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

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.

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

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

Introduction to ALKS 4230

Craig Hopkinson, M.D.

Chief Medical Officer and Executive Vice President of Research & Development

Alkermes, Inc.

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 potently 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.

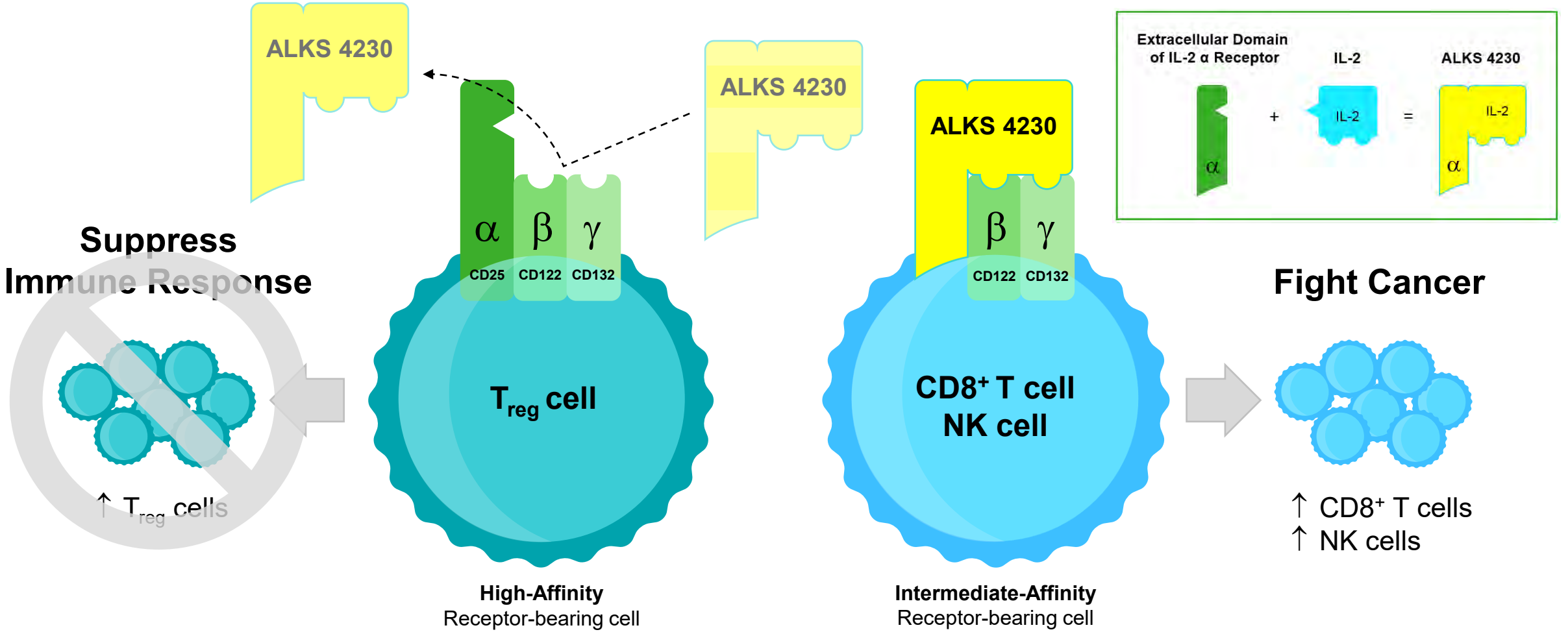
Proleukin should be administered in a hospital setting under the supervision of a qualified physician experienced in the use of anticancer agents. An intensive care facility and specialists skilled in cardiopulmonary or intensive care medicine must be available.

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



For illustrative purposes only; T_{reg}: Regulatory T cell; NK cell: natural killer cell

Non-Clinical Data Summary

ALKS 4230 Features	Model
Preferentially binds and signals through the intermediate-affinity IL-2R[1]	✓ *In vitro*
Selectively activates and expands circulating NK cells and $CD8^+$ T cells[1]	✓ Mouse, Non-human Primates (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, Flick 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) 591; DOI: 10.1158/1538-7445.AM2017-591
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

Overview of ALKS 4230 Clinical Development Program

Overview of ALKS 4230 Clinical Development Program

ARTISTRY-1
Phase 1/2

- 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

- Subcutaneous dosing: Refractory advanced solid tumors
- Six-week monotherapy lead-in followed by ALKS 4230 + pembrolizumab combination
  - Evaluating once-weekly and once-every-three-weeks dosing
- Efficacy expansion phase planned

ARTISTRY-3
Phase 2

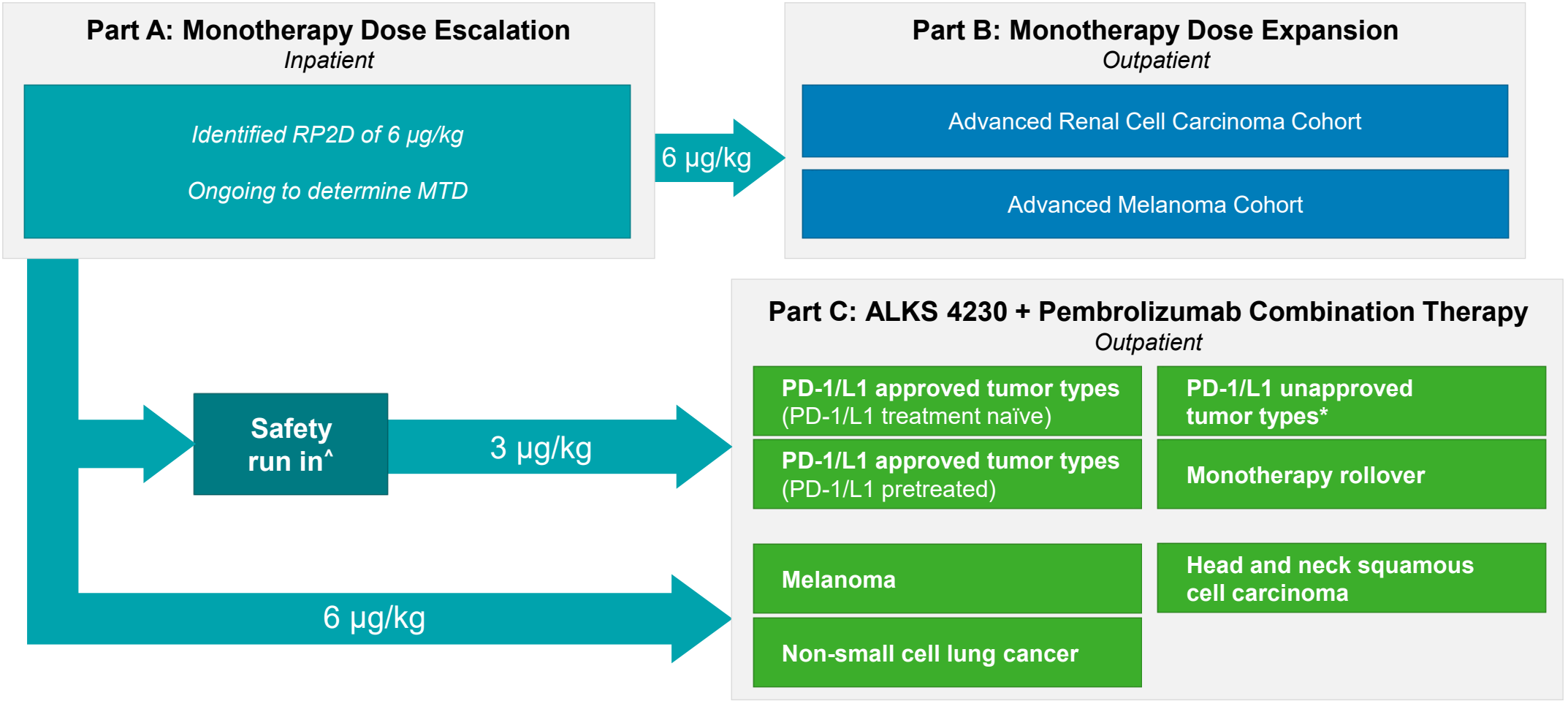
- IV dosing: Refractory advanced solid tumors, with accessible lesions for biopsy
- Five-week monotherapy lead-in followed by ALKS 4230 + pembrolizumab combination
- Assessment of tumor microenvironment from paired biopsies

