

ALKS 4230 ESMO Conference Call Script

September 18, 2020



ALKS 4230: A Novel, Engineered Interleukin-2 (IL-2) Variant Immunotherapy

Clinical Data Updates from ARTISTRY-1 Trial

2020 European Society for Medical Oncology (ESMO) Virtual Meeting

Investor Presentation

September 18, 2020



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Sandy Coombs

Thank you and welcome to the Alkermes plc conference call and webcast to discuss new clinical data and updates from our ongoing ARTISTRY-1 clinical trial of ALKS 4230, our investigational agent in oncology. These data are being presented as a mini oral presentation at the European Society for Medical Oncology 2020 virtual meeting.

Please note that during today's call we will reference slides that are available on the webcast. If you have not done so already, please go to the Investors section of our website, [Alkermes.com](https://www.alkermes.com), to access the webcast player. A PDF of the slides will be made available on our website following the conclusion of this call.

Forward-Looking Statements

Certain statements set forth in this presentation constitute “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: achievement of the design rationale for ALKS 4230; the potential therapeutic benefit and safety profile of ALKS 4230 when used as monotherapy or in combination across multiple tumor types; and clinical development plans for ALKS 4230, including details of the ARTISTRY clinical development program and the ION-01 study. The company cautions that forward-looking statements are inherently uncertain. Although the company believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, the forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those expressed or implied in the forward-looking statements due to various risks, assumptions and uncertainties. These risks, assumptions and uncertainties include, among others: whether ALKS 4230, as a monotherapy or in combination, could be shown to be unsafe or ineffective; whether preclinical results and data from ongoing clinical studies for ALKS 4230—whether as a monotherapy or in combination—will be predictive of future or final results from such studies, results of future clinical studies or real-world results; whether future clinical trials or future stages of ongoing clinical trials for ALKS 4230 will be initiated or completed on time or at all, and whether the results of such activities will be positive; changes in the cost, scope and duration of, and clinical trial operations for, development activities for ALKS 4230, including changes relating to the impact of the novel coronavirus (COVID-19) pandemic; and those risks, assumptions and uncertainties described under the heading “Risk Factors” in the company’s most recent Annual Report on Form 10-K and in subsequent filings made by the company with the U.S. Securities and Exchange Commission (“SEC”), which are available on the SEC’s website at www.sec.gov and on the company’s website at www.alkermes.com in the “Investors—SEC filings” section. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by law, the company disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this presentation.



During this presentation, we will be making forward-looking statements based on our current expectations relating to, among other things, the clinical development of ALKS 4230 and the potential therapeutic value of ALKS 4230. These forward-looking statements are neither promises nor guarantees and are subject to a high degree of uncertainty and risk. Please see slide 2 of the Investor Presentation accompanying this webcast, our press release issued this morning, and our most recent annual and quarterly reports filed with the SEC for important risk factors that could cause our actual performance and results to differ materially from those expressed or implied in the forward-looking statements. We undertake no obligation to update or revise the statements provided on this call as a result of new information or future results or developments.

Our prepared remarks today will include recent data from certain ongoing clinical trials in our ARTISTRY development program. This dataset will evolve as patient enrollment continues and as more patient data becomes available, and may not be indicative of future data or the final study results from such ongoing trials or results of future clinical trials.

Today's Speakers



Craig Hopkinson, M.D.

*Chief Medical Officer and
Executive Vice President
of R&D, Alkermes, Inc.*



Ulka N. Vaishampayan, M.D.

*Professor, Internal Medicine,
Division of Hematology/Oncology,
University of Michigan*



With me today for the prepared remarks are:


- Craig Hopkinson, our Chief Medical Officer and Executive Vice President of Research and Development,
- and special guest, Dr. Ulka Vaishampayan, Professor of Internal Medicine, Division of Hematology and Oncology at the University of Michigan, and Lead Investigator of the ARTISTRY-1 clinical trial.

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Agenda

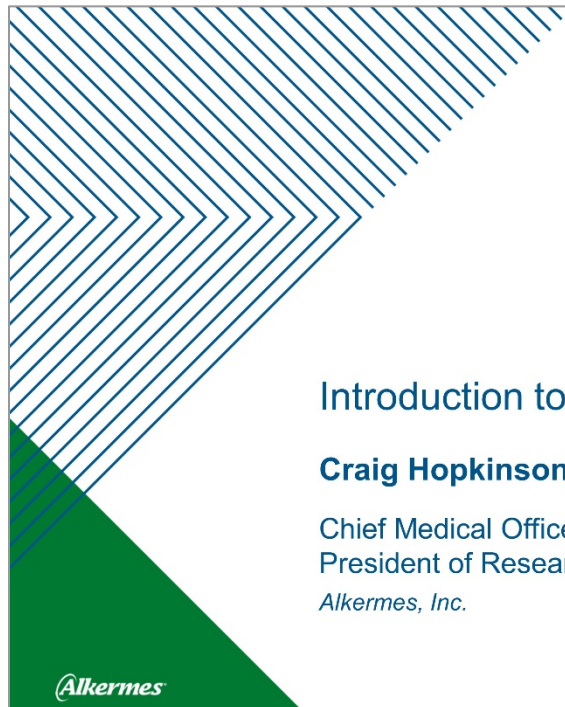
- Introduction to ALKS 4230
- Overview of ALKS 4230 Clinical Development Program
- ARTISTRY-1 Clinical Data Updates at the 2020 ESMO Virtual Congress
- ALKS 4230 Program Updates and Next Steps
- Q&A



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After the prepared remarks, we'll open the call for Q&A with Dr. Hopkinson. Now, I'd like to turn the call over to Craig.


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Introduction to ALKS 4230

Craig Hopkinson, M.D.
Chief Medical Officer and Executive Vice
President of Research & Development
Alkermes, Inc.



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Dr. Craig Hopkinson

Thank you, Sandy, and good morning everyone.

I'm delighted to be on the call today to share important new ALKS 4230 data being presented at ESMO with the clinical and investor communities. Efficacy, safety and tolerability data from the ARTISTRY development program have been accumulating in both the monotherapy and combination settings and now provide a clearer picture of ALKS 4230's potential clinical profile and utility.

In addition to the dataset being presented at ESMO as a mini oral presentation, this morning we will also provide an update on our ARTISTRY-1 monotherapy melanoma cohort, including data on an additional response that occurred subsequent to our ESMO data cutoff. As outlined in the press release we issued this morning, with two partial responses already observed in the first 6 evaluable patients in the monotherapy melanoma cohort, we have met the protocol-defined criteria to expand this cohort for further enrollment. We believe this is an important indicator of ALKS 4230's monotherapy activity profile.

This morning, I will begin with an introduction to ALKS 4230 followed by an overview of our clinical development program for ALKS 4230.

Dr. Vaishampayan will then share clinical data from ARTISTRY-1 that were presented at ESMO, after which I will elaborate on the most recent monotherapy response data, and discuss enrollment trends and next steps for the ALKS 4230 development program.

IL-2 Therapy Has Proven Anti-Tumor Efficacy, but is Associated With Serious Toxicities

- Recombinant human IL-2 (rhIL-2), known as PROLEUKIN® (aldesleukin), is approved for metastatic renal cell carcinoma (RCC) and metastatic melanoma based on complete and durable remissions
- IL-2 potentially activates the high-affinity IL-2 receptor found on vascular endothelial cells, resulting in poor tolerability and toxicities
 - Black box warning for vascular leak syndrome, pulmonary edema, hypotension, heart toxicities and more
- Toxicity profile of IL-2 significantly limits its broad use, despite its established anti-tumor efficacy

PROLEUKIN® (aldesleukin)
for injection, for intravenous infusion
Rx Only

WARNINGS

Therapy with Proleukin® (aldesleukin) should be restricted to patients with normal cardiac and pulmonary functions as defined by thallium stress testing and formal pulmonary function testing. Extreme caution should be used in patients with a normal thallium stress test and a normal pulmonary function test who have a history of cardiac or pulmonary disease.

Proleukin should be administered in a hospital setting under the supervision of a qualified physician experienced in the use of anticancer agents. An intensive care facility and specialists skilled in cardiopulmonary or intensive care medicine must be available.

Proleukin administration has been associated with **capillary leak syndrome (CLS) which is characterized by a loss of vascular tone and extravasation of plasma proteins and fluid into the extravascular space. CLS results in hypotension and reduced organ perfusion which may be severe and can result in death. CLS may be associated with cardiac arrhythmias (supraventricular and ventricular), angina, myocardial infarction, respiratory insufficiency requiring intubation, gastrointestinal bleeding or infarction, renal insufficiency, edema, and mental status changes.**

Proleukin treatment is associated with impaired neutrophil function (reduced chemotaxis) and with an increased risk of disseminated infection, including sepsis and bacterial endocarditis. Consequently, preexisting bacterial infections should be adequately treated prior to initiation of Proleukin therapy. Patients with indwelling central lines are particularly at risk for infection with gram positive microorganisms. Antibiotic prophylaxis with oxacillin, nafcillin, ciprofloxacin, or vancomycin has been associated with a reduced incidence of staphylococcal infections.

Proleukin administration should be withheld in patients developing moderate to severe lethargy or somnolence; continued administration may result in coma.

