MURAL ONCOLOGY INVESTOR CALL

October 2023

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. The words “anticipate,” “believe,” “expect,” “may,” “will” and similar expressions are intended to identify forward-looking statements. Forward-looking statements made in this presentation include, but are not limited to, statements concerning: the protein engineering capabilities of the oncology business (“Mural Oncology”) of Alkermes plc (the “Company”); the Company’s expectations regarding timelines for and anticipated benefits and other impacts of the planned separation of the Company's oncology business; the potential therapeutic and commercial value, and anticipated safety profile, of the Company’s engineered cytokine programs and product candidates, including nemvaleukin alfa (“nemvaleukin”) as a cancer immunotherapy when used as monotherapy or in combination, and its broad potential utility across a wide array of tumor types and indications and its potential dosing optionality; the Company’s expectations regarding timelines and plans for the development of its engineered cytokines, including, for nemvaleukin, expectations related to ongoing clinical studies in the ARTISTRY development program, the ability of ongoing studies to support potential registration, and potential for expansion of the development program, including to explore novel combinations with other cancer treatments; and Mural Oncology's expected post-separation balance sheet and cash runway. You are cautioned 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 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: the inherent risks and uncertainties associated with competitive developments, preclinical development, clinical trials, recruitment of patients, product development activities and regulatory approval requirements; preclinical or interim results and data from ongoing clinical studies of the Company’s cytokine programs and product candidates may not be predictive of future or final results from such studies, results of future clinical studies or real-world results; future clinical trials or future stages of ongoing clinical trials may not be initiated or completed on time or at all; the Company’s product candidates, including nemvaleukin, could be shown to be unsafe or ineffective; changes in the cost, scope and duration of development activities; impacts of the COVID-19 pandemic on the Company’s clinical trials, business, operations or financial condition; the U.S. Food and Drug Administration (“FDA”) may make adverse decisions regarding the Company’s products and product candidates; whether the Company ultimately separates its oncology business on the anticipated timeline or at all; the potential separation may adversely impact the Company’s ability to attract or retain key personnel that support the Company’s oncology business; and those risks, assumptions and uncertainties described under the heading “Risk Factors” in the Company’s Annual Report on Form 10-K for the year ended December 31, 2022 and in subsequent filings made by the Company with the U.S. Securities and Exchange Commission (“SEC”), including the Company’s Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, which are available on the SEC’s website at www.sec.gov. 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.

This presentation does not constitute an offer to sell or a solicitation of an offer to buy securities, nor shall there be any sale of securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

This presentation does not purport to be all-inclusive or to contain or summarize all of the information, conditions, risks and other attributes of an investment in Mural Oncology. No investment, divestment or other financial decision or action should be based on the information in this presentation. Potential investors will be solely responsible for conducting due diligence on Mural Oncology in connection with any potential investment.

Agenda

1. Executive Summary – Caroline Loew, Ph.D.

2. Nemvaleukin Alfa
   - Josh Heiber, Ph.D.
   - Jessicca Rege, Ph.D.


3. Additional Pipeline Programs
   - Mark Whitmore, Ph.D.
   - Josh Heiber, Ph.D.


4. Financial Overview – Caroline Loew, Ph.D.

5. Question and Answer

MURAL ONCOLOGY

SECTION 1:

EXECUTIVE SUMMARY

Mural Oncology - Highlights

Mural Oncology

1. **Mural Oncology is the oncology business of Alkermes plc**; Mural Oncology is expected to be separated into a new, independent publicly traded company via a spin-off in 4Q 2023. Two key data readouts anticipated within 18 months
2. **Portfolio of novel, investigational cytokines** engineered to optimize the "known knowns" of native interleukins – retain their high potency while potentially overcoming their low tolerability
3. **Nemvaleukin is an intrinsically active, stable fusion protein which does not degrade into native-IL-2** and is designed to selectively bind to the intermediate-affinity IL-2 receptor, enabling a potentially enhanced therapeutic window
4. **Nemvaleukin has generated compelling clinical data to date,** with durable responses[1] in monotherapy and in PD-1 combination across a range of tumor types. Exploring alternative dosing regimens. ARTISTRY-6 and ARTISTRY-7 readouts both expected in 1Q 2025[2]
5. **IL-18 and IL-12 programs in preclinical development** with potentially differentiated therapeutic properties and leveraging advanced protein engineering capabilities. Candidate nominations expected in 2024

1. Durable response defined as a response with a duration that exceeds the response generally observed with standard of care treatment; in the context of high unmet disease states such as mucosal melanoma and platinum-resistant ovarian cancer ("PROC"), a response that exceeds six months is considered durable
2. Subject to patient enrollment

Abbrev.: **IL-2:** interleukin-2: **IL-12:** interleukin-12; **IL-18:** interleukin-18

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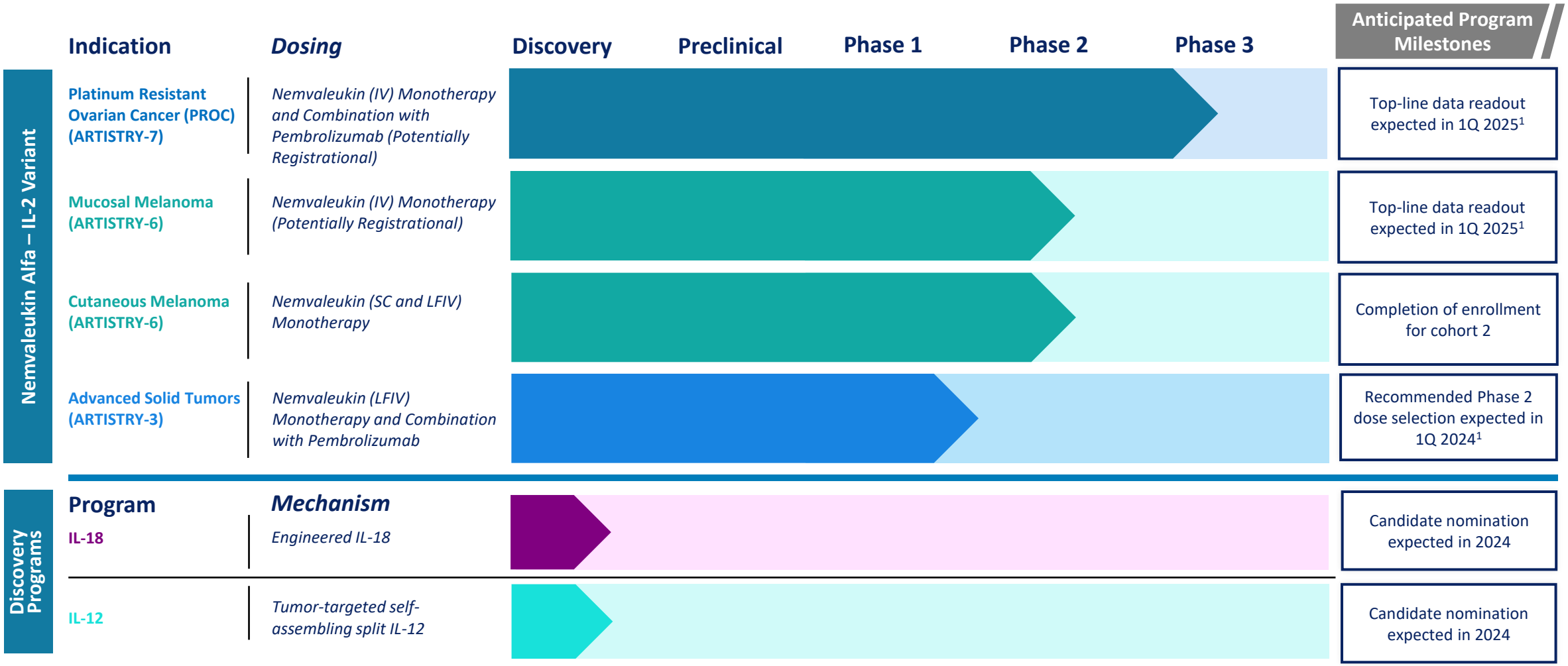
Pipeline Overview – Milestone Rich Near-Term Future



1. Subject to patient enrollment

Abbrev.: **IV**: intravenous; **SC:** subcutaneous; **LFIV:** less frequent IV dosing

MURAL ONCOLOGY

Building World Class Board and Management Team

Board of Directors

Susan Altschuller, Ph.D., MBA
Cerevel, Immunogen, Alexion, Bioverativ, Biogen

Francis Cuss, M.B., B.Chir., FRCP
BMS, Schering-Plough, GSK

Benjamin Hickey, MBA
Mirati, Halozyme, BMS

Scott Jackson, MBA - Chairman
Celator, Eli Lilly, Smithkline Beecham, Imclone, J&J, Eximias

