CO; [3]Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL; [4]University of Michigan, Ann Arbor, MI; [5]Thomas Jefferson University, Philadelphia, PA; [6]Tennesse Oncology, Nashville, TN; [7]Merck & Co., Inc. Rahway, NJ; [8]Kineta Inc., Seattle, WA; [9]UCLA, Santa Monica, CA.

Background

VISTA (V-domain Ig suppressor of T cell activation) is a strong driver of immunosuppression in the tumor microenvironment (TME)

- A negative immune checkpoint that suppresses T cell function in a variety of solid tumors
- Highly expressed in cold tumors and correlates with poor outcomes in cancer patients
- Up-regulated after checkpoint inhibitor therapy and associated with treatment failure
- Blocking VISTA induces a polyfunctional immune response that addresses immunosuppression and drives anti-tumor responses. Noelle et al. *Front Oncol (2023)*

KVA12123 is a VISTA-blocking immunotherapy in development as a twice-weekly infusion

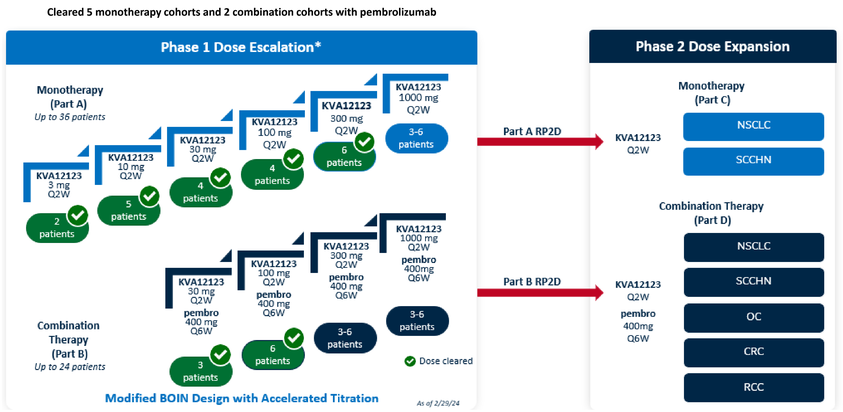
- An engineered IgG1 mAb that binds to a unique epitope at acidic and neutral pHs
- Induces a strong anti-tumor response as a single agent and in combination with anti-PD1 in multiple preclinical tumor models
- Well tolerated and does not induce the release of CRS-associated cytokines in non-human primates or in human whole blood
- May be an effective immunotherapy for many types of cancer, including NSCLC, colorectal (CRC), renal cell carcinoma (RCC), head and neck (SCCHN), and ovarian (OC) cancers
- Iadonato et al. A highly potent anti-VISTA antibody KVA12123 - a new immune checkpoint inhibitor and a promising therapy against poorly immunogenic tumors. *Front Immunol (2023)*

VISTA-101 study objectives

VISTA-101: Phase 1/2 open-label clinical trial of KVA12123 alone and in combination with pembrolizumab in patients with advanced solid tumors (NCT05708950)

- **Primary**: safety and tolerability, recommended Phase 2 dose (RP2D) or maximum tolerated dose (MTD) of KVA12123
- **Secondary**: pharmacokinetics, immunogenicity, tumor response in subjects with advanced solid tumors per iRECIST (ORR)
- **Exploratory**: biomarker and receptor occupancy

Cleared five monotherapy cohorts and first two cohorts in combination with pembrolizumab



The study was approved by the WCG Institutional Review Board (IRB)-approved protocol No. 20230297 and by the University of California, Los Angeles (UCLA) IRB-approved protocol No. IRB#22-002003. The patients provided written informed consent to participate in this study.

A Clinical Trial of KVA12123 Treatment Alone and in Combination With Pembrolizumab In Advanced Solid Tumors (VISTA-101) *
https://clinicaltrials.gov/ct2/show/NCT05708950

Clinical Trial Page (NCT05708950)

* This study is in collaboration with Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA

Baseline patient characteristics and Demographics

Characteristic Statistic	PART A 3mg IV Q2W (N=2)	PART A 10mg IV Q2W (N=5)	PART A 30mg IV Q2W (N=4)	PART A 100mg IV Q2W (N=4)	PART A 300mg IV Q2W (N=4)	PART B 30mg IV Q2W + Pemb. (N=3)	PART B 100mg IV Q2W + Pemb. (N=5)	Total
Gender (n %)								
Female	1 (50)	4 (80)	2 (50)	1 (25)	2 (50)	1 (33)	2 (40)	13 (48)
Male	1 (50)	1 (20)	2 (50)	3 (75)	2 (50)	2 (67)	3 (60)	14 (52)
Race (n %)								
Black or African American	0 (0)	1 (20)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	2 (7)
Other	0 (0)	2 (40)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	3 (11)
White	2 (100)	2 (40)	3 (75)	4 (100)	4 (100)	3 (100)	4 (80)	22 (81)
Age (Years)								
Mean	62.5	62.0	57.8	65.0	63.2	60.0	73.2	63.9
Median	62.5	64.0	56.5	64.0	68.0	61.0	75.0	64.0
Min, Max	62.0, 63.0	47.0, 72.0	53.0, 65.0	55.0, 77.0	47.0, 70.0	49.0, 70.0	57.0, 87.0	47.0, 87.0
Baseline ECOG PS (n %)								
Grade 0	0 (0)	2 (40)	0 (0)	1 (25)	1 (25)	2 (67)	0 (0)	6 (22)
Grade 1	2 (100)	3 (60)	4 (100)	3 (75)	3 (75)	1 (33)	5 (100)	21 (78)