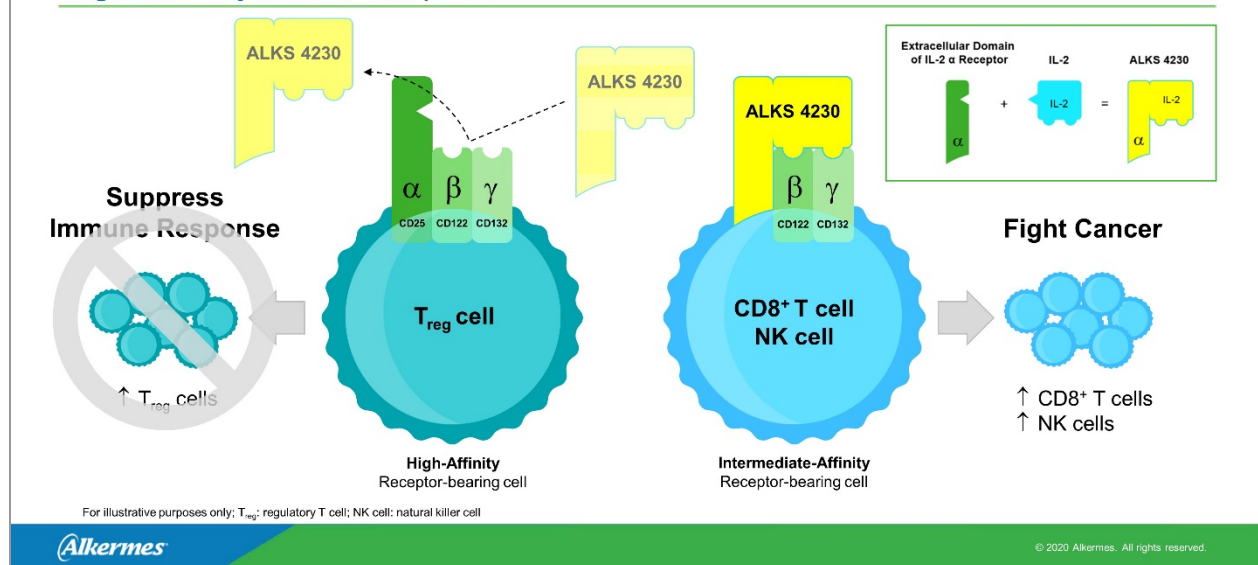
ALKS 4230 owes its roots to Proleukin or Recombinant Human IL-2, one of the first immunotherapies approved for metastatic melanoma and renal cell carcinoma that demonstrated complete and durable anti-tumor responses due to its activation of CD8+ T cells and Natural Killer cells associated with cancer-fighting immune responses.

Broader adoption of the therapy has been limited by its tolerability profile, notably vascular leak syndrome and severe hypotension.

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ALKS 4230 is 'Sterically Occluded' From Binding to the High-Affinity IL-2 Receptor

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ALKS 4230 was designed to retain the therapeutic benefits of recombinant human IL-2 by selectively activating anti-tumor effector cells while mitigating the IL-2-associated expansion of immunosuppressive regulatory T cells, or T regs, and activation of vascular endothelial cells.

4230 is a stable fusion protein, consisting of IL-2 and the alpha subunit of the high-affinity IL-2 receptor. This design allows ALKS 4230 to preferentially bind to the intermediate affinity IL-2 receptor located on CD8⁺ T cells and NK cells— shown here on the right. At the same time, it is sterically occluded from binding to the high-affinity receptor, which has been associated with certain undesirable effects of IL-2.

ALKS 4230 is administered as an inherently active drug, does not require any metabolic conversion, and does not degrade to native IL-2.

For a more detailed discussion on 4230's mechanism, I encourage you to refer to our SITC investor presentation from last year, available on our company website.

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Non-Clinical Data Summary

ALKS 4230 Features	Model
Preferentially binds and signals through the intermediate-affinity IL-2R ¹	✓ <i>In vitro</i>
Selectively activates and expands circulating NK cells and CD8 ⁺ T cells ¹	✓ Mouse, NHP
Negligible effects on T _{regs} ^{1,2}	✓ Mouse, NHP
Demonstrated superior anti-tumor efficacy compared to rhIL-2 ¹	✓ Mouse
Demonstrated enhanced anti-tumor activity in combination with a variety of immunotherapies including anti-PD-1, anti-CTLA-4 ² and a tyrosine kinase inhibitor, lucitanib ³	✓ Mouse

1. Lopes JE, Fisher JL, Pick HL, et al., ALKS 4230: a novel engineered IL-2 fusion protein with an improved cellular selectivity profile for cancer immunotherapy. *Journal for Immunotherapy of Cancer* 2020;8:e000673. doi: 10.1136/jitc-2020-000673
2. Losey HC, Lopes JE, Dean RL, et al., *Cancer Res* July 1 2017 (77) (13 Supplement) 581. DOI: 10.1158/1538-7445.AM2017-581
3. Lopes JE, Dusek RL, Robillard L, et al., *Cancer Res* Aug 15 2020 (80) (16 Supplement) 2202. DOI: 10.1158/1538-7445.AM2020-2202




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Our design concept for 4230 has been validated in preclinical models – which showed the desired pharmacokinetic and pharmacodynamic cell expansion profile, superior anti-tumor efficacy compared to recombinant human IL-2 as monotherapy, and enhanced anti-tumor activity in combination with a variety of immunotherapies including anti-PD-1, anti-CTLA-4 and the angiogenesis inhibitor, lucitanib.

These data support further exploration of ALKS 4230's potential clinical utility, as monotherapy and in combination with a variety of immunotherapies and other cancer treatments.

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Overview of ALKS 4230
Clinical Development Program

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The clinical development program for ALKS 4230 is progressing on multiple fronts.

Overview of ALKS 4230 Clinical Development Program

ARTISTRY-1 Phase 1/2	<ul style="list-style-type: none"> Intravenous (IV) dosing: Refractory advanced solid tumors Part A: Monotherapy dose escalation Part B: Monotherapy dose expansion Part C: ALKS 4230 + pembrolizumab combination
ARTISTRY-2 Phase 1/2	<ul style="list-style-type: none"> Subcutaneous dosing: Refractory advanced solid tumors Six-week monotherapy lead-in followed by ALKS 4230 + pembrolizumab combination <ul style="list-style-type: none"> Evaluating once-weekly and once-every-three-weeks dosing Efficacy expansion phase planned
ARTISTRY-3 Phase 2	<ul style="list-style-type: none"> IV dosing: Refractory advanced solid tumors, with accessible lesions for biopsy Five-week monotherapy lead-in followed by ALKS 4230 + pembrolizumab combination Assessment of tumor microenvironment from paired biopsies
ION-01 Phase 2	<ul style="list-style-type: none"> IV dosing: Anti-PD-1 pre-treated HNSCC patients ALKS 4230 + pembrolizumab combination Assessment of tumor microenvironment from paired biopsies Predictive biomarker assessments Collaboration with Fred Hutchinson Cancer Research Center

HNSCC: Head and neck squamous cell carcinoma



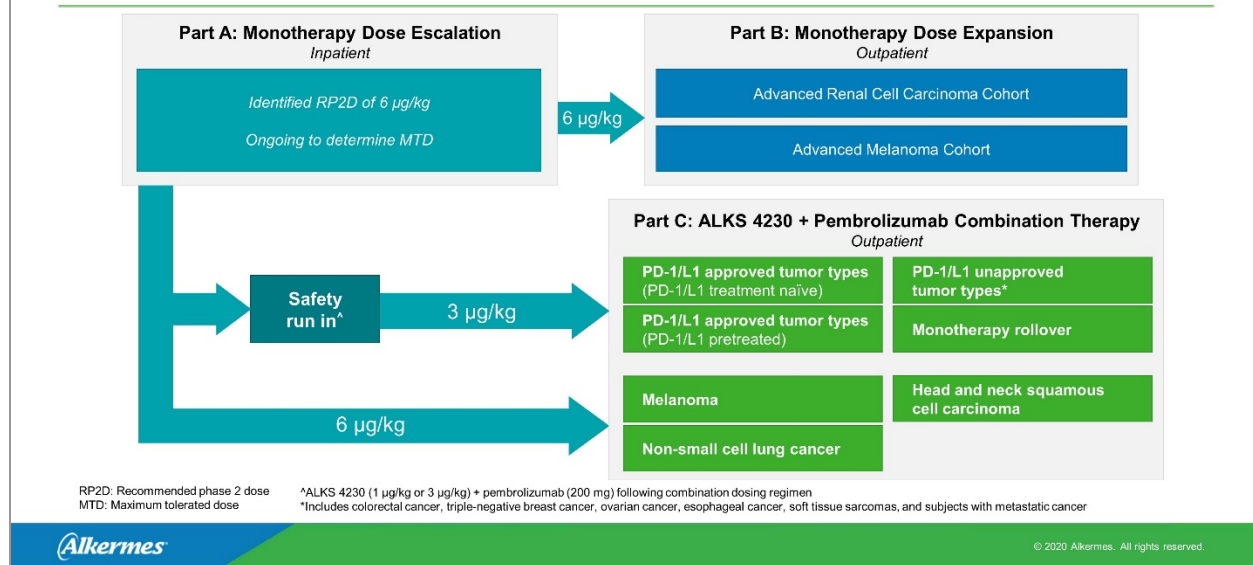
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In our ARTISTRY development program, we have two ongoing phase 1/2 studies, as well as a recently-initiated phase 2 study.

- ARTISTRY-1, evaluating ALKS 4230 administered intravenously, is the most advanced in enrollment and the subject of today's data presentation.
- ARTISTRY-2 is our subcutaneous dosing study, and is evaluating the safety, tolerability and efficacy of 4230 in both once-weekly and once-every-three-week dosing regimens.
- Both of these studies are evaluating ALKS 4230 as a monotherapy and in combination with pembrolizumab.
- We also recently announced the initiation of ARTISTRY-3, a phase 2 study to further evaluate the clinical and immunologic activity of ALKS 4230 monotherapy on the tumor microenvironment in advanced solid tumors. Findings from this study may help us answer important mechanistic questions and identify the tumor types for which ALKS 4230 could offer the most clinical benefit.

In addition, our phase 2 ION study, being conducted in collaboration with the Fred Hutchinson Cancer Research Center, is ongoing.