ION-01
Phase 2

- 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

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



RP2D: Recommended phase 2 dose
MTD: Maximum tolerated dose

^ALKS 4230 (1 µg/kg or 3 µg/kg) + pembrolizumab (200 mg) following combination dosing regimen
*Includes colorectal cancer, triple-negative breast cancer, ovarian cancer, esophageal cancer, soft tissue sarcomas, and subjects with metastatic cancer

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

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

ARTISTRY-1: Clinical Data Update

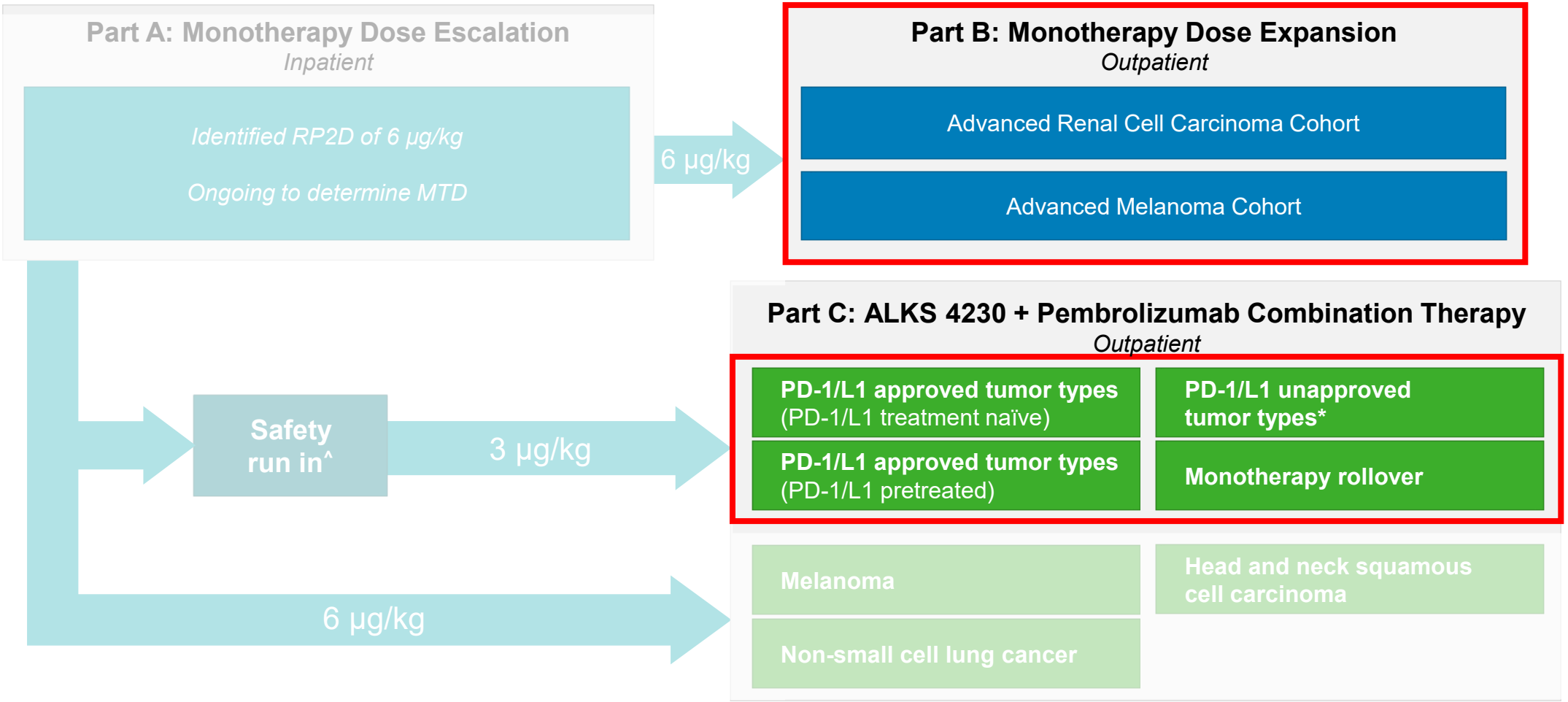
Ulka N. Vaishampayan, M.D.

Professor, Internal Medicine

Division of Hematology/Oncology, University of Michigan

Alkermes

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



RP2D: Recommended phase 2 dose
MTD: Maximum tolerated dose

^ALKS 4230 (1 µg/kg or 3 µg/kg) + pembrolizumab (200 mg) following combination dosing regimen
*Includes colorectal cancer, triple-negative breast cancer, ovarian cancer, esophageal cancer, soft tissue sarcomas, and subjects with metastatic cancer

ARTISTRY-1 Patient Baseline Characteristics

	Part B: ALKS 4230 Monotherapy		Part C: ALKS 4230 + Pembrolizumab			
Characteristic	**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

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)

- Chills and pyrexia: Most frequently reported adverse events (AEs); anticipated effects of cytokine administration
  - Transient, all grades ≤2 in severity
- Hypotension: Mostly grades ≤2 in severity
  - 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