Caroline Loew, Ph.D.
Glympse Bio, BMS, Merck, PhRMA

Management Team

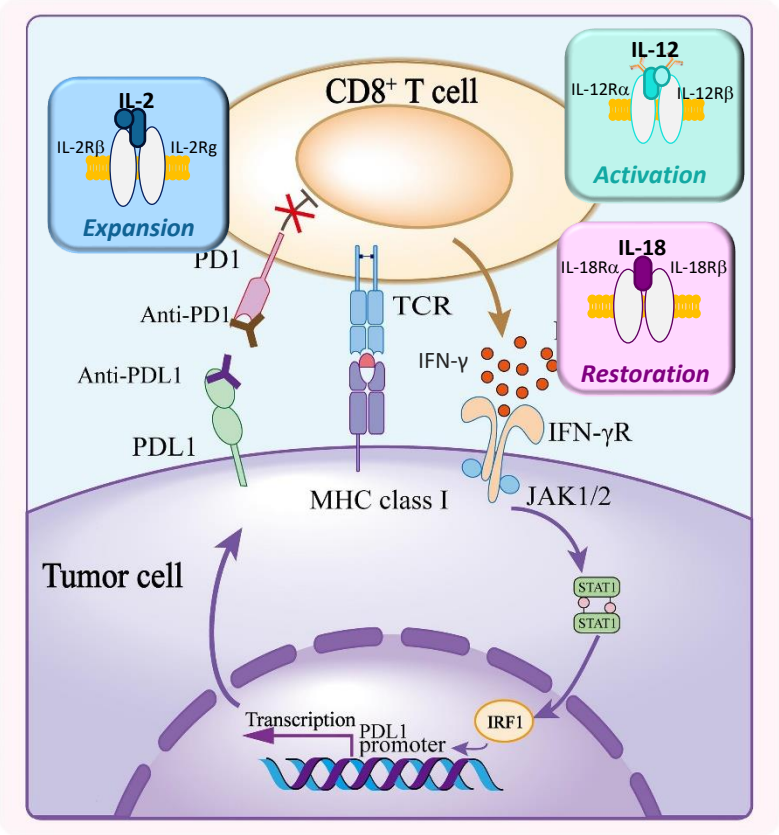
Caroline Loew, Ph.D. – CEO
Glympse Bio, BMS, Merck, PhRMA

Vicki Goodman, M.D. – CMO
Exelixis, Merck, BMS

Maiken Keson-Brookes - CLO
Rubius, Synlogic, uniQure, Forum, Biogen

Board members other than Dr. Loew who is currently a board member, expected to serve upon effectiveness of Registration of Form 10. Management expected to serve upon completion of separation

Cytokines Play an Important Role in Immuno-Oncology (IO)



- **Checkpoint modulation has driven the growth of the IO field - $88 billion in sales projected by 2027 [1] - but a significant unmet need still exists**
  - Only a minority of solid tumor patients experience a response to anti-PD-(L)1 therapy
  - Responders to existing immunotherapies often experience disease progression
- Cytokines are biologically active proteins that play an essential role in immune cell functions
- In cancer, cytokines can help prime, expand, activate, and/or enhance activity of the immune system to recognize and eliminate tumor cells
- **Mural Oncology focuses on optimizing immune cell activity, a key driver of immune response to cancer cells**
  - **EXPANSION**: IL-2 expands tumor-killing immune cells, including CD8+ T cells and NK cells
  - **RESTORATION**: IL-18 reinvigorates T cell exhaustion and mature dendritic cells
  - **ACTIVATION**: IL-12 drives pro-inflammatory responses by potently activating CD8+ T and NK cells
- **Mural Oncology's engineered cytokines may lead to new therapies for significant patient populations where checkpoint inhibitors failed to achieve a response or had a limited response**

Extracted from Lei Q, et al. Front. Cell Dev. Biol. 2020;8:00672

1. GlobalData Thematic Research: Immuno-Oncology

Abbrev.: **rhIL-2**: high-dose recombinant human IL-2

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Leveraging Core Competencies to Optimize Cytokines

Our Deep Understanding of Biology

- Modulate multiple immune pathways and investigate several phases of the cancer immunity cycle
- Explore treatment regimens to target different steps in the cancer immunity cycle designed to enhance efficacy
- Focus on targets with strong biologic rationales in areas of unmet medical need

Protein Engineering Capabilities

- Apply protein engineering solutions to address identified technical challenges associated with binding selectivity, tumor-targeting, half-life modification, and stable fusion proteins
- Design cytokines to overcome certain negative effects associated with unmodified cytokines
- Goal is a portfolio of molecules designed to expand, activate and reinvigorate T cells and NK cells

Abbrev.: **NK:** natural killer

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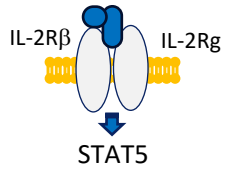
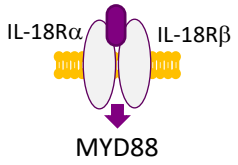
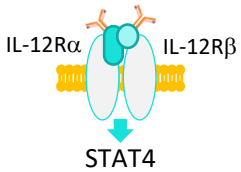
Leveraging Core Competencies: IO Programs Grounded in Strong Scientific Rationale

Program		Technical challenge	Protein engineering solution
Nemvaleukin alfa[1] (IL-2)		• Systemic toxicities due to overexpansion of T_{regs} related to high-affinity IL-2R binding	• Fusion of circularly permuted IL-2 with the IL-2Rα subunit resulting in only activating intermediate-affinity IL-2R
Engineered IL-18		• Limited clinical efficacy due to IL-18BP tightly binding to IL-18, neutralizing IL-18 receptor activation	• Engineered IL-18 designed with a half-life extension and to be resistant to IL-18BP neutralization, while retaining and optimizing the activity of IL-18
Tumor-targeted split IL-12		• Limited rhIL-12 clinical utility due to severe toxicities where tolerable systemic dosing regimens are not efficacious	• Separate inactive tumor-targeted IL-12 subunits assemble and activate in the tumor

1. Intrinsically active stable, not degraded fusion protein, sterically occluded from binding to the high-affinity IL-2R

Abbrev.: Tregs: regulatory T cells; **rhIL:** recombinant human IL; **IL-2R:** IL-2 receptor; **IL-2Rα**: IL-2R alpha, **IL-18BP:** IL-18 binding protein

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SECTION 2:

NEMVALEUKIN ALFA

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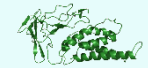
Nemvaleukin: A Disciplined and Systematic Approach to Developing an Engineered IL-2 Variant

Development Stage Gates

Novel Design

- Fusion protein of IL-2 and IL-2Rα, designed to expand the therapeutic benefits of high-dose recombinant human IL-2 (rhIL-2) while mitigating its hallmark toxicities
- Stable, intrinsically active without the need for metabolic or proteolytic conversion


Nemvaleukin

Pharmacological PoC

- Dose-dependent expansion of NK and $CD8^+$ T cells
- Minimal non-dose dependent effects on T_{regs}

Clinical Validation

- Monotherapy responses observed in melanoma and RCC in patients previously treated with a CPI
- Observed responses in combination with pembrolizumab
- IV QDx5 every 3 weeks dosing modeled after high dose IL-2

Potential Approval and Indication Expansion

- Two near-term potentially registrational data readouts
  - PROC: FDA Fast Track designation
  - Mucosal Melanoma: FDA Fast Track designation and Orphan Drug designation; MHRA ILAP Innovation Passport designation
- Focus on additional dosing approaches, including less frequent IV dosing regimens
- Potential for indication expansion with initial focus on cutaneous melanoma and earlier lines of treatment for ovarian cancer

Abbrev: **RCC**: Renal Cell Carcinoma; **CPI:** Checkpoint Inhibitor; **FDA**: Food and Drug Administration; **MHRA:** Medicines and Healthcare products Regulatory Agency; **ILAP:** Innovative Licensing and Access Pathway. **IL-2R**: IL-2 receptor; **rhIL-2:** recombinant human IL-2; **IL-2Rα:** IL-2R alpha

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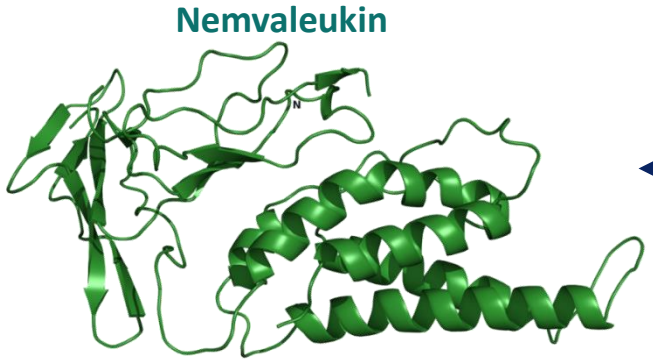
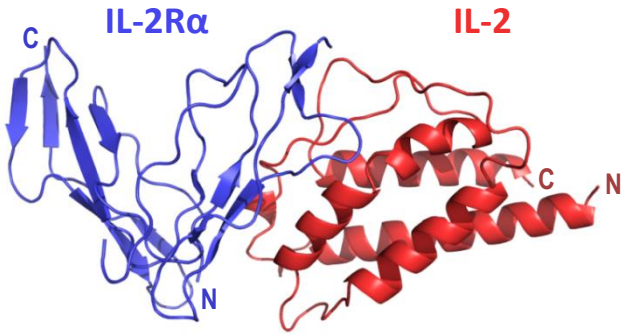
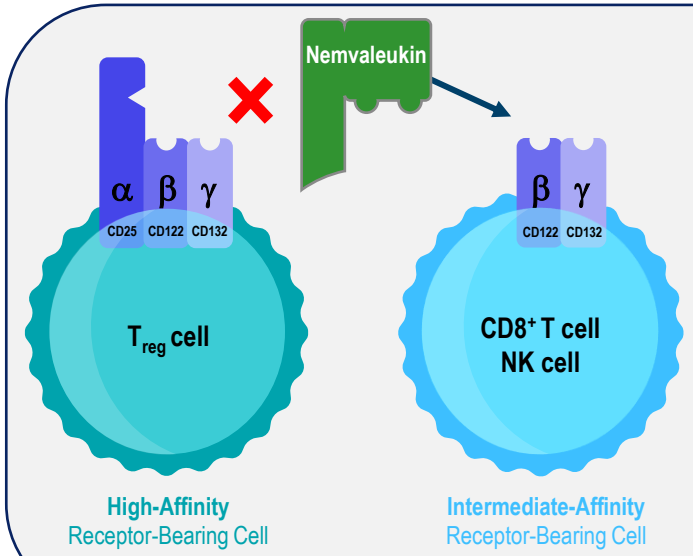
Nemvaleukin Meaningfully Differentiated from High-Dose IL-2