Characteristic Statistic	PART A 3mg IV Q2W (N=2)	PART A 10mg IV Q2W (N=5)	PART A 30mg IV Q2W (N=4)	PART A 100mg IV Q2W (N=4)	PART A 300mg IV Q2W (N=4)	PART B 30mg IV Q2W + Pemb. (N=3)	PART B 100mg IV Q2W + Pemb. (N=5)	Total
Cancer Type (n %)								
Bladder	1 (50)	1 (20)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	3 (11)
Breast	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	1 (4)
Colon	0 (0)	1 (20)	0 (0)	1 (25)	2 (50)	0 (0)	0 (0)	4 (15)
Endometrial	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	1 (4)
Lung	0 (0)	1 (20)	1 (25)	0 (0)	0 (0)	1 (33)	0 (0)	3 (11)
Other	1 (50)	0 (0)	0 (0)	3 (75)	0 (0)	1 (33)	5 (100)	10 (37)
Pancreatic	0 (0)	1 (20)	2 (50)	0 (0)	0 (0)	0 (0)	0 (0)	3 (11)
Renal	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	1 (33)	0 (0)	2 (7)
TNM Stage at Initial Dx (n %)								
I	0 (0)	1 (20)	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	2 (7)
II	0 (0)	1 (20)	1 (25)	0 (0)	0 (0)	1 (33)	1 (20)	4 (15)
III	0 (0)	0 (0)	0 (0)	0 (0)	2 (50)	1 (33)	0 (0)	3 (11)
IV	1 (50)	3 (60)	2 (50)	2 (50)	0 (0)	1 (33)	2 (40)	11 (41)
Missing	1 (50)	0 (0)	1 (25)	2 (50)	1 (25)	0 (0)	2 (40)	7 (26)

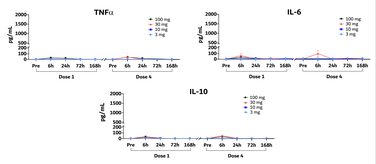
Heavily pretreated patients with multiple prior lines of therapy

KVA12123 was well tolerated in evaluated mono and combotherapy cohorts with no evidence of CRS-associated cytokine induction after KVA12123 administration

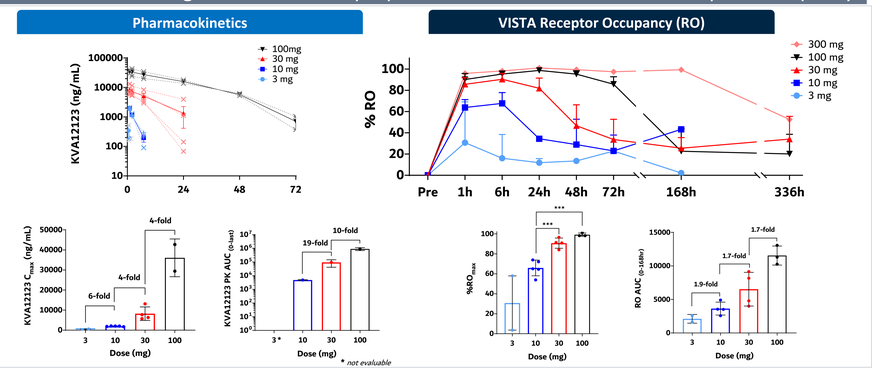
No dose limiting toxicities (DLT) were observed

MedDRA Preferred Term	3mg N=2 (%)	10mg N=5 (%)	30mg N=4 (%)	100mg N=4 (%)	300mg N=4 (%)	30mg IV Q2W + Pemb. (N=3)	100mg IV Q2W + Pemb. (N=5)	All doses N=27 (%)
Total Subjects With Any Related TEAE	1 (50)	4 (80)	3 (75)	2 (50)	2 (50)	2 (67)	2 (40)	16 (59)
Chills	0 (0)	1 (20)	1 (25)	1 (25)	0 (0)	1 (33)	1 (20)	5 (19)
Infusion related reaction	0 (0)	2 (40)	2 (50)	0 (0)	0 (0)	0 (0)	0 (0)	4 (15)
Fatigue	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	1 (33)	1 (20)	3 (11)
Blood bilirubin increased	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	1 (33)	0 (0)	2 (7)
Constipation	1 (50)	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)	2 (7)
Diarrhoea	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	2 (7)
Myalgia	1 (50)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)	0 (0)	2 (7)
Pyrexia	0 (0)	0 (0)	1 (25)	0 (0)	1 (25)	0 (0)	0 (0)	2 (7)