ALKS 4230: ARTISTRY-1 Phase 1/2 Study Design



Today we will focus on ARTISTRY-1.

The intent of this study is to evaluate the anti-tumor efficacy, safety, tolerability and pharmacodynamic effects of ALKS 4230, in both monotherapy and combination settings. There are 3 parts to the study.

Data from Part A, the ongoing monotherapy dose-escalation phase, led us to the identification of the 6 µg/kg/day dose as our recommended phase 2 dose, or RP2D, last year.

Part B is a monotherapy dose expansion phase evaluating ALKS 4230 at the RP2D in refractory melanoma and refractory renal cell carcinoma, which are the approved indications for recombinant human IL-2. For both of these tumor types, patients often have limited treatment options following disease progression on PD-1 therapy.

Understanding the single-agent activity of ALKS 4230 is an important aspect of its clinical profile and will help inform the potential therapeutic contributions of 4230 in possible combinations.

Today Dr. Vaishampayan will review ARTISTRY-1 study data as of the data cut of July 24th 2020, that is being presented at ESMO. As I mentioned earlier, since the time of that data cut, a subsequent partial response was observed in the monotherapy melanoma cohort. With this second partial response in that cohort, we achieved the protocol-defined response criteria for the Simon two-stage design enrollment, triggering expansion of the melanoma cohort to enroll up to a total of 41 patients.

I will speak to this in more detail later on this call.

Slide 11 (continued)

I will also note that patients in the Part B monotherapy expansion stage are eligible to roll over into the Part C combination stage of the study at the investigators' discretion, following four cycles in good standing or upon progressive disease.

Turning to Part C of ARTISTRY-1, this part of the study is evaluating two biologically active doses of ALKS 4230 in combination with pembrolizumab in a variety of advanced solid tumor types. The 3 $\mu\text{g/kg}$ dose is being evaluated in PD-1 approved tumor types in both refractory and treatment naïve patients, as well as certain PD-1-unapproved tumor types and a cohort of monotherapy rollover patients. These basket cohorts are designed to provide important signal seeking information and help inform future development strategies.

The 6 $\mu\text{g/kg}$ dose of 4230 is also being studied in combination with pembro in dedicated Part C cohorts in melanoma, non-small cell lung cancer and head and neck squamous cell carcinoma.

Anti-tumor response and duration of response assessments are based on RECIST 1.1 criteria and investigator-assessed, immune-related response, or iRECIST criteria. Unless otherwise noted, the safety data for all cohorts and the efficacy data for the monotherapy cohorts are from a data cutoff date of July 24th, while the efficacy data for the combination cohorts are from a data cutoff of August 7th.

ARTISTRY-1: Designed to Assess Safety, Tolerability and Anti-Tumor Activity of ALKS 4230 as Monotherapy and in Combination

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Establish Pharmacokinetic/Pharmacodynamic Profile

- Dose-dependent, selective expansion of NK and CD8⁺ T cells
- Negligible expansion of T_{regs} in the periphery
- PK/PD profile of ALKS 4230 remained consistent when used in combination with pembrolizumab



Demonstrate Anti-Tumor Efficacy

- Single-agent activity in monotherapy melanoma cohort
- Durable responses in combination with pembrolizumab
- Responses in multiple tumor types (in PD-1/L1 approved and unapproved cohorts) with combination therapy

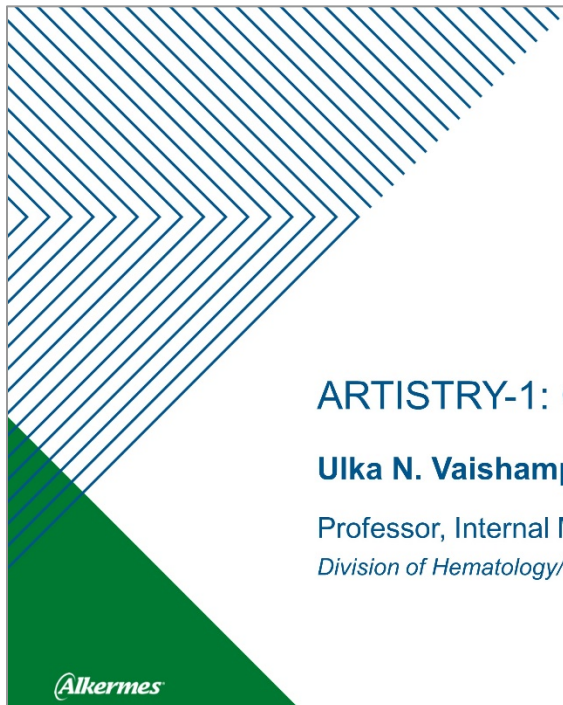


Establish Safety and Tolerability Profile

- Most frequently observed treatment-emergent adverse events were transient fever and chills, consistent with anticipated effects of immunotherapy (*Data as of July 24, 2020*):
 - Safety profile in combination with pembrolizumab generally consistent with monotherapy profile
 - In combination, no emerging evidence of additive toxicities to that already established for pembrolizumab alone
 - No vascular leak syndrome reported

As we have advanced through development of ALKS 4230, we have been accumulating evidence supporting our design hypothesis. In ARTISTRY-1, ALKS 4230 has shown:

- Dose-dependent, selective expansion of effector cell populations with negligible expansion of T_{regs}.
- Monotherapy efficacy activity, with evidence of disease stabilization and partial responses in melanoma, which will be discussed by Dr. Vaishampayan shortly.
- We have also seen durable and deepening responses for 4230 in combination with pembro, in both anti-PD1 approved and unapproved tumor types.
- In the combination cohorts, we have seen clinical benefit – including stable disease or partial responses – in patients who entered the study with difficult-to-treat, progressive disease. Certain of these patients have remained on treatment for more than 6 months, with some remaining on treatment for more than a year.
- And we have seen a clinically manageable safety profile with the most frequently observed treatment-emergent adverse events consistent with anticipated effects of immunotherapy, and no incidents of vascular leak.




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ARTISTRY-1: Clinical Data Update

Ulka N. Vaishampayan, M.D.

Professor, Internal Medicine
Division of Hematology/Oncology, University of Michigan



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Now, to provide an update from our ARTISTRY-1 clinical trial from the ESMO Virtual Congress, I'm pleased to introduce the ARTISTRY-1 lead investigator, Dr. Ulka Vaishampayan.

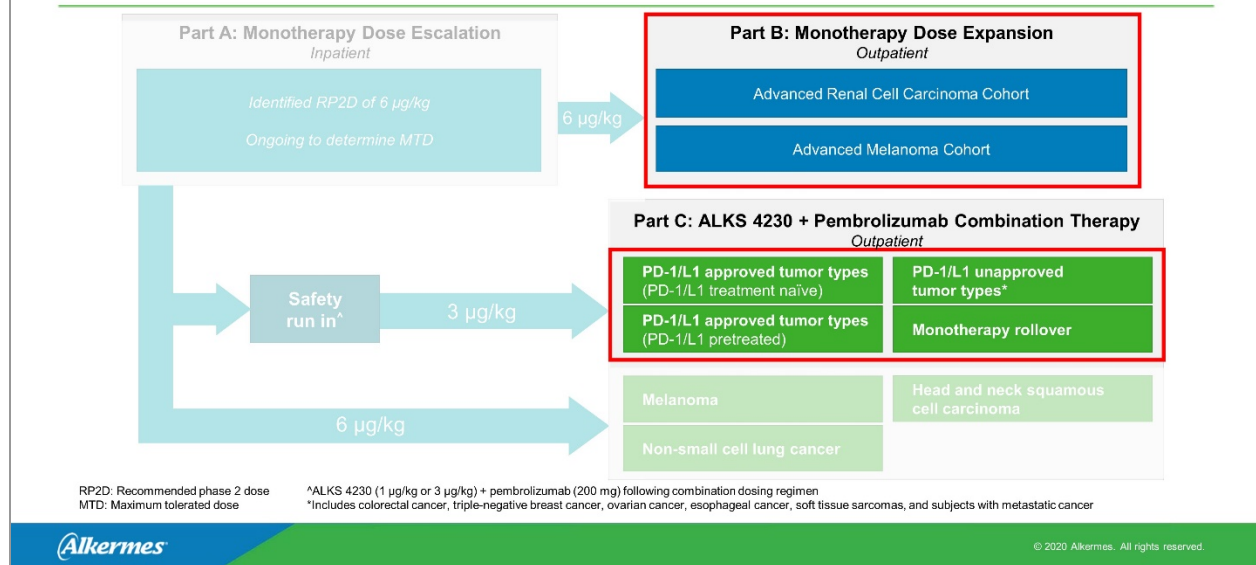
Dr. Vaishampayan is a professor of internal medicine within the division of hematology/oncology at the University of Michigan. Her research is primarily in translational drug development and early phase clinical trials in cancer with a focus on genitourinary malignancies.

Welcome, Dr. Vaishampayan, and thank you for joining us today.

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ALKS 4230: ARTISTRY-1 Phase 1/2 Study Design



Dr. Ulka Vaishampayan

Thank you, Craig, and good morning everyone.

Today, I will focus on new data from the Part B monotherapy cohort of patients who received the RP2D of 6 µg/kg of ALKS 4230 and the Part C combination cohorts of patients who received the 3 µg/kg dose of ALKS 4230 together with pembrolizumab.