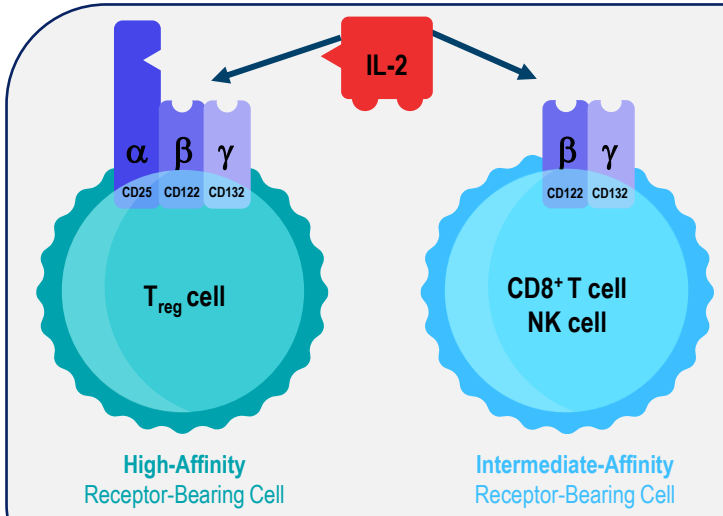
- Intrinsically active stable fusion protein
- Does not require metabolic or proteolytic conversion
- Does not degrade to native IL-2







- Nemvaleukin is sterically occluded from binding to the high-affinity IL-2R
- Nemvaleukin selectively binds the intermediate-affinity IL-2R to preferentially activate and expand CD8⁺ T cells and NK cells, with minimal expansion of T_{regs}



- IL-2 more potently activates the high-affinity IL-2R, preferentially expressed on immunosuppressive T_{reg} cells
- The high doses of rhIL-2 required for anti-tumor activity are associated with T_{reg} expansion, which may limit responses and lead to potentially acute life-threatening toxicities

Abbrev.: **IL-2R**: IL-2 receptor; **rhIL-2:** recombinant human IL-2; **IL-2Rα:** IL-2R alpha

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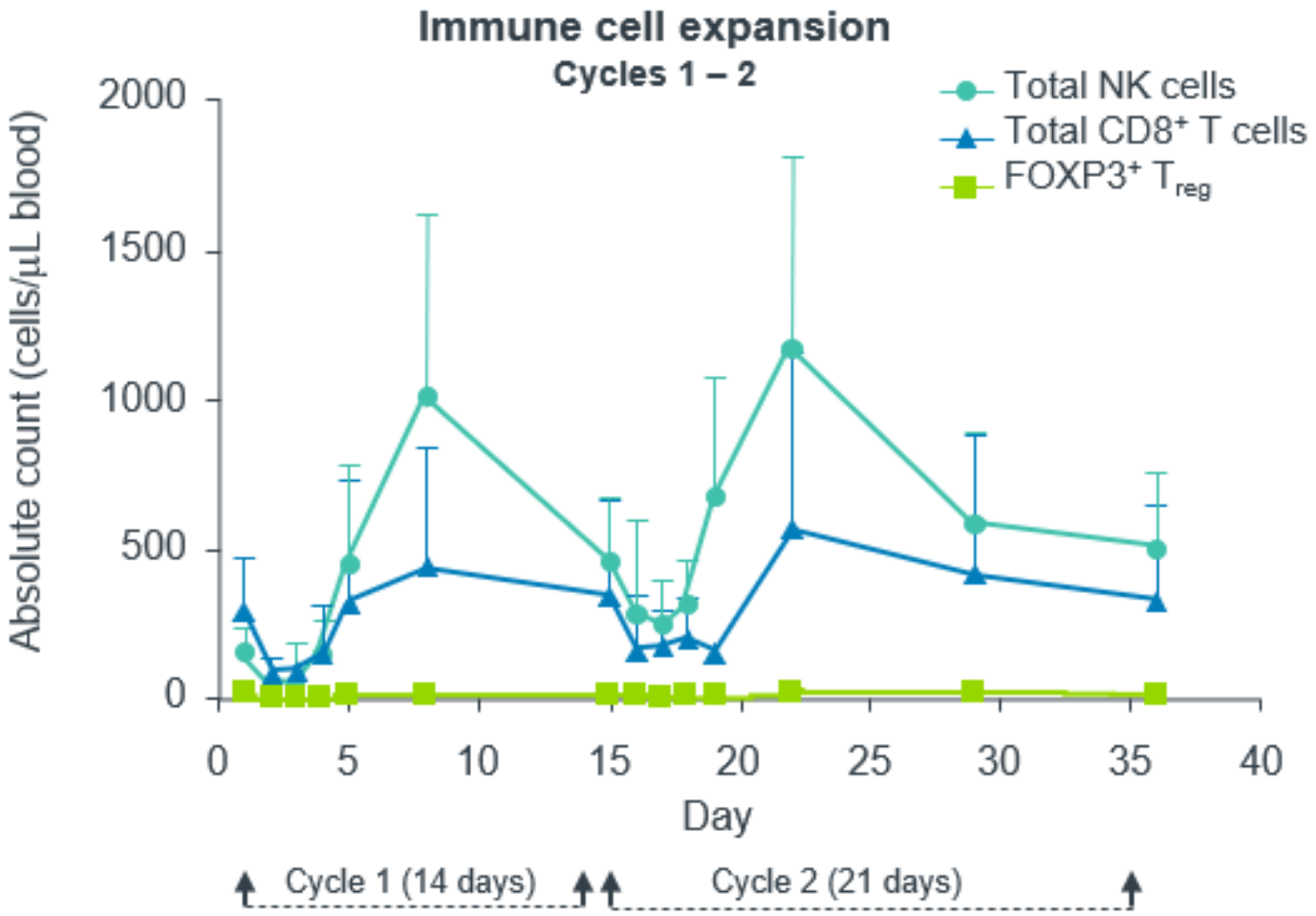
Clinical Pharmacodynamic Effects of Nemvaleukin[1,2]



CD8+ and NK cells expanded while T_{reg} cells remained suppressed

Nemvaleukin data are from the 6 µg/kg cohort in Part A of the study. For fold change plots, data are mean + SE (N=10). For time course plot, data are mean + SD (N=12).
1. Bhatt et al. Poster P123 presented at SITC 2018. 2. Vaishampayan et al. Oral Abstract 2500 presented at ASCO 2022. Fmax, maximum fold change; HD, high-dose; IL-2, interleukin-2; IV, intravenous; NK, natural killer; PD, pharmacodynamic; SD, standard deviation; SE, standard error; TID, 3 times daily; Treg, regulatory T cell

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Nemvaleukin: Deliberate and Focused Development Program

Type of Clinical Trial	Trial Name / Phase	Tumor Types	Dosing	Mono or Combo? Status
Foundational	ARTISTRY-1 Phase 1/2	Advanced solid tumors	Daily IVx5	- Multiple responses in mono and combo - Enrollment complete
Alternative Dosing	ARTISTRY-2 Phase 1/2	Advanced solid tumors	SC Q1W	- Combo with pembro - Data maturing
	ARTISTRY-3 Phase 1/2	Select advanced solid tumors	Less frequent IV	- Mono and pembro combo - RP2Ds expected 1Q 2024
Registrational enabling	ARTISTRY-6 Phase 2	Mucosal melanoma	All of the above	- Monotherapy - Enrollment ongoing
	ARTISTRY-7 Phase 3	Platinum-resistant ovarian cancer	Daily IVx5	- Pembro combo - Enrollment ongoing

Abbrev.: **IV**: Intravenous; **LFIV:** Less frequent IV; **SC:** Subcutaneous

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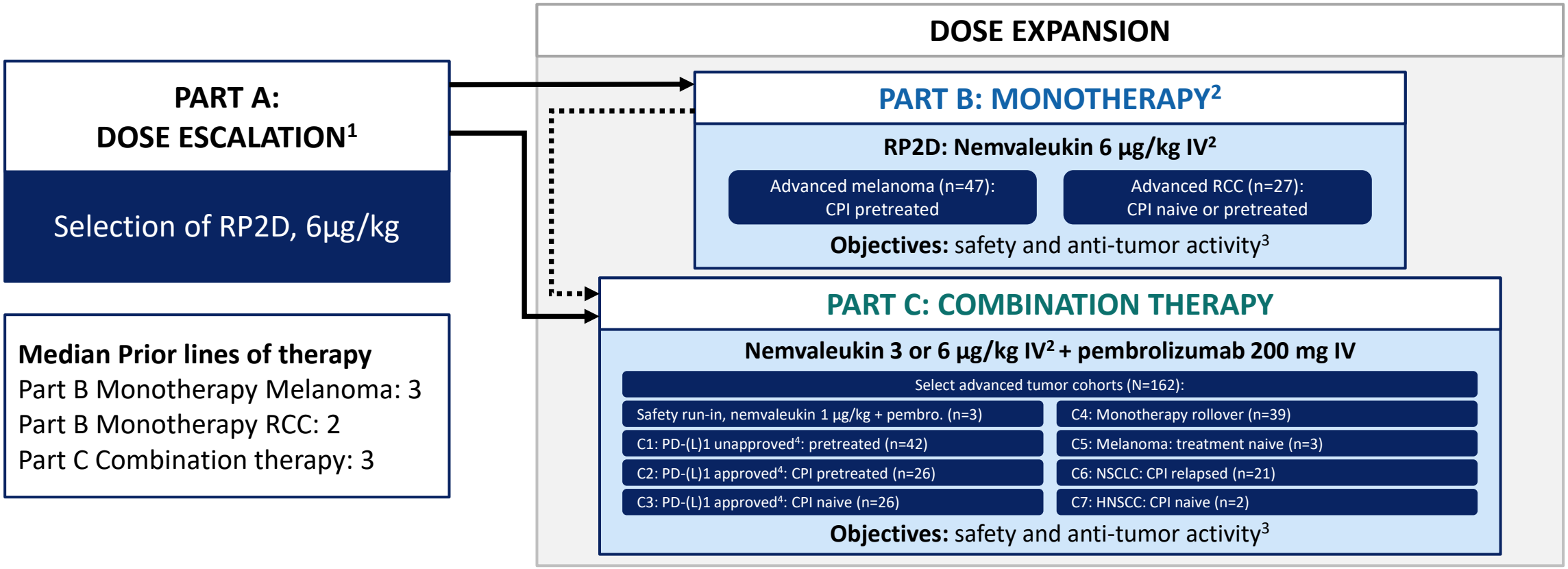
ARTISTRY-1: First-In-Human Study of IV Nemvaleukin
Global, Multicenter, Open-Label Phase 1/2 Study