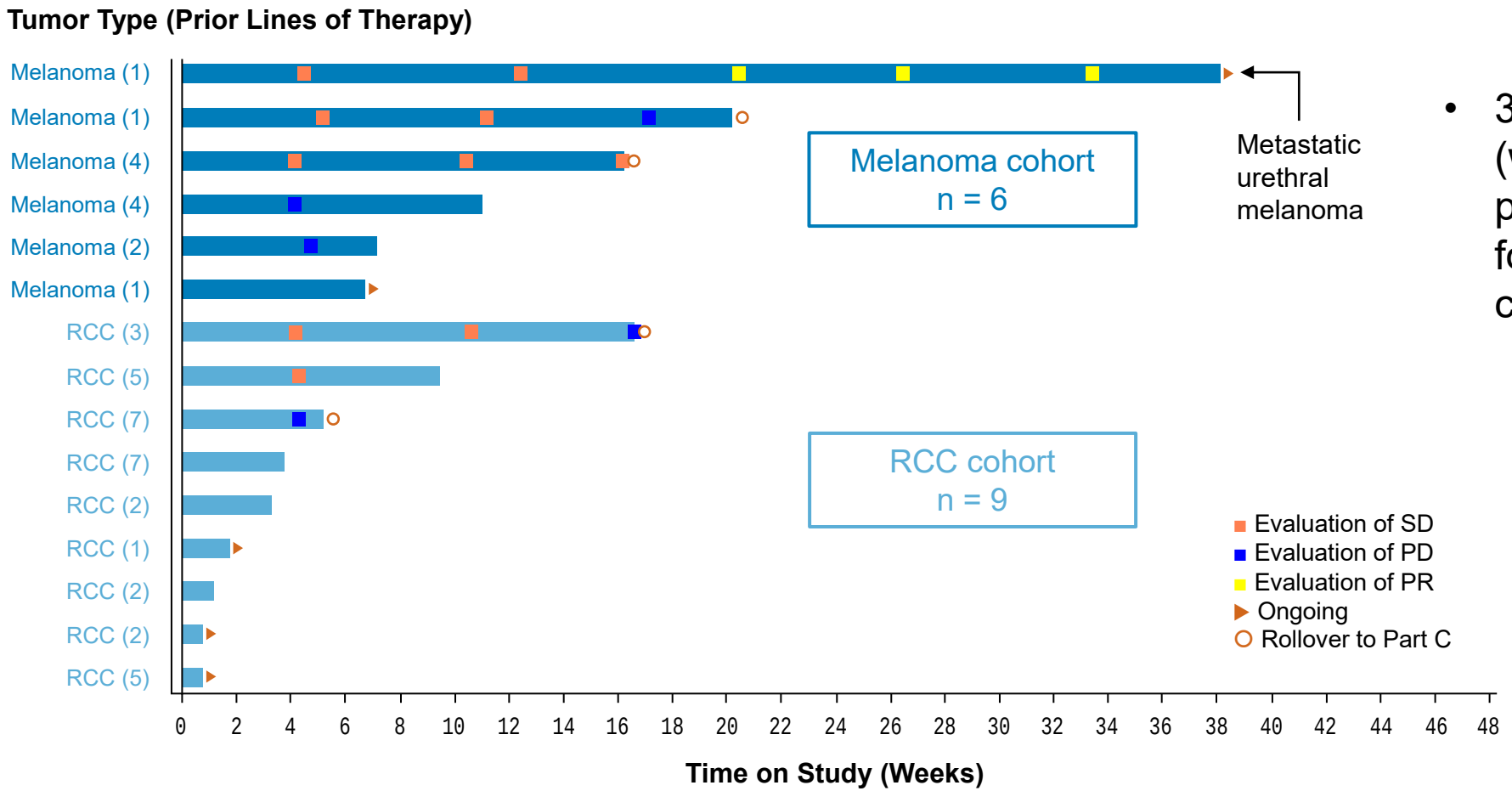
Combination with Pembrolizumab (Part C)*

- Chills and pyrexia: Most frequently reported AEs; anticipated effects of cytokine administration
  - 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
  - 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). ^Second death occurred after the data cutoff date of 24 Jul 2020

† Data as of 24 Jul 2020^

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

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

Data as of 24 Jul 2020

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

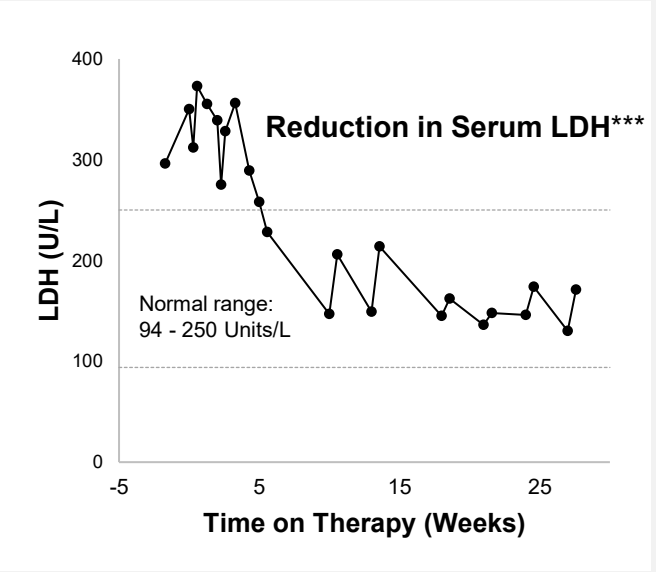
- Cystectomy and pelvic node dissection for urethral melanoma in June 2017, followed by one year of adjuvant nivolumab treatment (Sept 2017 – Sept 2018)
- No treatment between Sept 2018 and Sept 2019
- Recurrence: Sept 2019