ARTISTRY-1 Patient Baseline Characteristics

Characteristic	Part B: ALKS 4230 Monotherapy		Part C: ALKS 4230 + Pembrolizumab			
	Melanoma 6 µg/kg (n = 6)	RCC 6 µg/kg (n = 9)	PD-1/L1 Unapproved 3 µg/kg (n = 41)	PD-1/L1 Approved and PD-1/L1 Pretreated 3 µg/kg (n = 8)	PD-1/L1 Approved and PD-1/L1 Treatment Naïve 3 µg/kg (n = 11)	Monotherapy Rollover 3 µg/kg (n = 7)
Median age, years (range)	62.5 (43-73)	63 (38-73)	56.0 (34-83)	57.5 (24-71)	62.0 (48-73)	63.0 (43-73)
Male sex, n (%)	3 (50.0)	9 (100.0)	14 (34.1)	6 (75.0)	5 (45.5)	4 (57.1)
ECOG performance status, n (%)						
0	4 (66.7)	5 (55.6)	9 (22.0)	3 (37.5)	5 (45.5)	3 (42.9)
1	2 (33.3)	4 (44.4)	32 (78.0)	5 (62.5)	6 (54.5)	4 (57.1)
Total Prior Lines of Therapy						
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	3 (50.0)	1 (11.1)	2 (4.9)	1 (12.5)	3 (27.3)	1 (14.3)
2	1 (16.7)	3 (33.3)	10 (24.4)	1 (12.5)	2 (18.2)	1 (14.3)
3	0 (0.0)	1 (11.1)	11 (26.8)	4 (50.0)	4 (36.4)	2 (28.6)
4	2 (33.3)	0 (0.0)	5 (12.2)	2 (25.0)	2 (18.2)	1 (14.3)
5+	0 (0.0)	4 (44.4)	13 (31.7)	0 (0.0)	0 (0.0)	2 (28.6)

ECOG: Eastern Cooperative Oncology Group

Data as of 24 Jul 2020



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Shown here on slide 15 are the patient baseline characteristics for the data set being presented at ESMO. A total of 15 patients were enrolled in the monotherapy cohorts and 67 patients were enrolled in the 3 µg/kg combination cohorts. At the time of enrollment, all patients had rapidly progressing disease. All of these patients were pretreated, with the majority having received multiple lines of prior therapy.

ARTISTRY-1 Safety Summary†

- Safety profile of ALKS 4230 in combination with pembrolizumab generally consistent with monotherapy profile
- In combination, no emerging evidence of additive toxicities to that already established for pembrolizumab alone
- No vascular leak syndrome reported

Monotherapy (Part B)	Combination with Pembrolizumab (Part C)*
<ul style="list-style-type: none"> • Chills and pyrexia: Most frequently reported adverse events (AEs); anticipated effects of cytokine administration <ul style="list-style-type: none"> – Transient, all grades ≤2 in severity • Hypotension: Mostly grades ≤2 in severity <ul style="list-style-type: none"> – One patient had a grade 3 transient hypotension that was managed with fluids • No discontinuations occurred due to treatment-related AEs • No deaths due to AEs were reported 	<ul style="list-style-type: none"> • Chills and pyrexia: Most frequently reported AEs; anticipated effects of cytokine administration <ul style="list-style-type: none"> – Transient, all grades ≤2 in severity • Hypotension: Mostly grades ≤2 in severity • Discontinuations due to ALKS 4230 included: fatigue, pneumonitis, infusion-related reaction (as assessed by the investigator) • Two deaths occurred in pancreatic cancer patients <ul style="list-style-type: none"> – First due to underlying cancer and assessed as unrelated to treatment – Second† due to inanition (starvation) and assessed as related to both study drugs

*Overall data based on all patients enrolled in Part C of the trial (all cohorts). *Occurred after the data cutoff date of 24 Jul 2020

† Data as of 24 Jul 2020*



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This slide outlines the safety data observed for these cohorts, as of the July 24th cutoff date, unless otherwise noted.

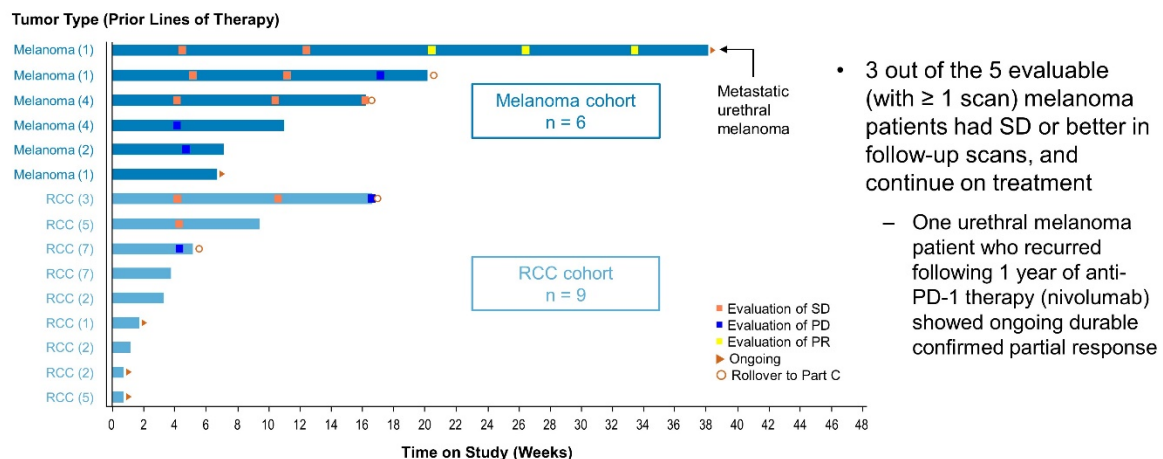
ALKS 4230 given in combination with pembrolizumab did not demonstrate any additive toxicity to that established with pembrolizumab alone.

The side effect profile across the monotherapy and combination cohorts was generally consistent with what one would expect to see with cytokine therapy, such as fever, chills and low-grade hypotension. Importantly, no signs of vascular leak syndrome—the hallmark toxicity associated with high-dose IL-2—were observed.

In the combination cohorts, two deaths were reported in patients with pancreatic cancer. One death was due to the underlying cancer and assessed as unrelated to treatment with ALKS 4230. The other was due to inanition, or starvation, and assessed as related to both study drugs. No deaths were reported in the Part B monotherapy cohorts.

Slide 17

ALKS 4230 6 µg/kg Monotherapy: Responses Among Melanoma and RCC Patients



- 3 out of the 5 evaluable (with ≥ 1 scan) melanoma patients had SD or better in follow-up scans, and continue on treatment
- One urethral melanoma patient who recurred following 1 year of anti-PD-1 therapy (nivolumab) showed ongoing durable confirmed partial response

Turning to efficacy data, I'll first review the overall response data from the monotherapy expansion cohorts. Efficacy data presented here are as of the cutoff date of July 24, 2020, unless otherwise noted.

In this cohort, 15 patients, 6 with melanoma and 9 with renal cell carcinoma, received the 6 µg/kg dose of ALKS 4230. This swimmer's plot shows the overall responses and the duration in those patients.

At the time of the data cut, out of the 5 evaluable melanoma patients who had received 1 or more scans, 3 patients had stable disease or better. Among these 3 patients, one had a confirmed partial response, and remained on ALKS 4230 monotherapy as of September 1st, and the other two demonstrated stable disease on at least two consecutive scans and have since rolled over into Part C.

Let's now take a closer look at the patient who had a confirmed partial response.

ALKS 4230 6 µg/kg Monotherapy:

Case Study: 66-Year-Old Female With Urethral Melanoma

Diagnosis

Melanoma

- Diagnosed with primary urethral mucosal melanoma in 2017

Treatment

- Cystectomy and pelvic node dissection for urethral melanoma in June 2017, followed by one year of adjuvant nivolumab treatment (Sept 2017 – Sept 2018)
- No treatment between Sept 2018 and Sept 2019
- Recurrence: Sept 2019

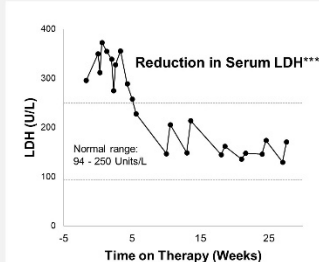
October 2019 – present*
(On treatment > 11 months; Ongoing)

- ALKS 4230 therapy
 - 6 µg/kg IV ALKS 4230

On-Study Benefits

	Change in Target Lesions from Baseline
Cycle 2	Stable Disease (SD)**: 8% increase
Cycle 4	SD: 17% reduction
Cycle 6	Partial Response (PR)** : 32% reduction
Cycle 8	Confirmed PR : 35% reduction
Cycle 10	PR: 38% reduction
Cycle 12	PR: 39% reduction

- Reduction in size of peritoneal implants, ascites, and retroperitoneal lymph nodes
- Patient had immune-related serious AEs: Grade 2 iritis / vitritis successfully treated with steroid eye drops
- Patient had a grade 3 serious AE of transient hypotension managed with fluids*



*Patient continued on therapy as of 01 Sept 2020
**Per RECIST criteria

*Hypotension occurred on study day 242 and resolved within the same day. Immune-related AEs occurred on study day 98 and are still ongoing ***LDH: Lactate Dehydrogenase

Data as of 27 Jul 2020 unless noted otherwise

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This is a case study of a 66-year-old female patient who was diagnosed with metastatic urethral mucosal melanoma in 2017. The patient completed one year of nivolumab in September 2018, followed by one year without any treatment. Her disease recurred in September 2019 and was progressive at the time of her enrollment into ARTISTRY-1 in October 2019.

Within the first 2 cycles of ALKS 4230 monotherapy, this patient experienced stable disease and her tumor began to shrink. She achieved a Partial Response by week 20 of treatment and a deepening of the response was observed through week 39 of treatment. As of her July 27th scan, her tumor had reduced by 39%.

Further, the patient's serum lactate dehydrogenase, or LDH, a known marker for treatment response in melanoma, normalized at Week 5, and has remained within the normal range.

This patient experienced grade 3 transient hypotension, which was managed with IV fluids.