NCTO2799095

1. Patients from Parts A and B could roll over to Part C upon progression or stable disease (after ≥ 4 cycles) on monotherapy.
2. Nemvaleukin daily Q5D, then off treatment for 9 days (cycle 1) or 16 days (cycle 2+).
3. ORR assessed by investigator (RECIST v1.1).
4. Nemvaleukin 3 µg/kg/d in C1-C4, 6 µg/kg/d in C5-C7. PD-(L)1 approved/unapproved indication based on FDA prescribing information and may have changed over time.

Abbrev.: **1-7**: Cohort 1-7; **CPI**: checkpoint inhibitor; **HNSCC**: head & neck squamous cell carcinoma; **IV**: intravenous; **NSCLC**: non-small cell lung cancer; **ORR**: overall response rate; **PD-(L)1**: programmed death (ligand) 1; **RCC**: renal cell carcinoma; **RECIST**: Response Evaluation Criteria In Solid Tumors; **RP2D**: recommended phase 2 dose

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Nemvaleukin's Adverse Event Profile in ARTISTRY-1 Was Consistent with Our Expectations Based on its Mechanism of Action

Monotherapy (Part B only; N=74) [1]

Event, n (%)	Overall N = 74
Any AE, regardless of causality	73 (99%)
Grade 3 or 4 nemvaleukin-related AE	56 (76%)
Nemvaleukin-related AEs leading to discontinuation	3 (4%)
Nemvaleukin-related AEs leading to death	0

- Most frequently (>30%) reported TRAEs include pyrexia, chills, neutropenia, increased AST, nausea, and hypotension; consistent with anticipated effects of cytokine administration
- Most frequent Grade 3-4 TRAE (>10%) was neutropenia
- Three patients discontinued due to TRAEs (Grade 3 failure to thrive in melanoma, Grade 2 ECG T wave abnormal and Grade 1 cardiac troponin I increase in melanoma, and Grade 3 bronchospasm in RCC)

Combination with Pembrolizumab (Part C only; N=166) [1]

Event, n (%)	Combination N = 166
Any AE, regardless of causality	162 (98%)
Grade 3 or 4 nemvaleukin-related AE	86 (52%)
Nemvaleukin-related AEs leading to discontinuation	6 (4%)
Nemvaleukin-related AEs leading to death	1 (1%)

- Chills and pyrexia were most frequently (>30%) reported TRAEs; and fatigue was most frequently reported nemvaleukin and pembrolizumab-related TRAE; consistent with anticipated effects of cytokine release and/or pembrolizumab administration (generally transient, majority Grade ≤2 in severity)
- Most frequent Grade 3-4 nemvaleukin-related AEs (>10%) were neutropenia and anaemia
- Discontinuations due to nemvaleukin-related AEs included: Grade 3 arthralgia, Grade 2 cytokine release syndrome, Grade 3 fatigue, Grade 2 infusion related reaction, Grade 3 pneumonitis, and Grade 5 starvation

1. Data as of March 27, 2023

Abbrev.: **AE:** Adverse Event; **TRAE:** Treatment Related Adverse Event; **AST:** aspartate aminotransferase; **RCC:** Renal Cell Carcinoma

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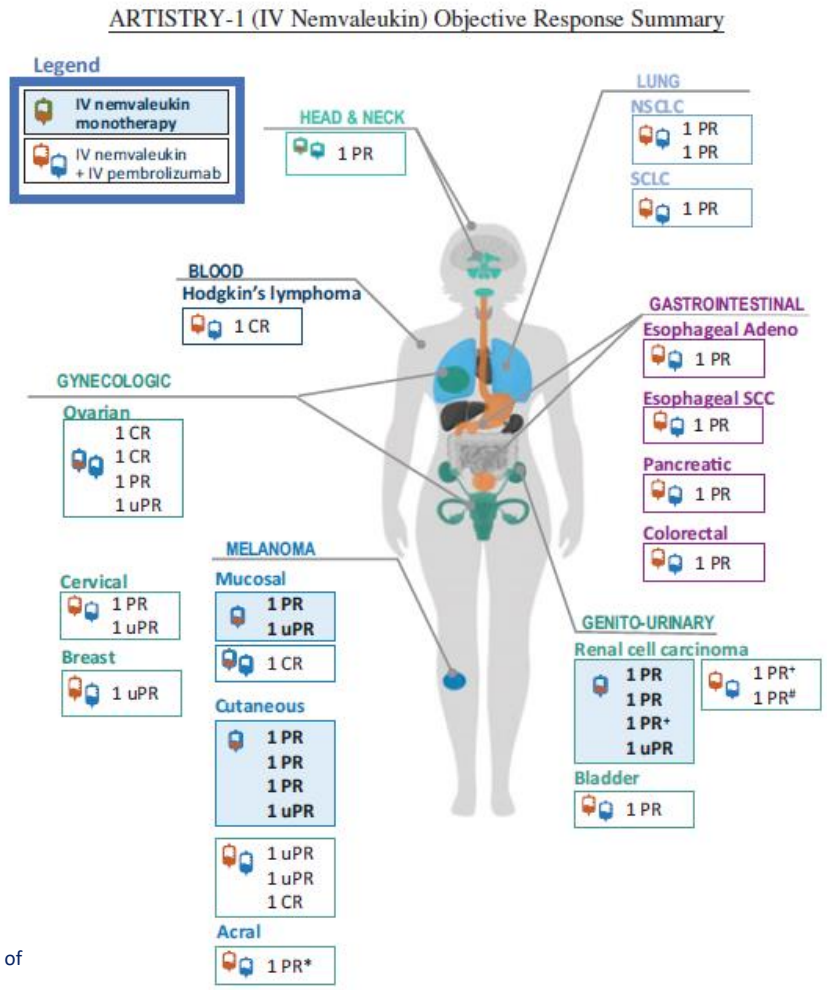
ARTISTRY-1: IV Nemvaleukin Demonstrated Durable[1] and Deepening[2] Responses in High Unmet Need Populations

Monotherapy activity (IV) in prior anti-PD-(L)1 treated melanoma and renal cell carcinoma

- **10 Objective responses (10 PRs (7 confirmed)) including:**
  - Clinically meaningful disease control rates
  - 2 PRs (1 confirmed) were observed in mucosal melanoma and 4 PRs (3 confirmed) were observed in cutaneous melanoma
  - 4 PRs (3 confirmed) were observed in RCC

Combination activity (IV) with pembrolizumab in a range of tumor types

- **24 Objective responses (5 CRs, 14 PRs, 5uPRs) including:**
  - **5 CRs - 2 in Platinum-Resistant Ovarian Cancer (PROC),** and 1 each in Mucosal Melanoma, Cutaneous Melanoma, and Hodgkin's lymphoma
  - **Additional responses** in a broad range of tumor types, both anti-PD-(L)1 approved and unapproved (Gastric, Esophageal, Breast, Cervical, Endometrial, NSCLC, Pancreatic, SCLC, SCCHN, RCC, PROC and Melanoma (acral, mucosal, cutaneous))



Data as of March 27, 2023

Patients achieved SD (*acral), PR (⁺RCC), and PD (#RCC) on nemvaleukin monotherapy, rolled over to combination therapy and achieved PR.

1. A durable response is defined as a response with a duration that exceeds the response generally observed with standard of care treatment; in the context of high unmet disease states such as mucosal melanoma and PROC, a response that exceeds six months is considered durable
2. A deepening response is defined as a response in which tumors have continued to shrink in subsequent scans

Abbrev.: **IV:** Intravenous; **NSCLC:** Non-small cell lung cancer; **SCLC:** Small cell lung cancer; **RCC:** Renal cell carcinoma; **SCCHN:** Squamous cell carcinoma of the head and neck **CR:** complete response; **PR:** partial response; **uPR:** unconfirmed PR; **SD**: stable disease; **PD**: progressive disease