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



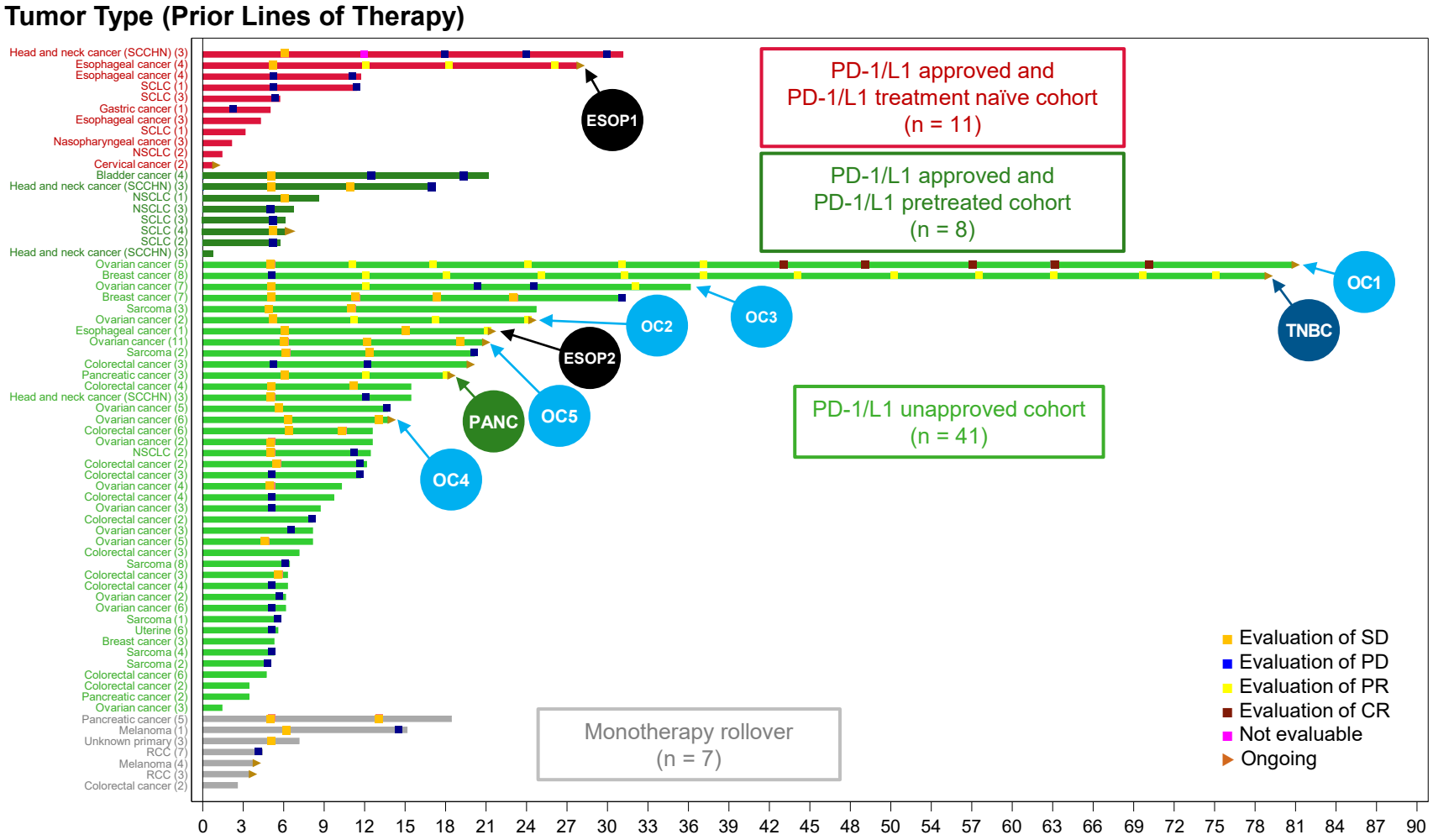
- Reduction in size of peritoneal implants, ascites, and retroperitoneal lymph nodes
- Patient had immune-related serious AEs: Grade 2 iritis / vitritis successfully treated with steroid eye drops
- Patient had a grade 3 serious AE of transient hypotension managed with fluids^

*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

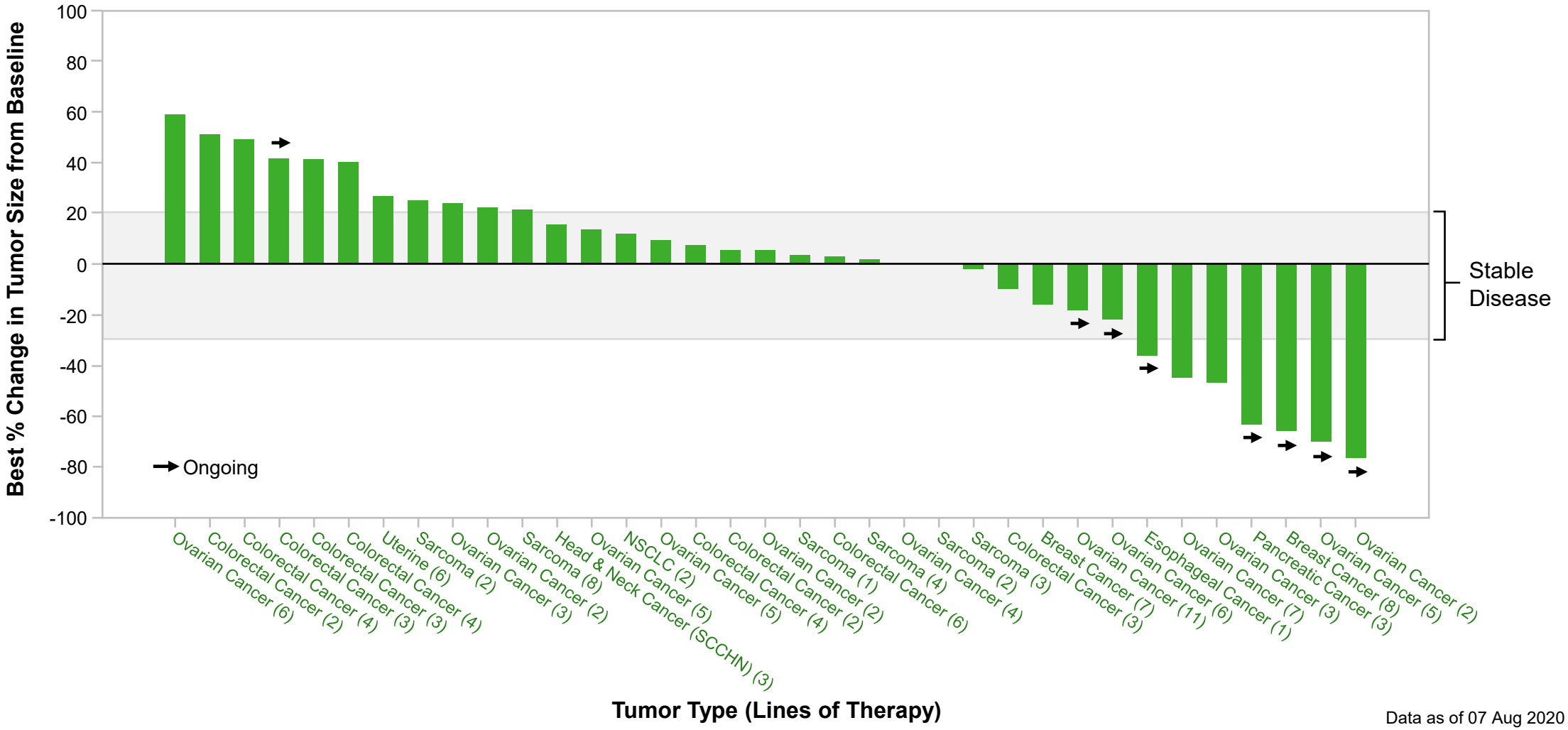
ALKS 4230 3 µg/kg in Combination With Pembrolizumab: Responses in Multiple Tumor Types