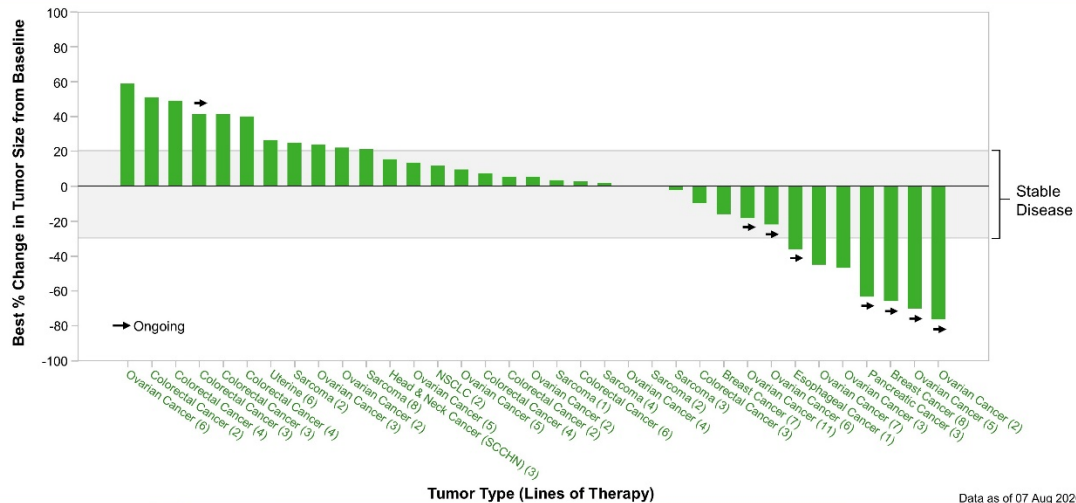
As of September 1st, this patient remained on ALKS 4230 monotherapy for more than 11 months.

I will also pause here to point out that this patient experienced iritis, an inflammation of the eye, which is an immune-related SAE. Immune-related adverse events like this are consistent with the anticipated effects of cytokine administration and may be a leading indicator of ALKS 4230's activity.

Taking a step back, the early responses observed with ALKS 4230 as a monotherapy treatment are an important element of its potential clinical utility.

Slide 20

ALKS 4230 3 µg/kg in Combination With Pembrolizumab: Best Response of Target Lesion in PD-1/L1 Unapproved Tumors



Data as of 07 Aug 2020

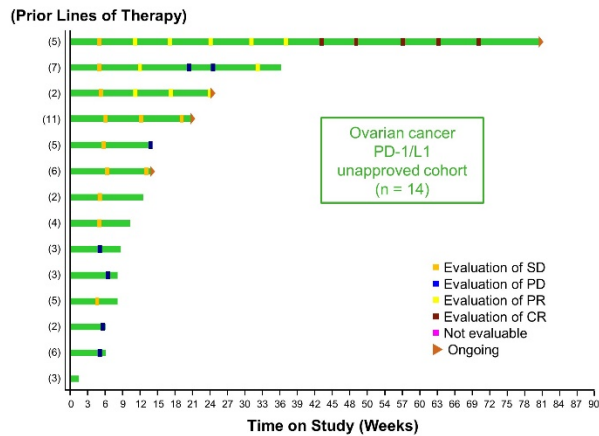
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Here is a waterfall plot on slide 20 of the best response by target lesion for the 35 evaluable patients from the PD-1 unapproved cohort. The area between the two gray horizontal lines indicates stable disease per RECIST criteria. As evidenced by the arrows, as of the data cutoff date of August 7th, 2020, eight patients continued on therapy with maturing data.

Slide 21

ALKS 4230 3 µg/kg in Combination With Pembrolizumab: Responses in Ovarian Cancer Patients



- 14 ovarian cancer patients enrolled; 13 evaluable (with ≥ 1 scan)
 - Patients were heavily pre-treated and had PD at the time of enrollment
- 9 of 13 patients had SD or better on at least one scan

CR: complete response; PD: progressive disease; PR: partial response; SD: stable disease

Data as of 07 Aug 2020

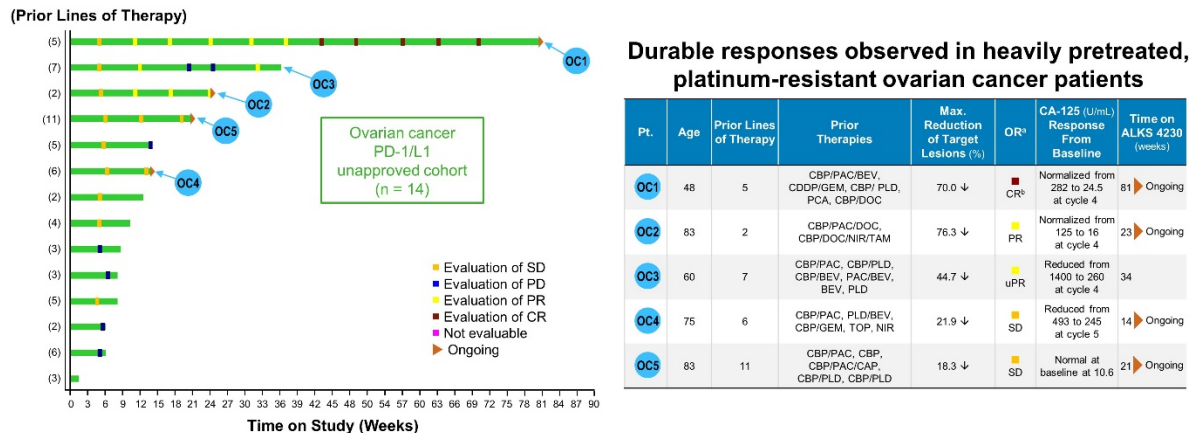
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Now, let's focus specifically on the ovarian cancer patients from the PD-1 unapproved group. This swimmer's plot on slide 21 shows the 14 ovarian cancer patients enrolled in this cohort, 13 of whom were evaluable at the time of the data cut. These patients entered the study with progressive ovarian cancer and were generally heavily pretreated.

Of these 13 evaluable patients, 9 patients showed stable disease on their first scan, as indicated by the orange boxes.

ALKS 4230 3 µg/kg in Combination With Pembrolizumab: Responses in Platinum-Resistant Ovarian Cancer Patients



*Assessed by investigator. *CR due to node shrinkage to < 10 mm short axis, which is considered normal
 BEV: bevacizumab; CAP: capecitabine; CBP: carboplatin; CDDP: cisplatin; CR: complete response; DOC: docetaxel; GEM: gemcitabine; Max: maximum; NIR: niraparib; OC: ovarian cancer; OR: objective response; PAC: paclitaxel; PCA: paclitaxel albumin; PD: progressive disease; PLD: pegylated liposomal doxorubicin hydrochloride; PR: partial response; SD: stable disease; TAM: tamoxifen; TOP: topotecan; uPR: unconfirmed partial response

Data as of 07 Aug 2020

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Among these patients, six received a second scan by the data cutoff and five of these six patients experienced stable disease or better during the course of the treatment with ALKS 4230 and pembro, including one patient who demonstrated a tumor burden reduction of 76%. All 5 of these patients received prior platinum-based chemotherapy and were assessed by the investigators as platinum-resistant. Some had also received prior bevacizumab and/or a PARP inhibitor. Of these five patients:

- o 3 patients – noted as patients OC 1, OC 2 and OC 3 on this slide – experienced clinical responses, including one confirmed complete response, one confirmed partial response, and one unconfirmed partial response.
- o The other 2 patients—noted here as patients OC 4 and OC 5—achieved stable disease and had tumor shrinkage of 22% and 18%, respectively, as of the August 7th data cut, and had remained on therapy for more than 14 weeks and 21 weeks, respectively.
- o As of August 7th, 4 of these 5 platinum-resistant ovarian cancer patients continued on therapy.

Next, I will go into greater detail on two of these patients, marked as OC1 and OC2 on this slide.

Slide 23

ALKS 4230 3 µg/kg in Combination With Pembrolizumab:

Case Study: 48-Year-Old Female With High-Grade, Progressive Ovarian Cancer

OC1

Diagnosis

High-Grade Serous Ovarian Cancer

- PD-L1 status: TPS = 20%
- *BRCA* status: wild-type
- Platinum-resistant

Treatment

- 5 prior lines of treatment[‡]
 - 4 lines of platinum-based chemo, bevacizumab
- No prior checkpoint inhibitor therapy

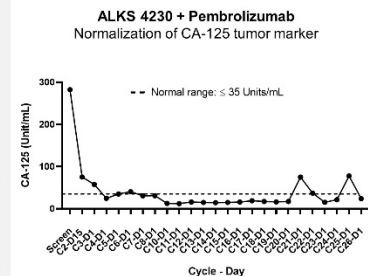
January 2019 – Present*
(On treatment > 1.5 years; Ongoing)

- ALKS 4230 + pembrolizumab therapy
 - 3 µg/kg IV ALKS 4230

On-Study Benefits

Cycle 2	Stable Disease (SD)*
Cycle 4	Partial Response (PR)*: 60% reduction in target lesions; Normalization of CA-125
Cycle 6	Confirmed PR
Cycle 10	Complete Response (CR)* : 70% reduction in target lesions
Cycles 12-22	Confirmed CR

- Tolerated therapy well
- No serious adverse events reported



*Patient continued on therapy as of 07 Aug 2020

TPS: Tumor proportion score; *Per RECIST criteria

[‡]Prior treatments: Carboplatin/TAXOL®/AVASTIN®, cisplatin/gemcitabine, carboplatin/DOXIL®, ABRAXANE®, carboplatin/TAXOTERE®

Data as of 07 Aug 2020

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Shown here on slide 23 are details for a 48-year-old female patient who enrolled in the study with a diagnosis of high-grade, progressive ovarian cancer, which was *BRCA* wild-type. She had received 5 prior lines of therapy.