No CRS associated cytokines were observed



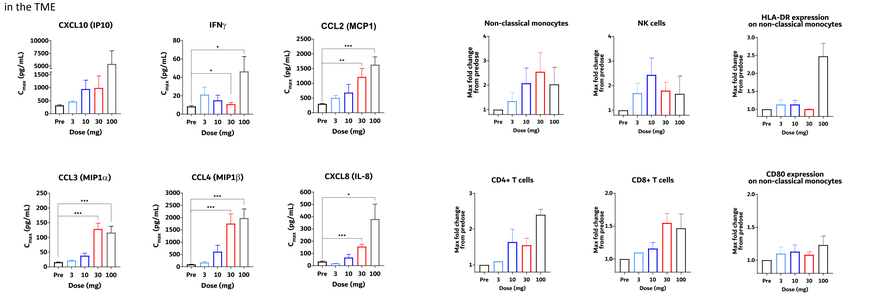
KVA12123 exhibits a greater than dose-proportional PK and > 90% VISTA Receptor Occupancy



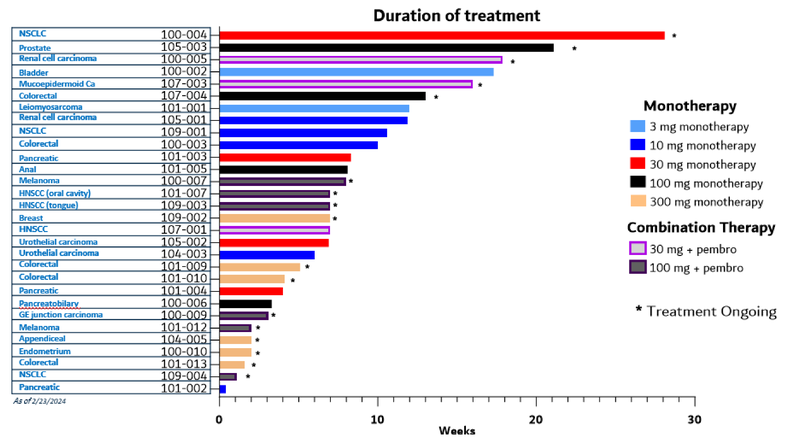
KVA12123 induces dose-proportional on-target biomarker responses

KVA12123 demonstrated dose proportional induction of pro-inflammatory myeloid derived cytokines/chemokines involved in immune cell activation and recruitment in the TME

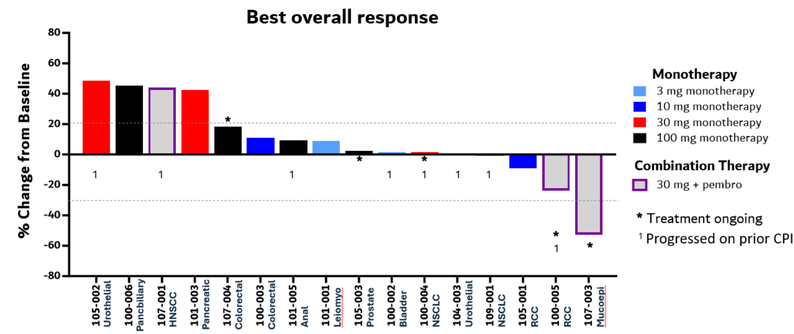
KVA12123 demonstrated VISTA on-target immune cell responses involved in anti-tumor activity



Duration of treatment



Best overall response (iRecist, patients with at least one follow up scan)



Conclusions

- *February 23rd 2024* - Cleared first five KVA12123 monotherapy cohorts (3, 10, 30, 100, 300 mg) with 21 patients dosed, and two KVA12123+pembrolizumab cohorts (30, 100 mg + 400 mg pembro) with 9 patients dosed
- Clinical safety profile: KVA12123 was well tolerated in evaluated monotherapy and combination therapy cohorts and no DLTs were observed
- No evidence of CRS-associated cytokines (IL-6, TNFα & IL-10) were detected after KVA12123 administration
- Achieved >90% VISTA RO across patients in >30 mg dosing cohorts with 300mg of KVA12123 approaching an optimal clinical dose
- Demonstrated efficacy-related cytokine secretion of CXCL10, IFNγ, CCL2, CCL3, CCL4, CXCL8 and on target changes in anti-tumor immune cell subpopulations
- Monotherapy: 9 of 12 patients who received at least 1 follow-up scan achieved stable disease (SD) as BOR and mean duration of SD is 15 weeks with the longest duration of 28 weeks in ongoing CPI-failed NSCLC
- Combotherapy: 3 patients received one follow-up scan, 1 Mucoepidermoid carcinoma patient achieved a **partial response** with **52.7% reduction** of target lesions and 1 RCC patient with SD and **23.7% reduction** of target lesions.
- VISTA-101 trial is advancing to the last monotherapy dose level and the last two cohorts in combination with pembrolizumab.