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

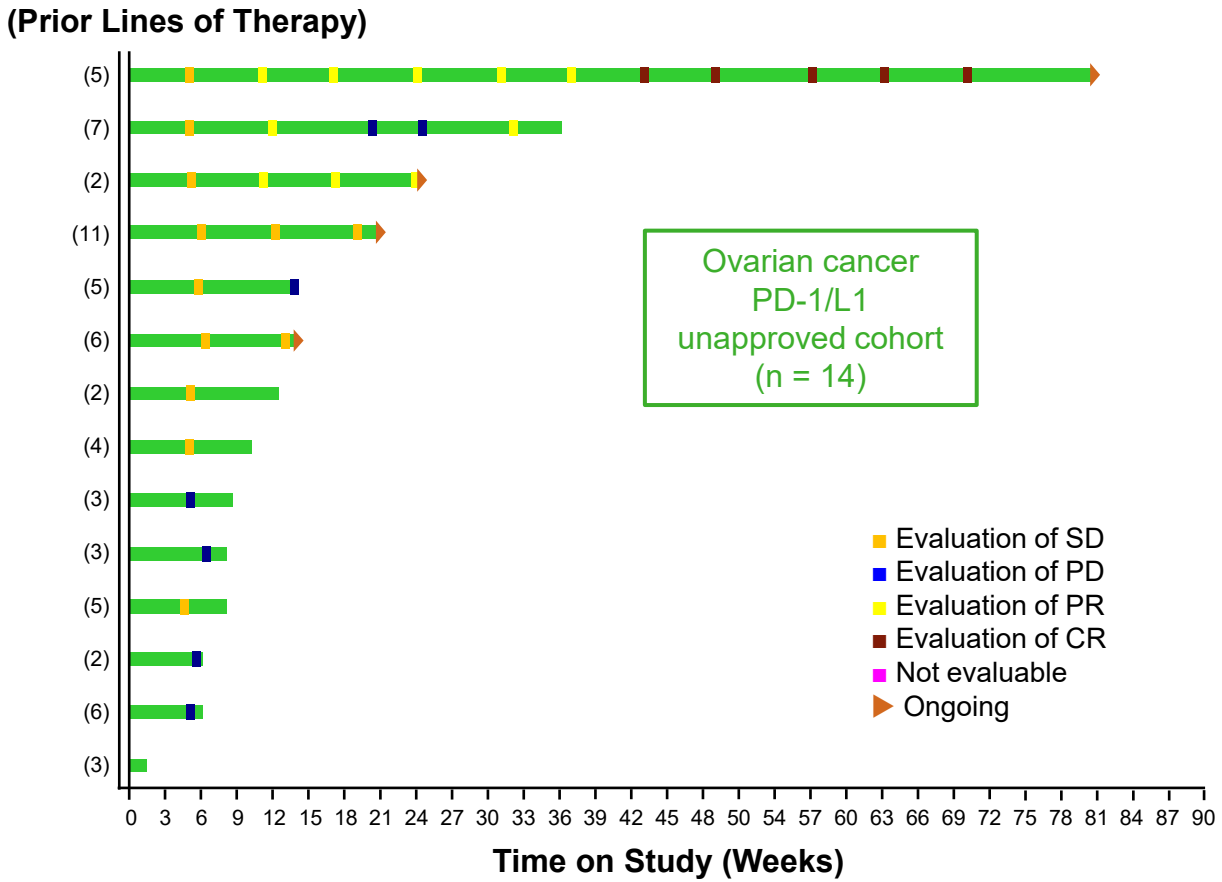
Data as of 07 Aug 2020

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

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

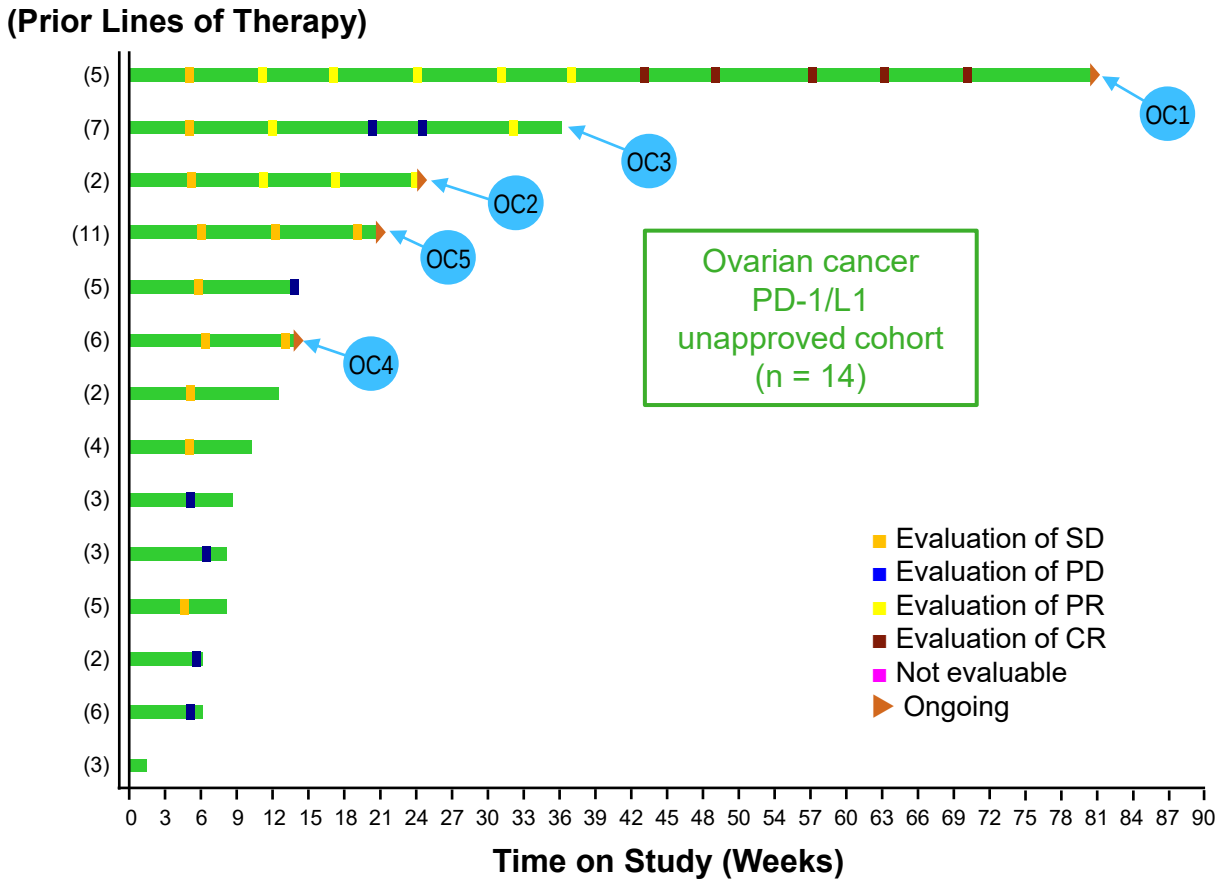


- 14 ovarian cancer patients enrolled; 13 evaluable (with ≥ 1 scan)
  - Patients were heavily pre-treated and had PD at the time of enrollment
- 9 of 13 patients had SD or better on at least one scan

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

Data as of 07 Aug 2020

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



Durable responses observed in heavily pretreated, platinum-resistant ovarian cancer patients