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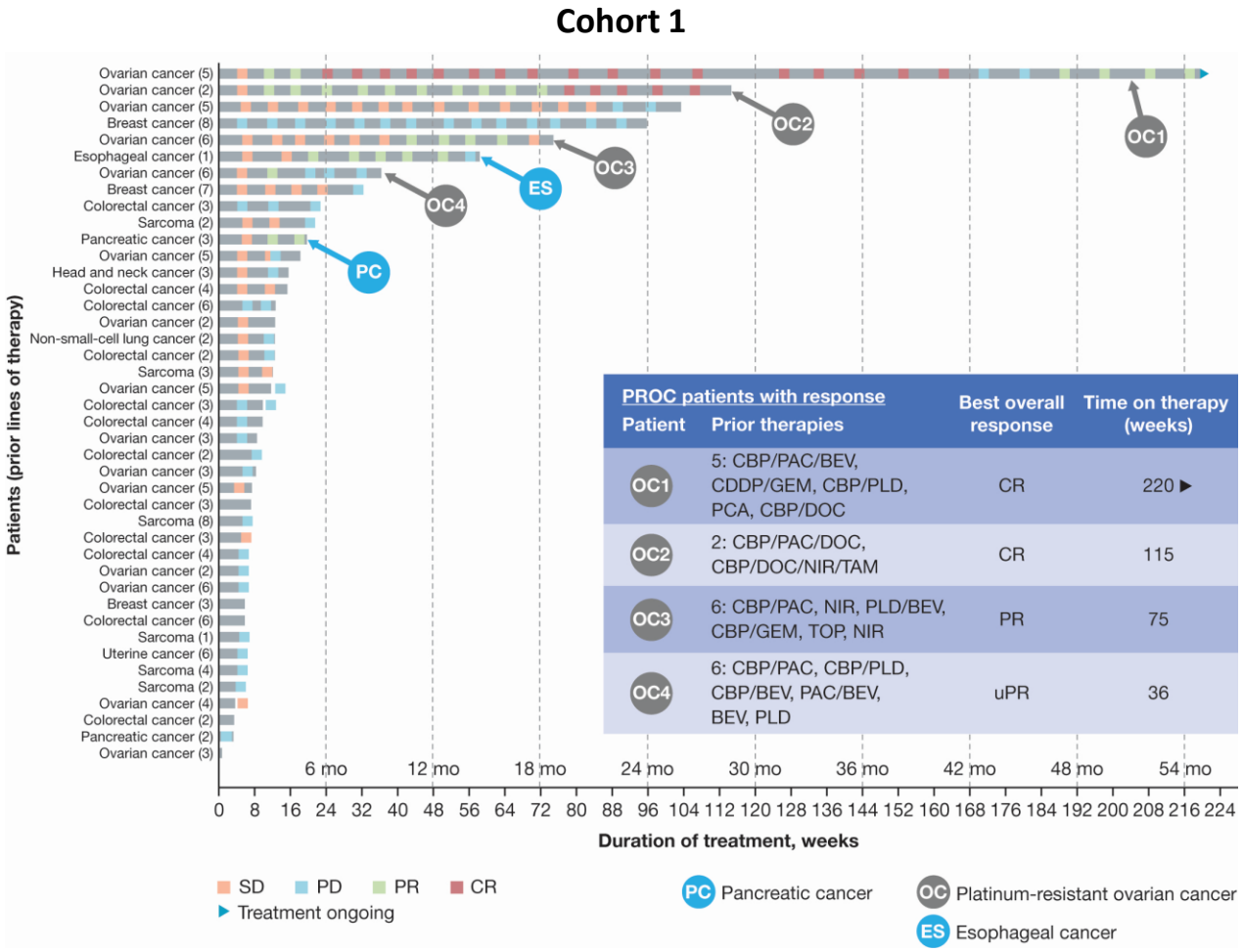
ARTISTRY-1: IV Nemvaleukin Combination Responses with Pembrolizumab (Part C, Cohort 1)



	PROC (n=14)
Best overall response, n (%)	
CR	2 (14.3%)
PR	2 (14.3)*
SD	6 (42.9)
PD	2 (33.3)
ORR, n (%)	4 (28.6)*
DCR, n (%)	10 (71.4)*
Median DOR in weeks	65.5

PD-(L)1 approved/unapproved indication based on FDA prescribing information and may have changed over time. Responses per RECIST v1.1

*Includes 1 confirmed PR, 1 unconfirmed PR

Data cut off Mar 27 2023

Abbrev.: **BEV**: bevacizumab; **CBP**: carboplatin; **CDDP**: cisplatin; **CR**: complete response; **DOC**: docetaxel; **FDA**: Food and Drug Administration; **GEM**: gemcitabine; **mo**: month; **NIR**: niraparib; **NSCLC**: non–small cell lung cancer; **PAC**: paclitaxel; **PCA**: paclitaxel albumin; **PD**: progressive disease; **PD-(L)1**: programmed death (ligand) 1; **PLD**: pegylated liposomal doxorubicin hydrochloride; **PR**: partial response; **PROC**: platinum-resistant ovarian cancer; **SCLC**: small-cell lung cancer; **SD**: stable disease; **TAM**: tamoxifen; **TOP**: topotecan; **uPR**: unconfirmed PR

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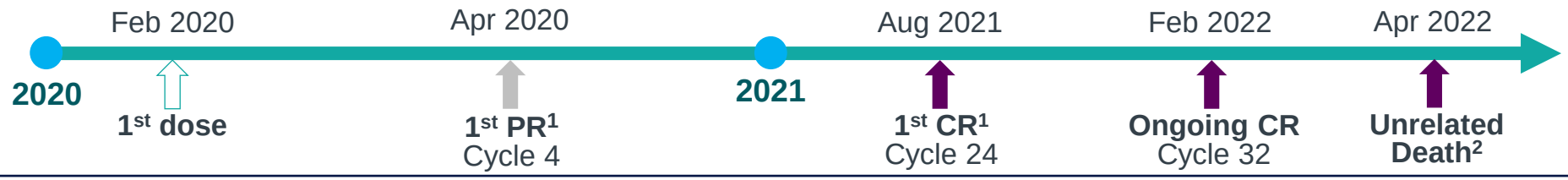
Complete Response in 83-Year-Old Patient with Platinum-Resistant Ovarian Cancer

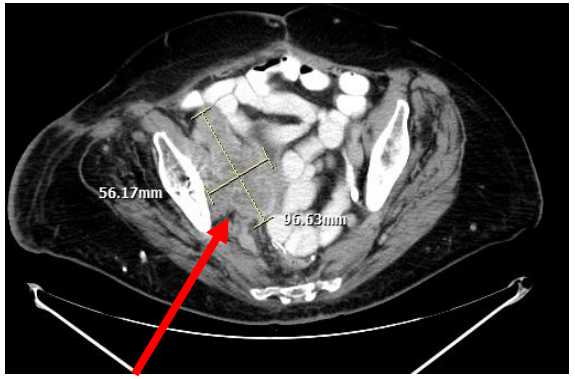
OC2 **83-year-old woman**

- Diagnosed in 2008 with high-grade serous ovarian cancer
- 2 prior lines of therapy

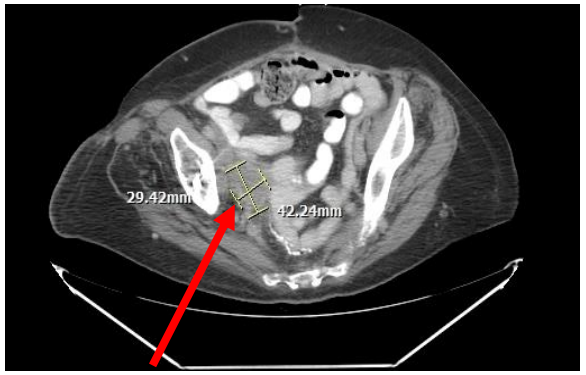
Nemvaleukin + pembrolizumab
Time on therapy 115 weeks