This patient initiated ALKS 4230 in combination with pembro in January 2019. At cycle 4, she demonstrated a partial response with a 60% decrease in target lesions, along with a complete normalization of her CA-125 levels, which is an established prognostic indicator in ovarian cancer.

At cycle 10, the patient had a complete response with a 70% decrease in target lesions, which was confirmed at cycle 12.

Throughout her treatment period, the patient tolerated therapy well and did not experience any serious adverse events.

As of August 7th, the patient had a sustained complete response and remained on study.

Slide 24

ALKS 4230 3 µg/kg in Combination With Pembrolizumab:

Case Study: 83-Year-Old Female With Progressive Ovarian Cancer

OC2

Diagnosis

Ovarian Cancer

- PD-L1 status: unknown
- BRCA status: negative
- Platinum-resistant

Treatment

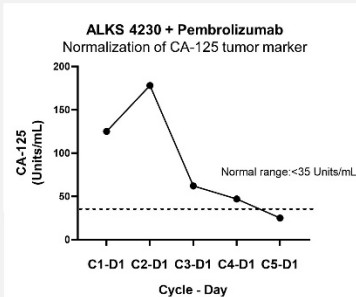
- 2 prior lines of treatment with best response of complete response[†]
 - Platinum-based chemo, PARP inhibitor
- No prior checkpoint inhibitor therapy

February 2020 – Present*
(On treatment > 6 months; Ongoing)

- ALKS 4230 + pembrolizumab therapy
 - 3 µg/kg IV ALKS 4230

On-Study Benefits

Cycle 2	Stable Disease (SD)*: 6% reduction in target lesions
Cycle 4	Unconfirmed Partial Response (PR)*: 55% reduction in target lesions Normalization of CA-125
Cycle 6	Confirmed PR: 68% reduction in target lesions
Cycle 8	76% reduction in target lesions



- No serious adverse events reported
- The only treatment-related grade ≥ 3 AE reported was grade 3 neutropenia

*Patient continued on therapy as of 07 Aug 2020

+per RECIST criteria; PARP: Poly (ADP-ribose) polymerase

†Prior treatments: TAXOL®/Carboplatin/TAXOTERE®, TAXOTERE®/Carboplatin/ZEJULA®/Tamoxifen

Data as of 07 Aug 2020

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The next case study is an 83-year-old female patient with ovarian cancer, which was BRCA negative. She had received 2 prior lines of therapy, and had progressive disease when she entered ARTISTRY-1 in February 2020.

At cycle 2 of treatment, the patient demonstrated stable disease with a 6% decrease in target lesions. Her tumor continued to shrink with treatment, and at cycle 8, she had a 76% decrease in target lesions.

As of the August 7th data cutoff, the patient had not experienced any serious adverse events and remained on therapy.

High Unmet Needs Remain for Treatment of Ovarian Cancer

Ovarian Cancer Burden	Limited Treatment Options
<ul style="list-style-type: none"> • Second most common gynecological cancer¹ <ul style="list-style-type: none"> – U.S. prevalence: ~233K cases in 2017² • Leading cause of gynecologic cancer-related deaths in the U.S.¹ <ul style="list-style-type: none"> – 5-year survival rate for stage IV ovarian cancer of 29%³ – Median overall survival (mOS) for platinum-resistant ovarian cancer is less than 12 months⁴ 	<ul style="list-style-type: none"> • 1L (Standard of Care) <ul style="list-style-type: none"> – Surgery + platinum-based chemotherapy +/- bevacizumab followed by bevacizumab and/or PARP inhibitor as maintenance⁵ – Many become platinum resistant (refractory) and progress < 6 months after completion of platinum-based chemotherapy⁶ • Few treatment options post-platinum chemotherapy; patients not treated with curative intent <ul style="list-style-type: none"> – In one study of non-platinum chemotherapy, objective response rate was 12% and median progression free survival (mPFS) was 3.4 months⁷ • Anti-PD-1/L1 (e.g., pembrolizumab, atezolizumab) have been shown to be ineffective for treatment of ovarian cancer^{8,9} <ul style="list-style-type: none"> – Pembrolizumab efficacy in ovarian cancer is ~10% for high PD-1/L1 expression⁸

1. <https://www.cdc.gov/cancer/ovarian/statistics/index.htm> 2. <https://seer.cancer.gov/statistics/html/ovary> 3. <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2020/cancer-facts-and-figures-2020.pdf> 4. <https://pubmed.ncbi.nlm.nih.gov/24607295/> 5. <https://www.frontiersin.org/articles/10.3389/fonc.2020.00782/full> 6. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2962713/> 7. Pujado-Lauraine E, Hilpert F, Weber S, et al. Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: The AURELIA open-label randomized phase III trial. *J Clin Oncol*. 2014;32(13):1302-1308. doi: 10.1200/JCO.2013.51.4489. 8. Matulonis UA, Shapira-Frommer R, Sardin AD, et al. Antitumor activity and safety of pembrolizumab in patients with advanced recurrent ovarian cancer: results from the phase II KEYNOTE-100 study. *Ann Oncol*. 2019;30(7):1080-1087. doi: 10.1093/annonc/mdz135. 9. Gonzalez-Martín A, Sanchez-Lorenzo L. Immunotherapy with checkpoint inhibitors in patients with ovarian cancer: Still promising? *Cancer*. 2019;126 Suppl 24:4616-4622. doi: 10.1002/cnecr.22520

As we think about the treatment landscape for ovarian cancer, the standard of care for first-line treatment is multi-modality, involving both surgery, and platinum-based chemotherapy, with or without bevacizumab and a PARP inhibitor as maintenance therapy for patients who are BRCA positive. It is important to note here that there are no anti-PD-1 treatments approved for ovarian cancer.

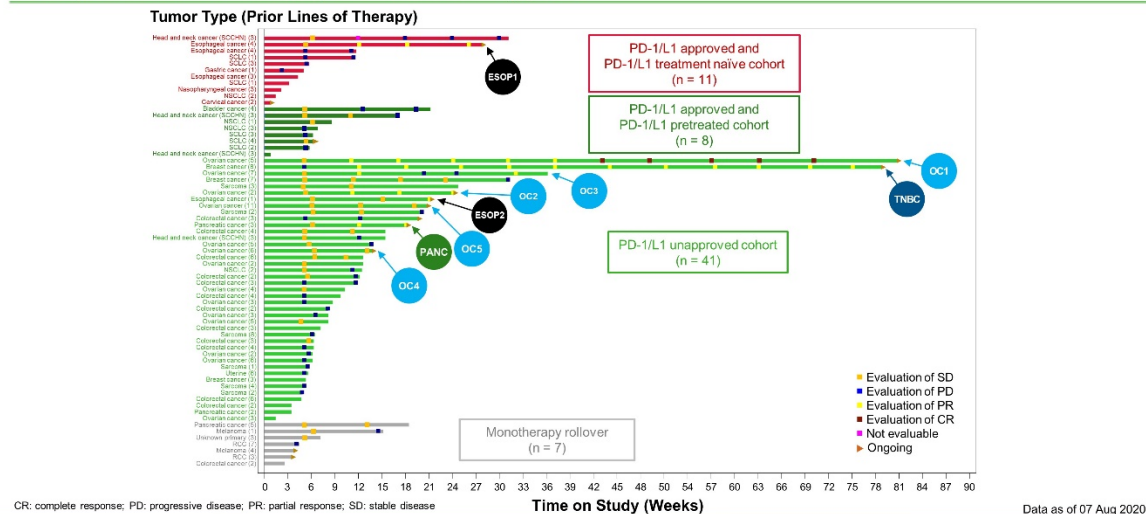
Following first-line platinum-based chemotherapy, many patients may become platinum resistant, and their disease often progresses within 6 months after completion of therapy.

Unfortunately, there are limited treatment options for patients with platinum-resistant ovarian cancer. Non-platinum chemotherapy has low response rates and is associated with short progression-free survival. The median overall survival for platinum-resistant ovarian cancer is less than 12 months.

Given the high unmet need for this patient population, I am really encouraged by the responses seen so far in ovarian cancer with ALKS 4230 in combination with pembro.

Slide 26

ALKS 4230 3 µg/kg in Combination With Pembrolizumab: Responses in Multiple Tumor Types



Let's take a closer look now at the responses we have seen in other tumor types.

Clinical responses associated with significant tumor burden reduction were observed in 4 additional patients in Part C. This includes one patient with triple-negative breast cancer, one patient with pancreatic cancer, and two patients with esophageal cancer.

Also, as shown by the orange boxes on slide 26, a number of these patients, all of whom entered the trial with progressive disease, experienced prolonged stable disease for two or more consecutive scans while on treatment with ALKS 4230 in combination with pembrolizumab.

I will now discuss the two esophageal responses.

Slide 27

ALKS 4230 3 µg/kg in Combination With Pembrolizumab:

Case Study: 54-Year-Old Female With Esophageal Cancer

Diagnosis

Adenocarcinoma of the GEJ

- Diagnosed: January 2014
- PD-L1 status: unknown

Treatment

- 4 prior lines of treatment with best response of stable disease[†]
- No prior checkpoint inhibitor therapy

January 2020 – Present* (On treatment 7 months; Ongoing)

- ALKS 4230 + pembrolizumab therapy
 - 3 µg/kg IV ALKS 4230

On-Study Benefits

Cycle 2	Stable Disease (SD)*: 1% reduction in target lesions from baseline
Cycle 4	Partial Response (PR)*: 28% reduction in target lesions from baseline
Cycle 6	Confirmed PR: 43% reduction in target lesions from baseline
Cycle 8	PR: 48% reduction in target lesions from baseline

- Grade 2 treatment-related arthralgias/arthritis managed with NSAIDs, hydroxychloroquine, and methotrexate

*Patient continued on therapy as of 07 Aug 2020
*Per RECIST criteria

[†]Prior treatments: paclitaxel/carboplatin, irinotecan, paclitaxel/ramucirumab, trastuzumab
GEJ: esophagogastric junction; NSAID: Non Steroidal Anti Inflammatory Drugs

Data as of 07 Aug 2020



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This case is a 54-year-old female patient who had an adenocarcinoma of the gastroesophageal junction. This tumor type is anti-PD1 approved, however, this patient had no prior checkpoint inhibitor therapy. She had received four prior lines of therapy, before entering the study in January 2020.