Pt.	Age	Prior Lines of Therapy	Prior Therapies	Max. Reduction of Target Lesions (%)	OR[a]	CA-125 (U/mL) Response From Baseline	Time on ALKS 4230 (weeks)
OC1	48	5	CBP/PAC/BEV, CDDP/GEM, CBP/ PLD, PCA, CBP/DOC	70.0 ↓	CR[b]	Normalized from 282 to 24.5 at cycle 4	81 ▶ Ongoing
OC2	83	2	CBP/PAC/DOC, CBP/DOC/NIR/TAM	76.3 ↓	PR	Normalized from 125 to 16 at cycle 4	23 ▶ Ongoing
OC3	60	7	CBP/PAC, CBP/PLD, CBP/BEV, PAC/BEV, BEV, PLD	44.7 ↓	uPR	Reduced from 1400 to 260 at cycle 4	34
OC4	75	6	CBP/PAC, PLD/BEV, CBP/GEM, TOP, NIR	21.9 ↓	SD	Reduced from 493 to 245 at cycle 5	14 ▶ Ongoing
OC5	83	11	CBP/PAC, CBP, CBP/PAC/CAP, CBP/PLD, CBP/PLD	18.3 ↓	SD	Normal at baseline at 10.6	21 ▶ Ongoing

[a]Assessed by investigator. [b]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

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

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

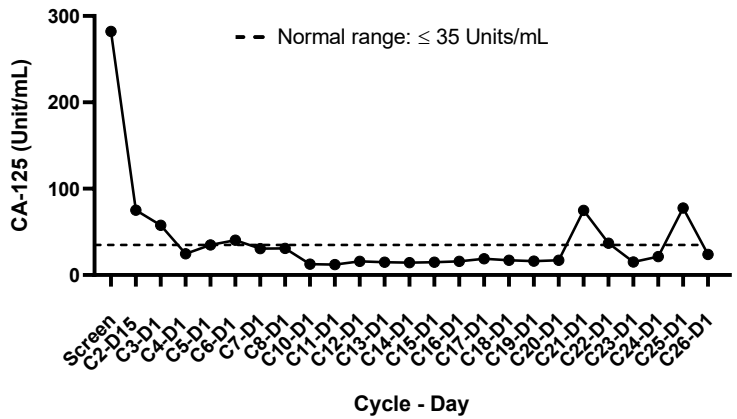
- ALKS 4230 + pembrolizumab therapy
  - 3 µg/kg IV ALKS 4230

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

ALKS 4230 + Pembrolizumab
Normalization of CA-125 tumor marker



*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

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

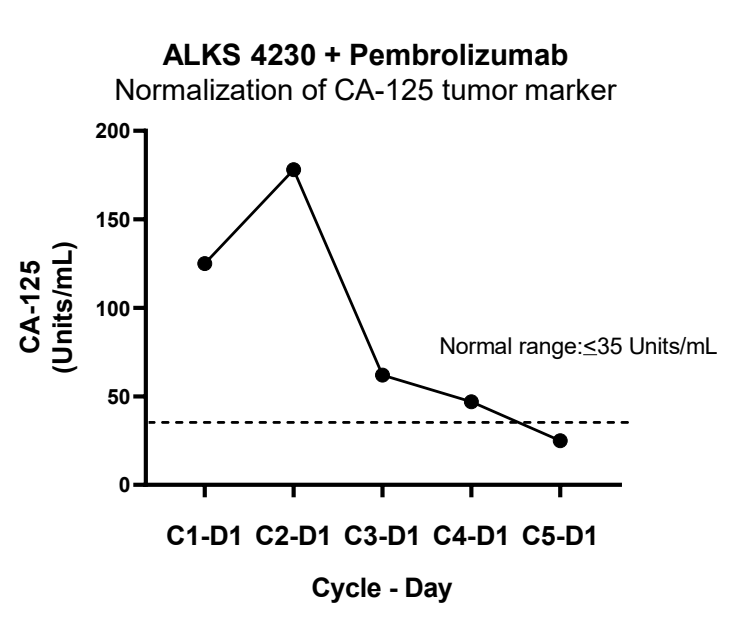
- 2 prior lines of treatment with best response of complete response‡
  - Platinum-based chemo, PARP inhibitor
- No prior checkpoint inhibitor therapy

Feb 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

High Unmet Needs Remain for Treatment of Ovarian Cancer

Ovarian Cancer Burden

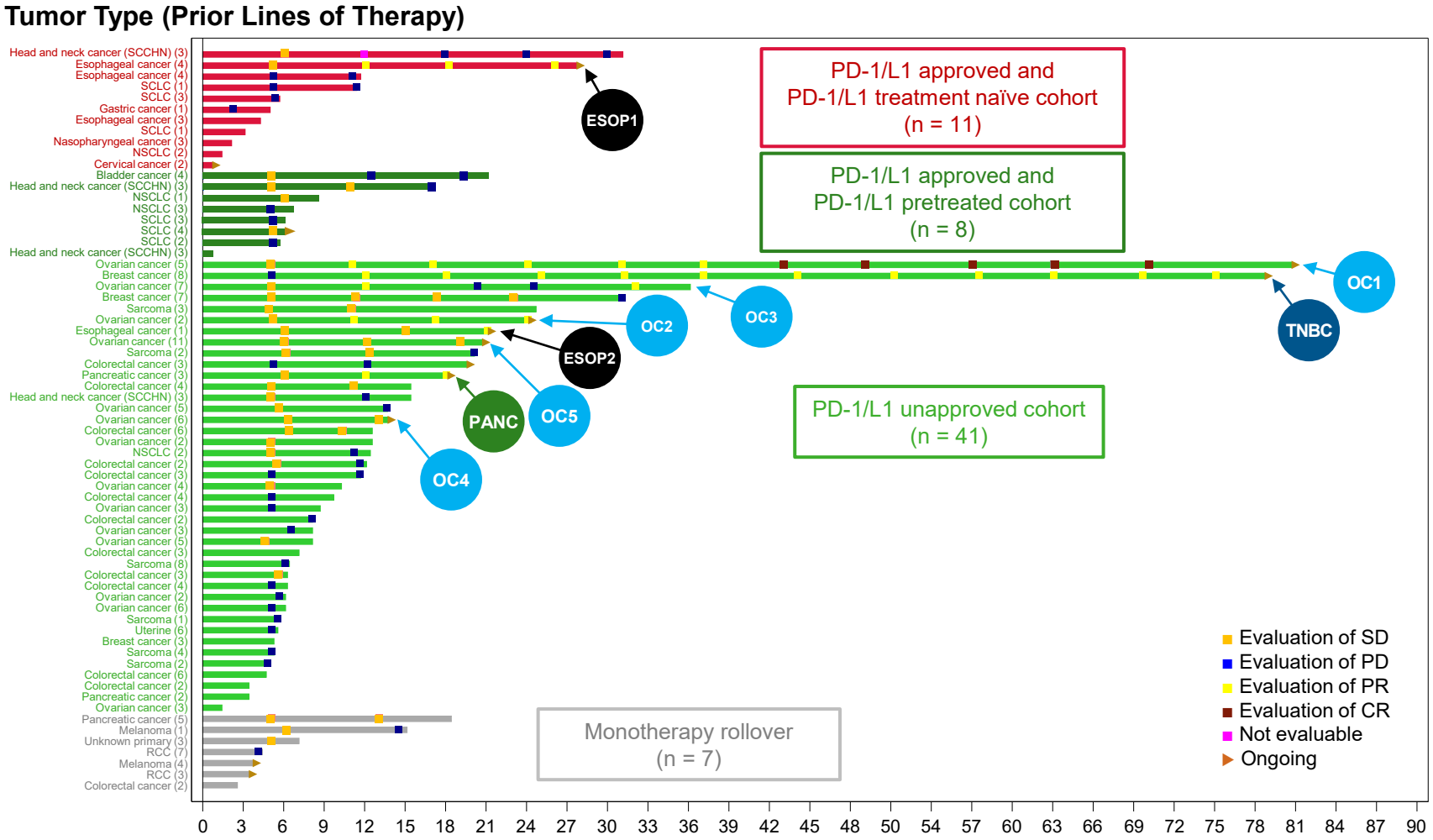
- Second most common gynecological cancer[1]
  - U.S. prevalence: ~233K cases in 2017[2]
- Leading cause of gynecologic cancer-related deaths in the U.S.[1]
  - 5-year survival rate for stage IV ovarian cancer of 29%[3]
  - Median overall survival (mOS) for platinum-resistant ovarian cancer is less than 12 months[4]