Right hemipelvic lesion

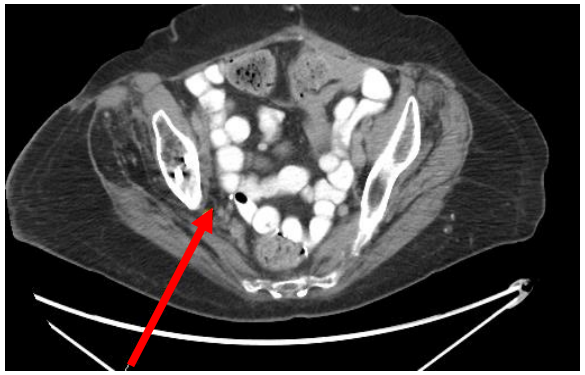


Jan 29, 2020
Baseline



Apr 21, 2020
Cycle 4

PR[1] 55% ↓ in target lesion



Aug 03, 2021
Cycle 24

CR[1] Max 100% ↓ in target lesion

1 Response per RECIST v1.1
2 Death unrelated to TX, subject remained in CR thru final response assessment

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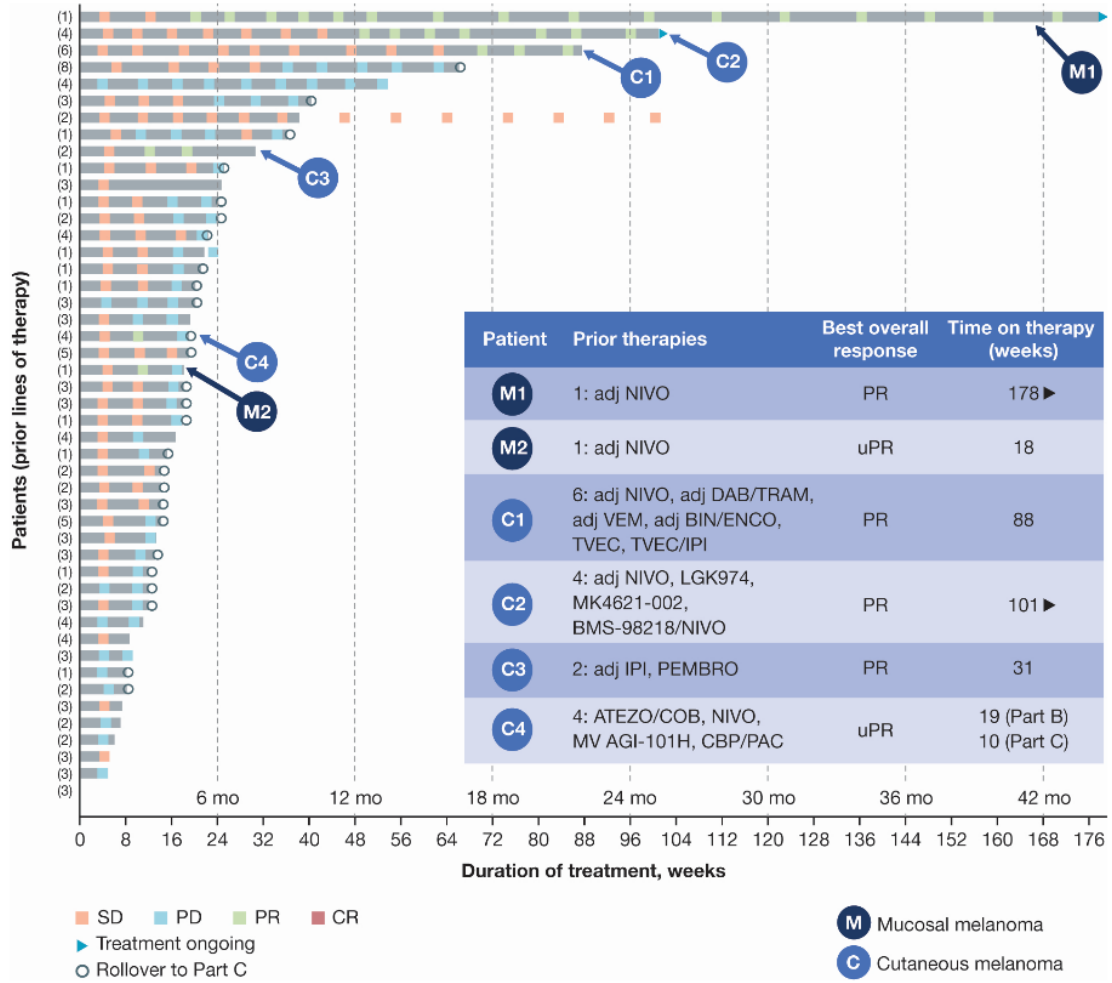
ARTISTRY-1: IV Nemvaleukin Demonstrated Monotherapy Responses in Melanoma (Part B)



Patient	Prior therapies	Best overall response	Time on therapy (weeks)
M1	1: adj NIVO	PR	178 ▶
M2	1: adj NIVO	uPR	18
C1	6: adj NIVO, adj DAB/TRAM, adj VEM, adj BIN/ENCO, TVEC, TVEC/IPI	PR	88
C2	4: adj NIVO, LGK974, MK4621-002, BMS-98218/NIVO	PR	101 ▶
C3	2: adj IPI, PEMBRO	PR	31
C4	4: ATEZO/COB, NIVO, MV AGI-101H, CBP/PAC	uPR	19 (Part B) 10 (Part C)

	All[a,b] (n=46)	Mucosal (n=6)
Best overall response, n (%)		
CR	0	0
PR	6 (13.0)[c]	2 (33.3)[d]
SD	30 (65.2)	2 (33.3)
PD	10 (21.7)	2 (33.3)
ORR, n (%) [95% CI]	6 (13.0) [4.9-26.3][c]	2 (33.3) [4.3-77.8][d]
DCR, n (%) [95% CI]	36 (78.3) [63.6-89.1] [c]	4 (66.7) [22.3-95.7] [d]
DOR in weeks[d], Mean (SD) Median (range)	40.77 (55.6) [c] 16.75 (6.1-150.3)	78.2 (101.9)[d] 78.2 (6.1-150.3)

[a] Excludes 1 patient who did not meet tumor-evaluable criteria. [b] Patients with mucosal, cutaneous, uveal, acral included in 'All'. [C] Includes 4 confirmed PRs, 2 unconfirmed PRs, [d] 1 confirmed PR. [e] DOR for Part B only and does not include patients who rolled over to Part C; some patients may still be on treatment

- All responders had been on prior CPI therapy and progressed
- FDA Orphan Drug and Fast Track designations, as well as MHRA's ILAP Innovation Passport, granted in mucosal melanoma
- Data supported design of ARTISTRY-6 study

Responses per RECIST v1.1

Data cut off Mar 27, 2023

Abbrev.: **adj**: adjuvant; **ATEZO**: atezolizumab; **BIN**: binimetinib; **CBP**: carboplatin; **CI**: confidence interval; **COB**: cobimetinib; **CPI**: checkpoint inhibitor; **CR**: complete response; **DAB**: dabrafenib; **DCR**: disease control rate (CR+PR+SD); **DOR**: duration of response; **ENCO**: encorafenib; **FDA**: US Food and Drug Administration; **IPI**: ipilimumab; **MV**: melanoma vaccine; **NA**: not applicable; **NIVO**: nivolumab; **ORR**: overall response rate; **PAC**: paclitaxel; **PD**: progressive disease; **PEMBRO**: pembrolizumab; **PR**: partial response; **SD**: stable disease; **TRAM**: trametinib; **TVEC**: talimogene laherparepvec; **VEM**: vemurafenib

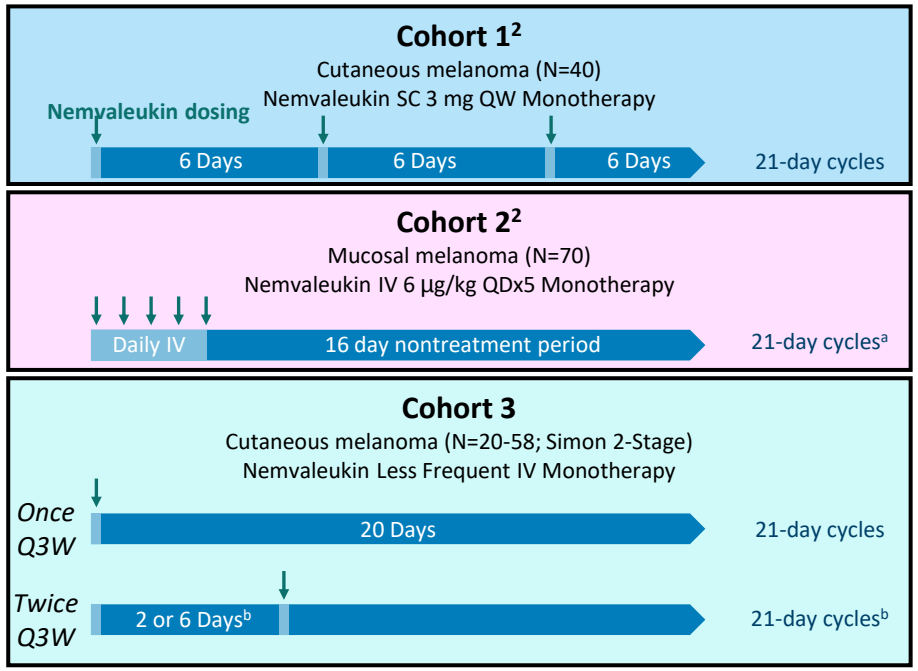
MURAL ONCOLOGY

ARTISTRY-6: Phase 2 / Potentially Registrational Study for Mucosal Melanoma

Investigational Nemvaleukin SC, IV or LFIV Monotherapy [1]

Key eligibility criteria [1]

- Unresectable and/or metastatic cutaneous or mucosal melanoma
- Patient has received anti–PD(L)-1 ± anti–CTLA-4 therapy
- No more than 1 prior systemic therapy
- Measurable disease per RECIST v1.1
- ECOG PS 0-1



Key endpoints (independent of cohort) [2]

- **Primary:** ORR per RECIST v1.1 (by independent central review)
- **Key secondary:** DOR, PFS, DCR, TTR per RECIST v1.1 (by independent central review)

[a] With the exception of Cycle 1, which is 14 days (daily IV for 5 days + 9 days nontreatment), all cycles were 21 days[3]
[b] Twice Q3W could be either D1/4 or D1/8 Q3W, to be informed by ARTISTRY-3

1. https://clinicaltrials.gov, NCT04830124
2. Lewis K, et al. Presentation at the Melanoma and Immunotherapy Bridge 2021 Virtual Congress; December 1-4, 2021
3. Data on file. ARTISTRY-6 Protocol Amendment 1 (Version 2.0). January 5, 2021

Abbrev.: **CTLA-4:** cytotoxic T-lymphocyte–associated antigen 4; **DCR**: disease control rate; **DOR**: duration of response; **ECOG PS**: Eastern Cooperative Oncology Group performance status; **IV**: intravenous; **ORR**: objective response rate; **PD-(L)1**: programmed death (ligand) 1; **PFS**: progression-free survival; q7d, every 7 days; **RECIST**: Response Evaluation Criteria in Solid Tumors; **SC**: subcutaneous; **TTR**: time to response

MURAL ONCOLOGY

ARTISTRY-7: Phase 3 / Potentially Registrational Study for Platinum-Resistant Ovarian Cancer