At cycle 6, she had a confirmed partial response with a 43% decrease in target lesions. At cycle 8, her response deepened to a 48% decrease.

The patient experienced grade 2 treatment-related joint pain, which was managed with medication. As of August 7th, the patient remained on study.

ALKS 4230 3 µg/kg in Combination With Pembrolizumab:

Case Study: 82-Year-Old Male With Esophageal Cancer



Diagnosis

Esophageal Squamous Cell Carcinoma

- Diagnosed: February 2018
- PD-L1 status: unknown

Treatment

- 1 prior line of treatment[‡]
- No prior checkpoint inhibitor therapy

March 2020 – Present* (On treatment 5 months; Ongoing)

- ALKS 4230 + pembrolizumab therapy
 - 3 µg/kg IV ALKS 4230

On-Study Benefits

Cycle 2	Stable Disease (SD) [†] : 5% reduction in target lesions from baseline
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Cycle 4	SD: 23% reduction in target lesions from baseline
---------	--

Cycle 6	Partial Response^{†*} : 36% reduction in target lesions from baseline
---------	---

- Grade 3 treatment-related adverse events: neutropenia, thrombocytopenia, lymphopenia, decrease in white blood cell count, fatigue
- No serious adverse events reported

*Patient continued on therapy as of 07 Aug 2020
*Awaiting confirmation

[‡]Prior treatment: carboplatin/TAXOL®
[†]Per RECIST criteria

Data as of 07 Aug 2020











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The next case is an 82-year-old male patient with esophageal squamous cell carcinoma. Unlike the previous esophageal patient, this patient's tumor type is not approved for treatment with anti-PD1 therapies.

He initiated ALKS 4230 combination treatment with pembro in March 2020. At cycle 4, his target lesions had decreased by 23%, and at cycle 6, he had a partial response awaiting confirmation with a 36% decrease in target lesions. This patient experienced transient grade 3 treatment-related AEs, including neutropenia and lymphopenia, and no serious AEs.

As of August 7th, the patient remained on study.

ALKS 4230 3 µg/kg in Combination With Pembrolizumab: Summary of Responses in Multiple Tumor Types

Cohort	Pt.	Age (years)	Prior Lines of Therapies	Prior Therapies	Max. Reduction of Target Lesions (%)	OR ^a	Time on ALKS 4230 (weeks)
PD-1/L1 unapproved cohort		47	5	DOX/CTX; PAC; PCA; TAM; CAP; PCA; ERI; GEM/CBP	66 ↓	 iPR	74 ▶ Ongoing
PD-1/L1 unapproved cohort		74	3	PCA/GEM; 5FU/IRI; 5-FU/IRI/calcium folinate	63 ↓	 PR	17*
PD-1/L1 approved; PD-1/L1 treatment naïve		54	4	CBP/PAC; CDDP/HER/5FU/IRI; PAC/RAM; Chk1i/GEM	48 ↓	 PR	28 ▶ Ongoing
PD-1/L1 unapproved cohort		82	1	CBP/PAC	36 ↓	 uPR	20 ▶ Ongoing

^aAssessed by investigator. *Patient died after the Aug 07 data cut off.
5-FU: fluorouracil; Chk1i: LY2880070; CTX: cyclophosphamide; DOX: doxorubicin hydrochloride; ERI: eribulin; ESOP: esophageal cancer patient; HER: trastuzumab; iPR: immune partial response; IRI: irinotecan; Max.: maximum; PANC: pancreatic cancer patient; RAM: ramucirumab; TNBC: triple-negative breast cancer

Data as of 07 Aug 2020

The responses we have seen with ALKS 4230 in combination with pembro in these non-ovarian tumor types are also encouraging, with reductions in target lesions of up to 66% and patients continuing on ALKS 4230 therapy for up to 74 weeks as of the August 7th cutoff. These data support further clinical evaluation of ALKS 4230 in combination with pembro.

Of note, the 66% reduction in tumor size was observed in a patient with triple-negative breast cancer. This patient's case was presented last year at SITC and she has continued on treatment for more than a year and a half with a sustained and deepening response.

It is important to note that these patients, except for the one pancreatic patient who unfortunately passed away, are doing well on treatment and remain in the study.

Summary: ARTISTRY-1 Part B Monotherapy and Part C Combination with Pembrolizumab

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ALKS 4230 is an investigational, novel agent with encouraging activity and tolerability

- Demonstrated a clinically manageable safety profile when used as monotherapy or in combination with anti-PD-1 therapy, with no vascular leak syndrome
- Pharmacokinetic and pharmacodynamic effects support selective activation of the intermediate-affinity IL-2 receptor complex and are not altered by the addition of pembrolizumab

Monotherapy (6 µg/kg dose)

3 of 5 melanoma patients with ≥ 1 scan had stable disease or better in follow-up scans, and continue on treatment

- A **durable and deepening response** was observed in 1 melanoma patient (previously treated with anti-PD-1 therapy) who received ALKS 4230 monotherapy

Combination Therapy (3 µg/kg dose)

There was an encouraging signal for the combination of ALKS 4230 with pembrolizumab in heavily pretreated **platinum-resistant ovarian cancer patients** who do not typically respond to pembrolizumab alone

- One ovarian cancer patient achieved a complete response

This study is ongoing and data support additional research of monotherapy and combination therapy with ALKS 4230

Data as of 24 Jul 2020



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In summary, these data provide encouraging evidence of antitumor efficacy for ALKS 4230 as both a monotherapy and in combination with pembro, with a safety profile generally consistent with the anticipated effects of cytokine therapy, but with no reports of vascular leak syndrome, which is otherwise a hallmark toxicity of high dose IL-2 treatment.

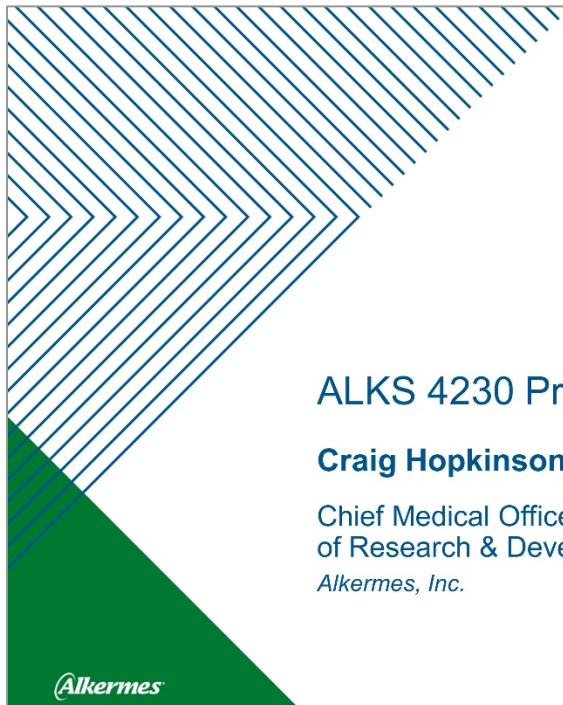
The most frequently observed adverse events regardless of causality in both the monotherapy and combination cohorts were transient fever and chills.

In terms of efficacy, we saw durable and deepening responses to ALKS 4230 as a monotherapy in melanoma and in combination with pembrolizumab in a diverse set of difficult-to-treat tumor types.

The data presented here provide new insights into the potential clinical value of ALKS 4230 as a novel treatment option in oncology and I believe future research for its use as monotherapy and in combination with other therapies is certainly warranted.

With that, I will turn it back over to Dr. Hopkinson.

Slide 31



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ALKS 4230 Program Updates and Next Steps

Craig Hopkinson, M.D.
Chief Medical Officer and Executive Vice President
of Research & Development
Alkermes, Inc.

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Dr. Craig Hopkinson

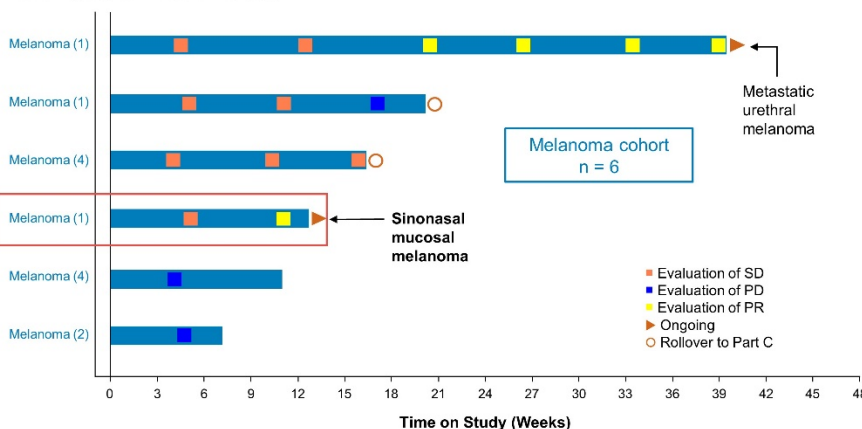
Thank you, Dr. Vaishampayan for your review of the data today, and for your participation in the ARTISTRY-1 study.