Limited Treatment Options

- **1L (Standard of Care)**
  - Surgery + platinum-based chemotherapy +/- bevacizumab followed by bevacizumab and/or PARP inhibitor as maintenance[5]
  - Many become platinum resistant (refractory) and progress < 6 months after completion of platinum-based chemotherapy[6]
- **Few treatment options post-platinum chemotherapy; patients not treated with curative intent**
  - In one study of nonplatinum chemotherapy, objective response rate was 12% and median progression free survival (mPFS) was 3.4 months[7]
- **Anti-PD-1/L1 (e.g., pembrolizumab, atezolizumab) have been shown to be ineffective for treatment of ovarian cancer[8,9]**
  - Pembrolizumab efficacy in ovarian cancer is ~10% for high PD-1/L1 expression[8]

1. https://www.cdc.gov/cancer/ovarian/statistics/index.htm 2. https://seer.cancer.gov/statfacts/html/ovary.html 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/24607285/ 5. https://www.frontiersin.org/articles/10.3389/fonc.2020.00782/full 6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2962713/ 7. Pujade-Lauraine E, Hilpert F, Weber B, 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, Santin 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-Martin A, Sanchez-Lorenzo L. Immunotherapy with checkpoint inhibitors in patients with ovarian cancer: Still promising? *Cancer.* 2019;125 Suppl 24:4616-4622. doi: 10.1002/cncr.32520.

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



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

Data as of 07 Aug 2020

ALKS 4230 3 µg/kg in Combination With Pembrolizumab:

Case Study: 54-Year-Old Female With Esophageal Cancer ESOP1

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

ALKS 4230 3 µg/kg in Combination With Pembrolizumab:

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

ESOP2

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
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

Alkermes

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	TNBC	47	5	DOX/CTX; PAC; PCA; TAM; CAP; PCA; ERI; GEM/CBP	66 ↓	iPR	74 ▶ Ongoing
PD-1/L1 unapproved cohort	PANC	74	3	PCA/GEM; 5FU/IRI; 5-FU/IRI/calcium folinate	63 ↓	PR	17*
PD-1/L1 approved; PD-1/L1 treatment naïve	ESOP1	54	4	CBP/PAC; CDDP/HER/ 5FU/IRI; PAC/RAM; Chk1i/GEM	48 ↓	PR	28 ▶ Ongoing
PD-1/L1 unapproved cohort	ESOP2	82	1	CBP/PAC	36 ↓	uPR	20 ▶ Ongoing

[a]Assessed 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

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

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

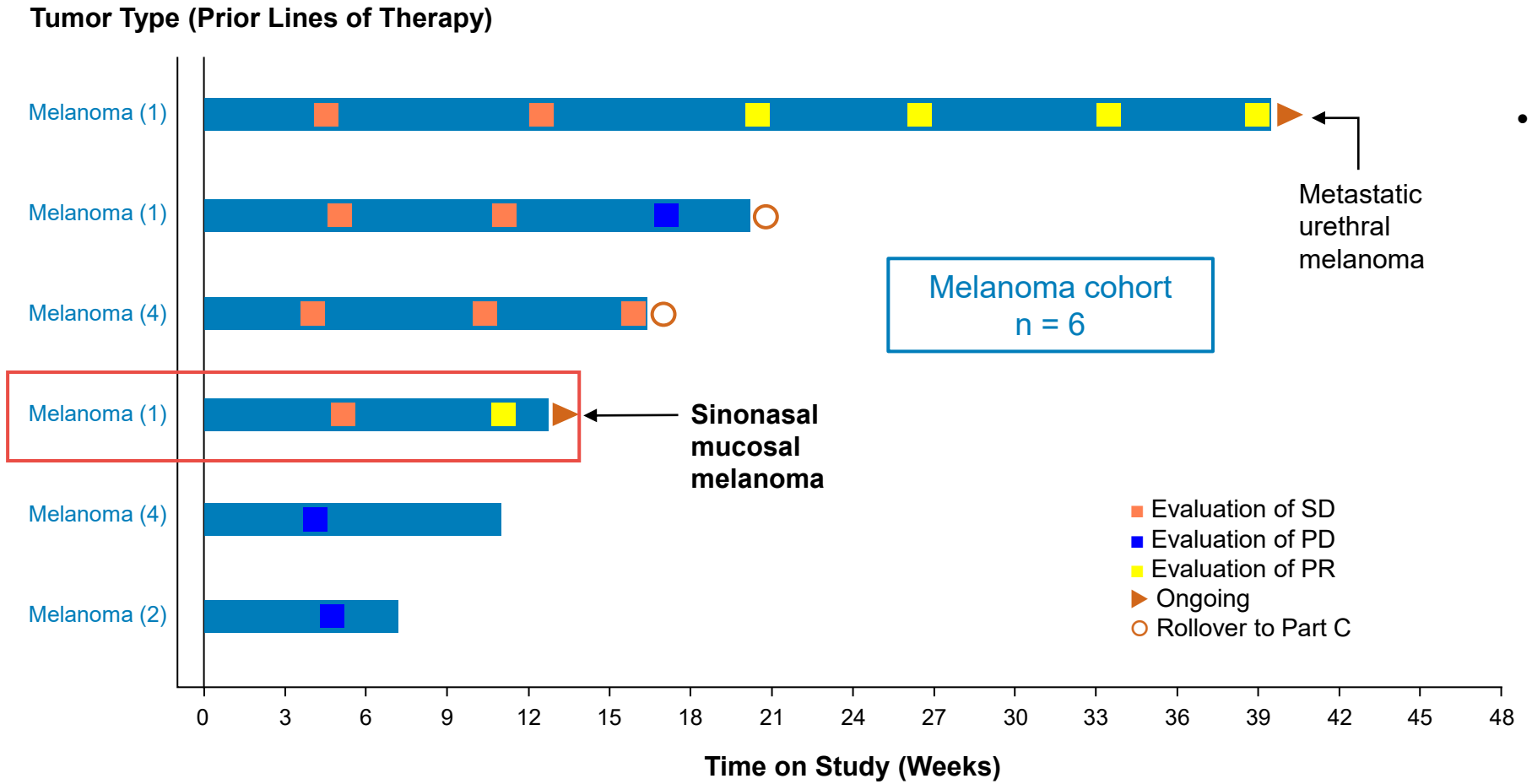
ALKS 4230 Program Updates and Next Steps

Craig Hopkinson, M.D.