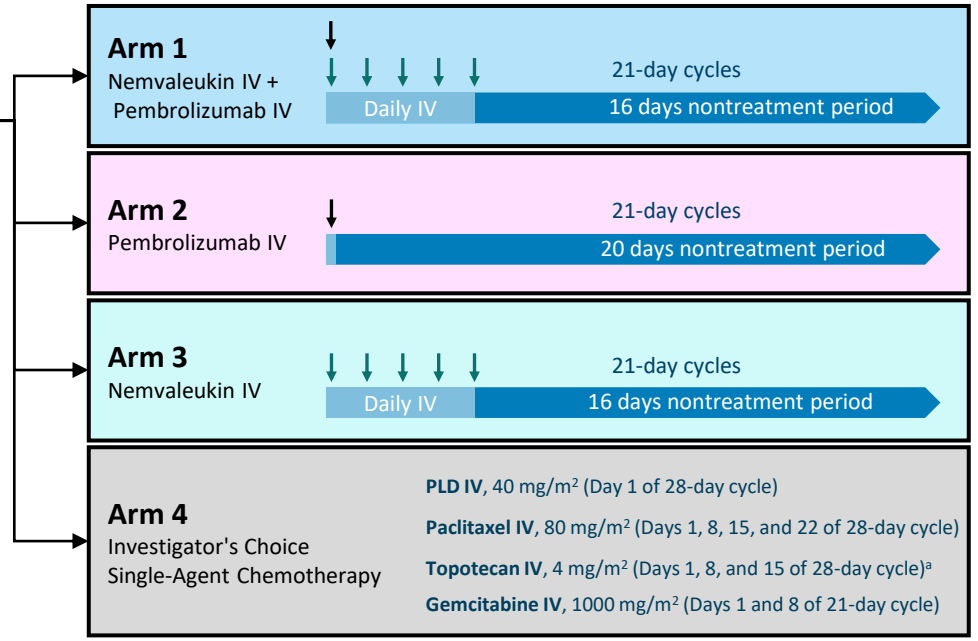
Investigational Nemvaleukin IV ± Pembrolizumab Versus Pembrolizumab Monotherapy or Chemotherapy

Estimated 376 participants

Randomization
3:1:1:3
Futility analysis planned for monotherapy arms [1]

Key eligibility criteria [2]

- Platinum-resistant/ refractory epithelial ovarian, fallopian tube, or primary peritoneal cancer
- At least 1L of systemic platinum therapy and ≤5L of systemic platinum-resistant therapy
- Prior bevacizumab treatment
- Measurable disease by RECIST v1.1



Key Endpoints

Primary outcome measure:

- Investigator assessed PFS[b]

Secondary outcome measures:

- ORR, DCR, DOR, and TTR[b]
- CA-125 response[c]
- OS and TEAEs

Clinical trial and supply agreement with MSD (a tradename of Merck & Co., Inc. Kenilworth, NJ, USA)

Conduct of trial is in association with The GOG Foundation, Inc. (GOG), the European Network of Gynaecological Oncological Trial groups (ENGOT), and the Asia-Pacific Gynecologic Oncology Trials Group (APGOT)

↓ Pembrolizumab dosing ↓ Nemvaleukin dosing

[a] Alternative topotecan regimen: 1.25 mg/m² on Days 1-5 of 21-d cycles
[b] Response per RECIST v1.1
[c] Response per GCIG

1. Herzog T et al. Poster presented at the Society for Gynecologic Cancers Annual Meeting (SGO), Phoenix, AZ, March 18-21, 2022
2. https://clinicaltrials.gov, NCT05092360

Abbrev.: **CA-125**: cancer antigen-125; **DCR**: disease control rate; **DOR**: duration of response; **GCIG**: Gynecologic Cancer InterGroup; **IV**: intravenous; **ORR**: objective response rate; **OS**: overall survival; **PFS**: progression-free survival; **PLD**: pegylated liposomal doxorubicin; **RECIST**: Response Evaluation Criteria in Solid Tumors; **TEAE**: treatment-emergent adverse event; **TTR**: time to response

MURAL ONCOLOGY

Focused on Initial, Potentially Registrational Indications with Compelling Expansion Opportunities

Initial Development
Two indications with unmet need

Platinum-Resistant Ovarian Cancer
13K Patients[1,2]

- FDA Fast Track Designation
- In combination with pembrolizumab
- Potential to provide an immunotherapy option to an indication where CPIs have failed

Mucosal Melanoma
2K Patients[1]

- FDA Fast Track and Orphan Drug Designation
- Opportunity to further establish monotherapy efficacy in a larger patient cohort
- Potential to be first approval specific to mucosal melanoma

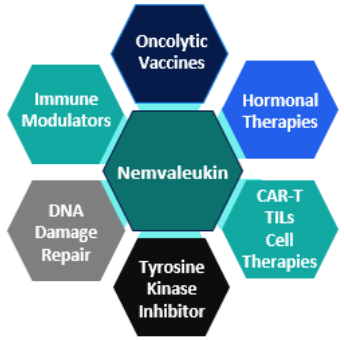
Planned Expansion Into Broader Cancer Indications
Evolution of a proven cytokine
provides opportunity to expand utility

Earlier Lines of Therapy in Ovarian and Cutaneous Melanoma

40K+
First line patients in each indication[1]

Multiple complete and partial responses
Observed in both cutaneous melanoma and ovarian cancer in combination with an anti-PD-(L)1 therapy

Other Mechanistic Combinations



Scientific rationale for many combinations to advance cancer treatment across a range of tumor types

Apply design and development approach to advance additional immunotherapy approaches

1. Clarivate Epidemiology; Estimated number of patients in the U.S. and Europe
2. Represents 3rd line PROC patients

Abbrev.: CPI: Checkpoint Inhibitor; **MOA**: Mechanism of Action; **RCC**: Renal Cell Carcinoma; **NSCLC**: Non-small cell lung cancer

MURAL ONCOLOGY

Exploration of Optimal Dose Administration and Schedule for Nemvaleukin to Establish Recommended Phase 2 Dose

- **Initial IV nemvaleukin dosing regimen:** 5x daily Q3W
  - Dosing modeled after the currently approved high-dose rhIL-2 dosing
- **Alternative dosing options being evaluated**
  - Explore potential broad utility and ability to offer flexible and convenient options to patients, caregivers, and providers
  - Exploring less frequent IV dosing: Days 1 and 4 Q3W; and Days 1 and 8 Q3W. RP2D selections expected in 1Q 2024
  - **ARTISTRY-3**: Phase 1/2 open label study of less frequent IV dosing options of nemvaleukin in patients with advanced solid tumors (cohort 2)
  - **ARTISTRY-6**: Dedicated cohort of patients with cutaneous melanoma (cohort 3) to establish proof of concept

1. Pending identification of the recommended Phase 2 dose for the less frequent IV dosing regimen currently being evaluated in ARTISTRY-3

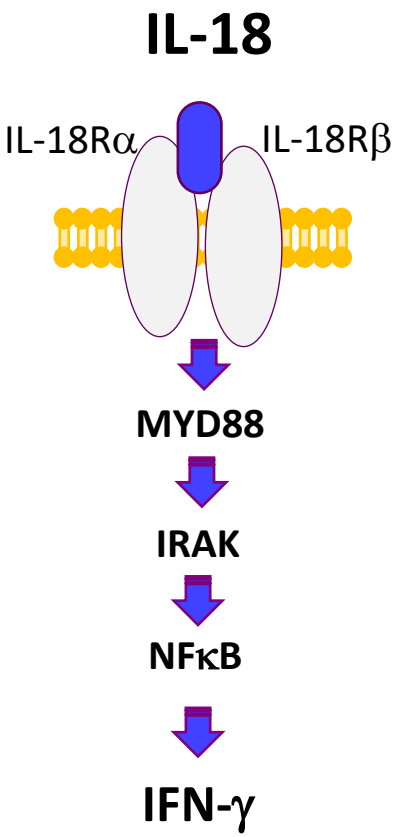
MURAL ONCOLOGY

SECTION 3:

ADDITIONAL PIPELINE PROGRAMS

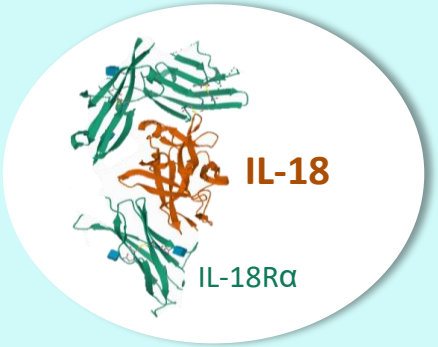
Anti-Tumor Immune-Biology of Native IL-18: A Potent Immuno-stimulator of Innate and Adaptive Immunity

Initially discovered as IFNγ–inducing factor



Distinctive biology vs. IL-2 and IL-12

Immunomodulation by IL-18[1,2]



1 Activates NK cells and antigen-experienced CD8⁺ T cells

- Anti-tumor cytotoxic activity
- Leads to IFNγ production for further immune activation

2 Re-invigorates dysfunctional T cells

- Reduces cancer immune evasion and increases tumor-killing

3 Matures dendritic cells (DCs)

- Increases antigen presentation
- Enhances activation of NK and T cells

PBMC: Peripheral Blood Mononuclear Cells. IL-18BP: IL-18 Binding Protein

Source: 1) Zhou, T. et al. (2020) *Nature* 583:609-14. 2) Alkermes internal data

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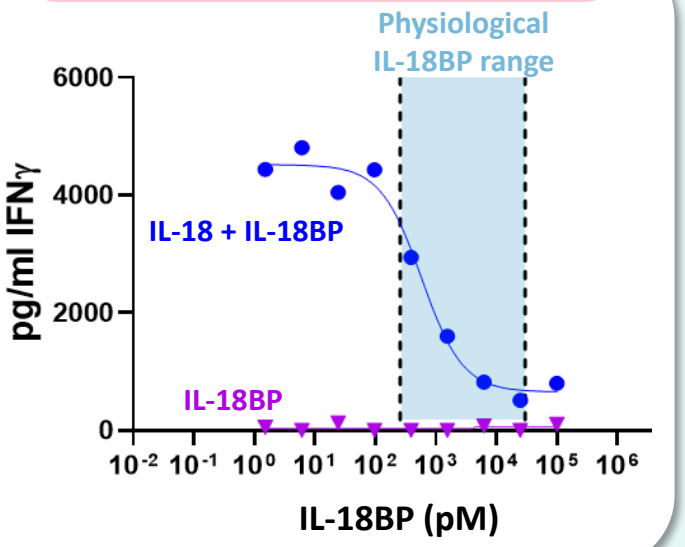
Native IL-18 is Limited by IL-18 Binding Protein