In addition to the review you just heard on ARTISTRY-1, as I mentioned at the start of the call, since the date of the data cut for the ESMO mini-oral presentation, an additional melanoma patient in the monotherapy cohort achieved a partial response, awaiting confirmation.

Slide 32

ALKS 4230 6 µg/kg Monotherapy: Melanoma Cohort Recent Updates Post-ESMO 2020 Data Cutoff Date

Tumor Type (Prior Lines of Therapy)



- A new **PR awaiting confirmation** observed in a sinonasal mucosal melanoma patient
 - 74-year-old male patient had prior nivolumab treatment and was progressive at the time of enrollment
 - **23% tumor shrinkage at cycle 2 (SD)**
 - **39% tumor shrinkage at cycle 4 (PR)**

PD: progressive disease; PR: partial response; SD: stable disease.

Data as of 01 Sept 2020

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This 74-year old male patient with sino-nasal mucosal melanoma had prior nivolumab treatment and had progressive disease at the time of enrollment into the ARTISTRY-1 study in June 2020.

At cycle 4 of monotherapy treatment with ALKS 4230, this patient demonstrated a 39% tumor shrinkage. As of September 1st, he remained on treatment.

Interestingly, both partial responses observed to date with ALKS 4230 monotherapy have been in patients with mucosal melanomas who had received prior PD-1 therapy. Mucosal melanoma is considered a particularly aggressive form of melanoma and is often not discovered until an advanced stage. Treatment options for this subtype of melanoma are very limited.

ALKS 4230 6 µg/kg Monotherapy: Melanoma Cohort Protocol-Defined Response Criteria Achieved, Expansion Ongoing

- Protocol-defined efficacy response criteria achieved, triggering expansion of this cohort:
 - 4 out of the first 6 evaluable patients (with ≥ 1 scan) had stable disease or better
 - 2 of these patients achieved a partial response
- Second stage of enrollment initiated, per Simon two-stage design enrollment (to enroll up to a total of 41 patients):

After the RP2D is determined, the second part of the study (ie, Part B) will begin. In this part of the study, up to 41 subjects with melanoma (including no more than 5 ocular melanoma subjects) and up to 41 subjects with RCC may be enrolled to receive ALKS 4230 at the RP2D. Enrollment to these cohorts will follow a PR (unconfirmed) Simon's two-stage design enrollment as outlined in Table 2. Response assessments will be based on the RECIST guidelines.

Table 2: Simon's Two-stage Design Enrollment for Subjects in Part B

	Undesirable rate	Desirable rate	N1	Enroll more if	N2	Total
Expansion Cohort B1: Refractory RCC	5%	20%	21	≥ 2 PR/CR	20	41
Expansion Cohort B2: Refractory Melanoma ^a	5%	20%	21	≥ 2 PR/CR	20	41

Abbreviations: CR=complete response; PR=partial response; RCC=renal cell carcinoma

^a No more than 5 ocular melanoma subjects may be enrolled into this cohort.

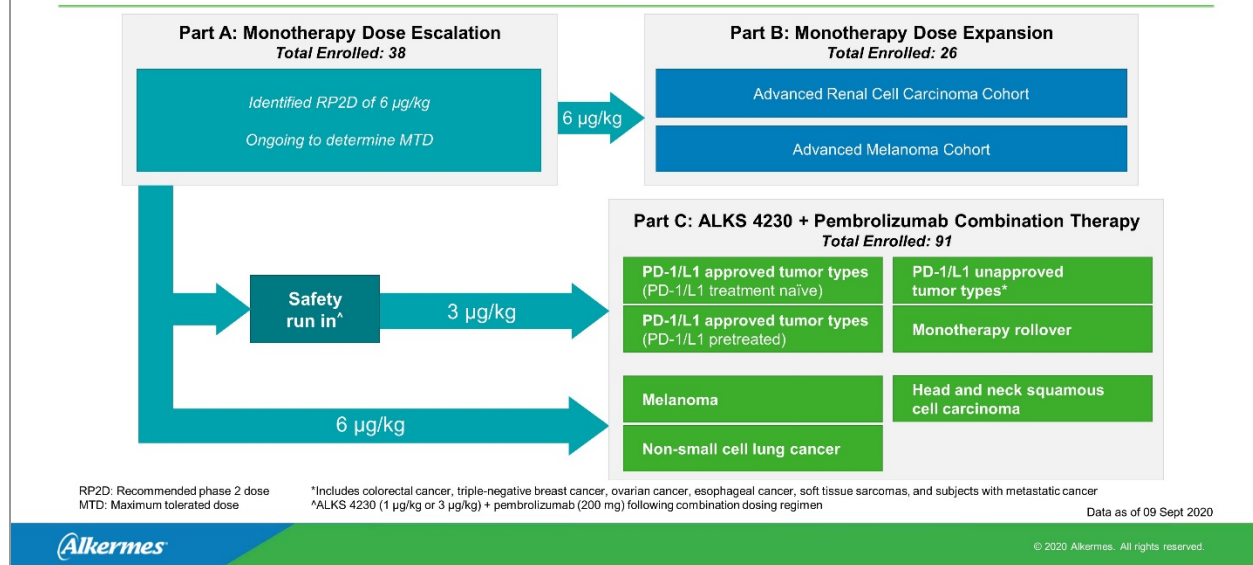
Data as of 01 Sept 2020

The recruitment of subjects in the monotherapy stage of ARTISTRY-1 follows a Simon two-stage study design, commonly used for phase 2 studies in oncology for practical and ethical considerations. The first stage was designed to enroll up to 21 patients in each of the melanoma and renal cell carcinoma cohorts. If protocol-defined response criteria are achieved in this first stage of 21 patients, the applicable cohort is expanded to recruit up to an additional 20 patients.

With two partial responses observed among the first 6 evaluable patients in the monotherapy melanoma cohort, the protocol-defined response criteria for expansion of this cohort were achieved, and up to an additional 20 patients will be enrolled in this cohort for a total of up to 41 patients.

These data are consistent with our design hypothesis for ALKS 4230 and the known monotherapy activity of recombinant human IL-2 in melanoma. We are encouraged by this evidence of single-agent anti-tumor efficacy for ALKS 4230 and look forward to enrolling more patients to further evaluate ALKS 4230 as monotherapy.

ALKS 4230: ARTISTRY-1 Phase 1/2 Study Updates

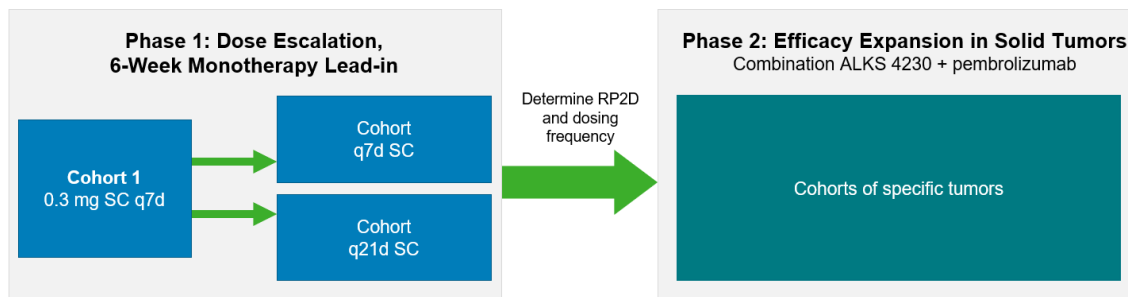


Across the ARTISTRY development program, overall patient enrollment has been accelerating despite certain COVID-19-related disruptions. Since January, we have enrolled 103 patients across the program, doubling our total number of enrolled patients. We believe these enrollment trends are an important indicator of investigator enthusiasm around the program.

In ARTISTRY-1, as of September 9th, 2020 – we had enrolled 38 patients in Part A, 26 patients in Part B and 91 patients in Part C, including full enrollment of the Part C PD-1 unapproved cohort. Following a delay related to COVID, our ex-U.S. sites have recently re-opened and are already contributing to enrollment, particularly in the Part B monotherapy cohorts.

ALKS 4230: ARTISTRY-2 Phase 1/2 Study Updates

Total enrolled as of September 2020: 43



- In phase 1 dose escalation: Patients receive 42 days of monotherapy lead-in of ALKS 4230 SC q7d or q21d, followed by combination of q21d pembrolizumab (200 mg) and either ALKS 4230 SC q7d or q21d
- Cohort 1 dosing of 0.3 mg was chosen as the starting dose based on predictive modeling

SC: Subcutaneous; RP2D: Recommended phase 2 dose; q7d: Administered once weekly; q21d: Administered once every three weeks

Data as of 09 Sept 2020

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One of the most distinctive features of the ALKS 4230 clinical development program is the potential for subcutaneous dosing. ARTISTRY-2, our subcutaneous study, is ongoing in its dose escalation phase for both the once-weekly and once-every-three-week dosing options. As of September 9th, 2020, we had enrolled a total of 43 patients in the study. We believe that we are narrowing in on the recommended phase 2 dose for subQ and hope to share updates from that study later this year.

Taking a step back, we have made significant progress in this development program, both in terms of new data accumulation and patient recruitment. I am particularly gratified that the responses we are seeing are occurring in patients that have failed multiple prior lines of therapy and may have few remaining potential treatment options. Each response is meaningful and I would like to express my sincere appreciation to the patients and investigators that have participated in the development program to date. We look forward to updating you on our progress as the program continues.

Slide 36



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Q&A

Ulka N. Vaishampayan, M.D., Professor, Internal Medicine,
Division of Hematology/Oncology, University of Michigan

Craig Hopkinson, M.D., Chief Medical Officer and
Executive Vice President of R&D, Alkermes, Inc.

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Sandy Coombs

Thank you, Craig and Dr. Vaishampayan. We will now open the call for questions.
Operator?

Slide 37

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