Chief Medical Officer and Executive Vice President
of Research & Development

Alkermes, Inc.

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



- 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 recruitment
  - **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

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

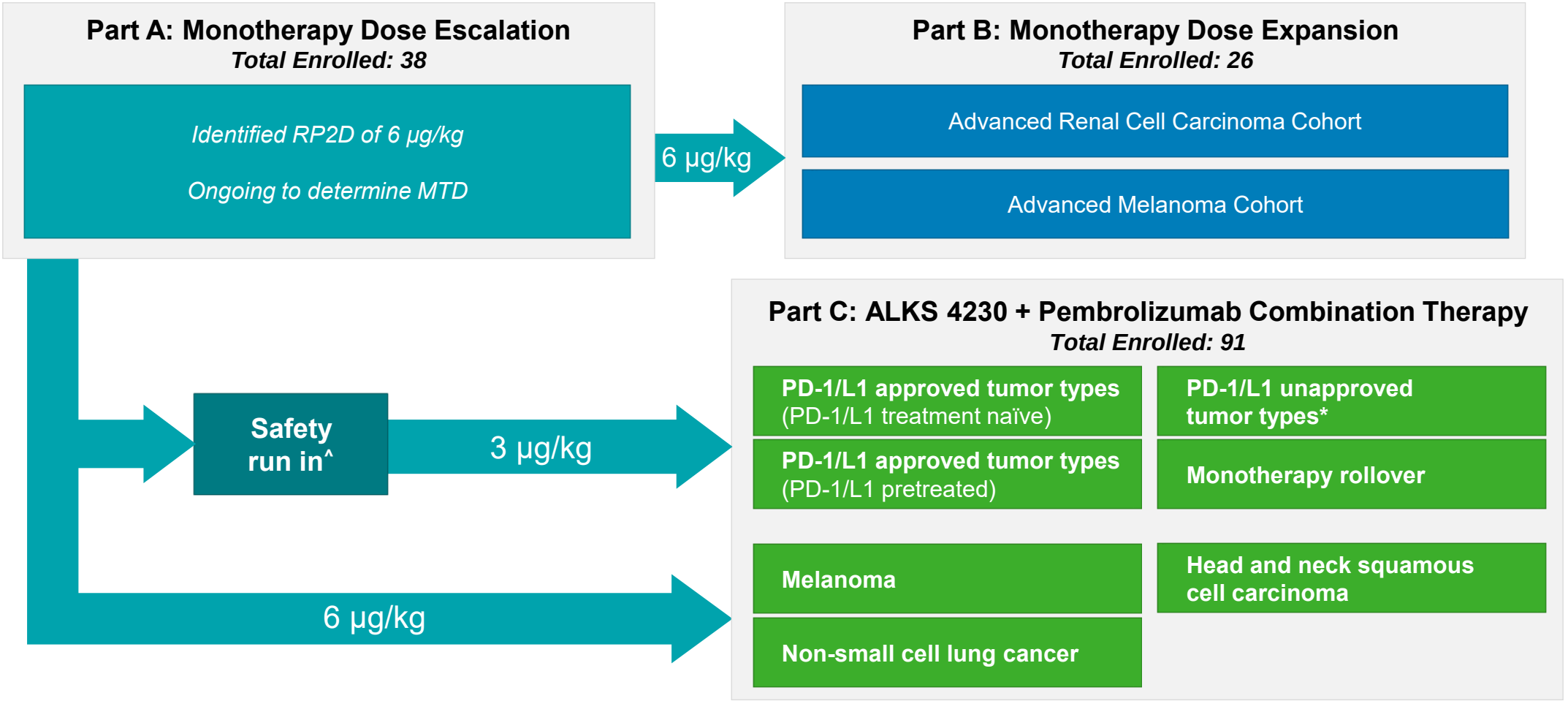
	Undesirable rate	Desirable rate	N1	Enroll more if	N2	Total
Expansion Cohort B1: Refractory RCC	5%	20%	21	≥2 PR/CR	20	41
Expansion Cohort B2: Refractory Melanoma[a]	5%	20%	21	≥2 PR/CR	20	41

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

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



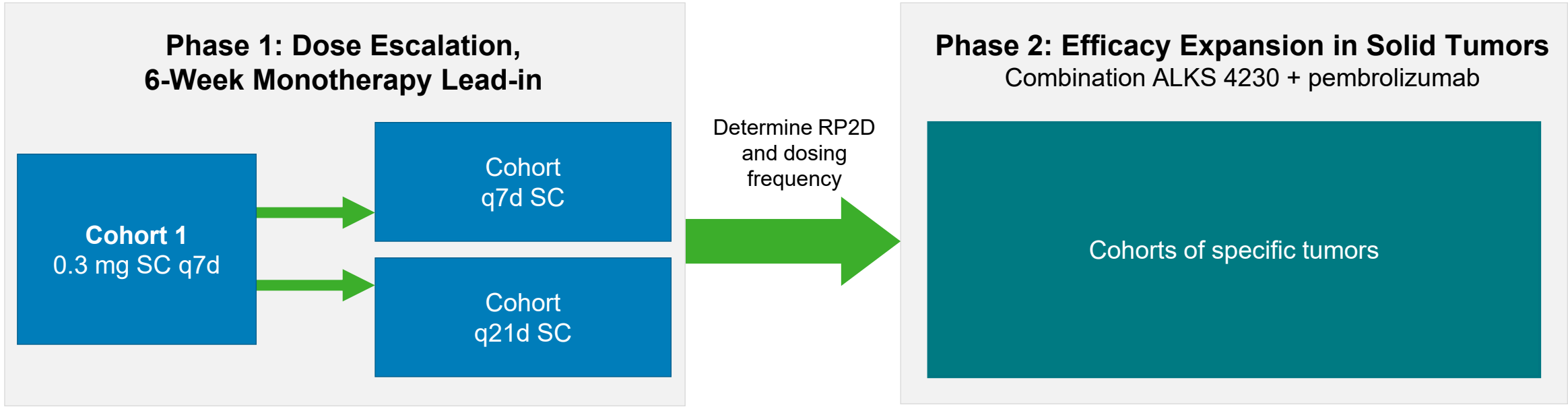
RP2D: Recommended phase 2 dose
MTD: Maximum tolerated dose

*Includes colorectal cancer, triple-negative breast cancer, ovarian cancer, esophageal cancer, soft tissue sarcomas, and subjects with metastatic cancer
^ALKS 4230 (1 µg/kg or 3 µg/kg) + pembrolizumab (200 mg) following combination dosing regimen

Data as of 09 Sept 2020

ALKS 4230: ARTISTRY-2 Subcutaneous 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

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.

www.alkermes.com