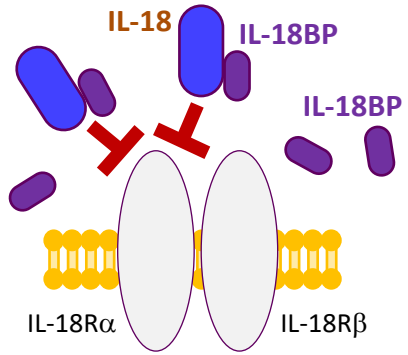
IL-18 Binding Protein (IL-18BP)[1]

- Soluble IL-18 decoy receptor
- Binds IL-18 and neutralizes interaction with IL-18Rα

Loss of IL-18 activity due to IL-18BP in vitro[2]

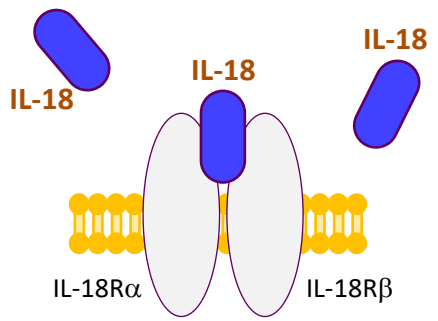


IL-18BP-rich TME



Minimal IL-18 Signaling
Lack of anti-tumor immunity

Ideal interaction



NK / CD8⁺ T / DCs

Re-invigorates exhausted T-cells
↑Anti-tumor immunity

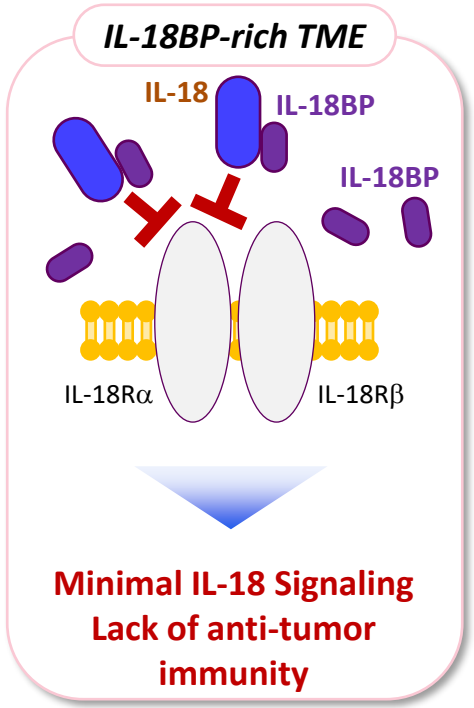
rhIL-18: Recombinant human IL-18. IFNγ: Interferon gamma. IL-18BP: IL-18 binding protein. DCs: Dendritic cells. TME: Tumor microenvironment

1. Robertson et al (2008). Clinical Cancer Research, 14(11), 3462-3469. 2. Alkermes internal data

MURAL ONCOLOGY

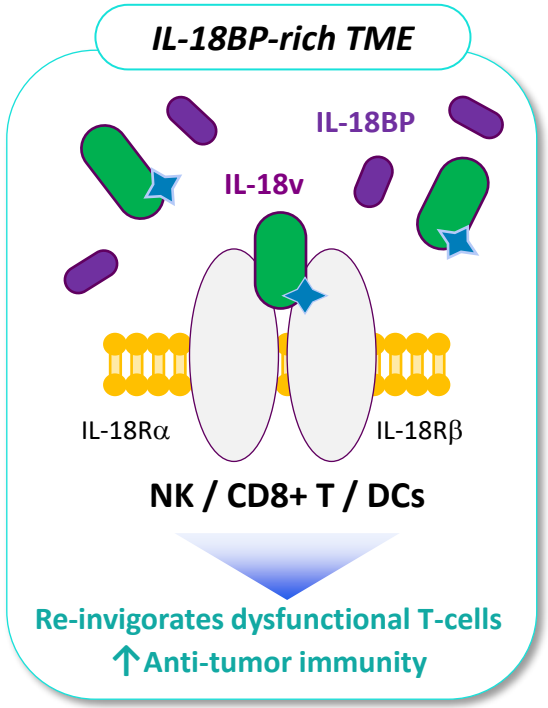
Mural Oncology IL-18 Engineering: Resist IL-18BP Checkpoint to Unleash the Therapeutic Potential of IL-18

Challenge to IL-18



Internal expertise in protein engineering

Mural Solution: design IL-18 variant resistant to IL-18BP

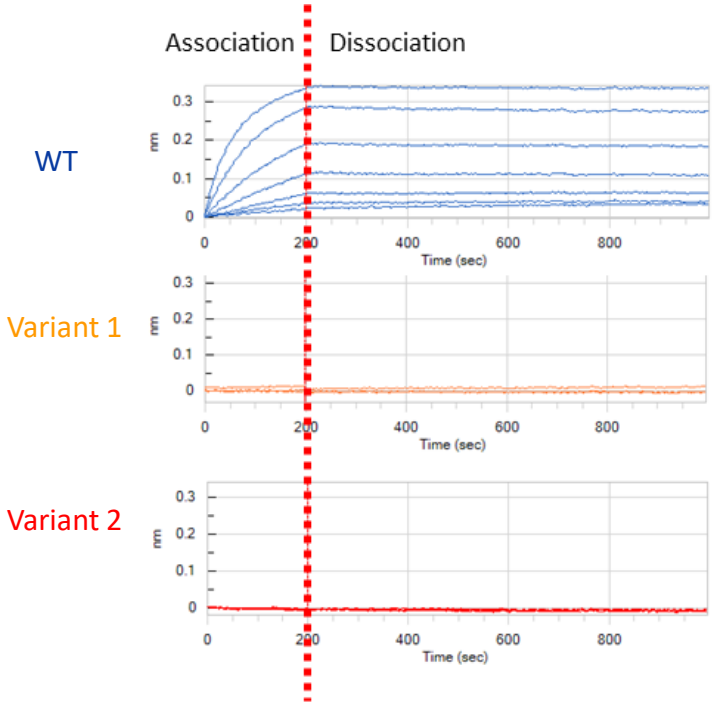


Design Approach via Mutation(s):

1. **Resist IL-18 neutralization by immune checkpoint IL-18BP**
2. **Retain and optimize IL-18 activity**

Mural Variants Do Not Bind IL-18BP in Preclinical Studies: Excellent Potency with Maximal Resistance to IL-18BP Inhibition

*No Detectable Binding Between Variants and IL-18BP

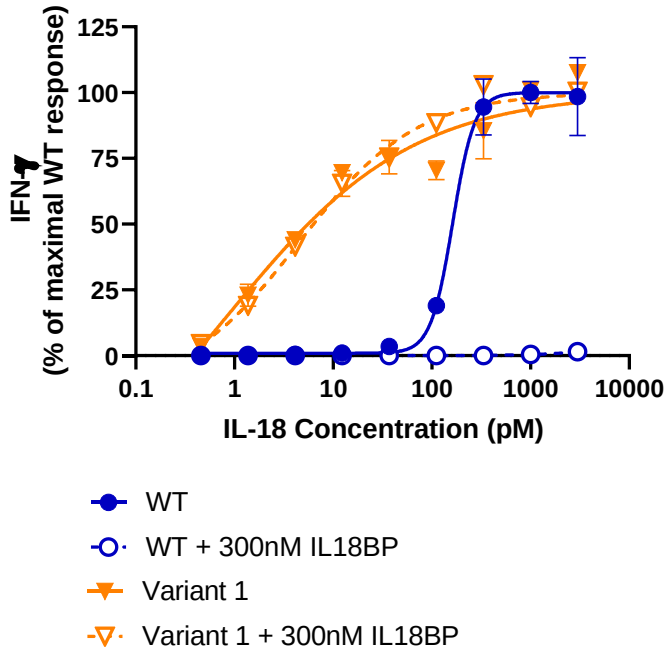


Note: No detectable binding between variants and hIL-18BP hIL18BP tested up to 1µM

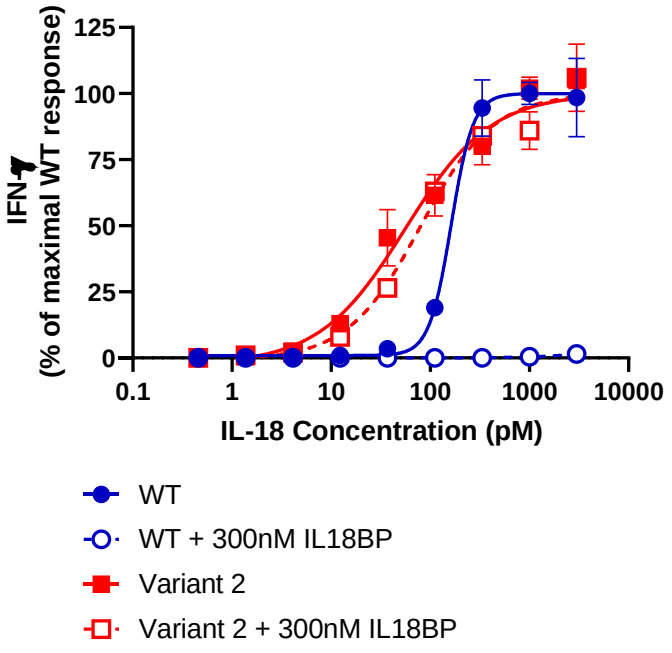
*Alkermes Internal Data

*Variants with Similar or Stronger Potency vs WT IL-18 with Resistance to IL-18BP Suppression

Maximal Resistance with Potency Stronger than WT

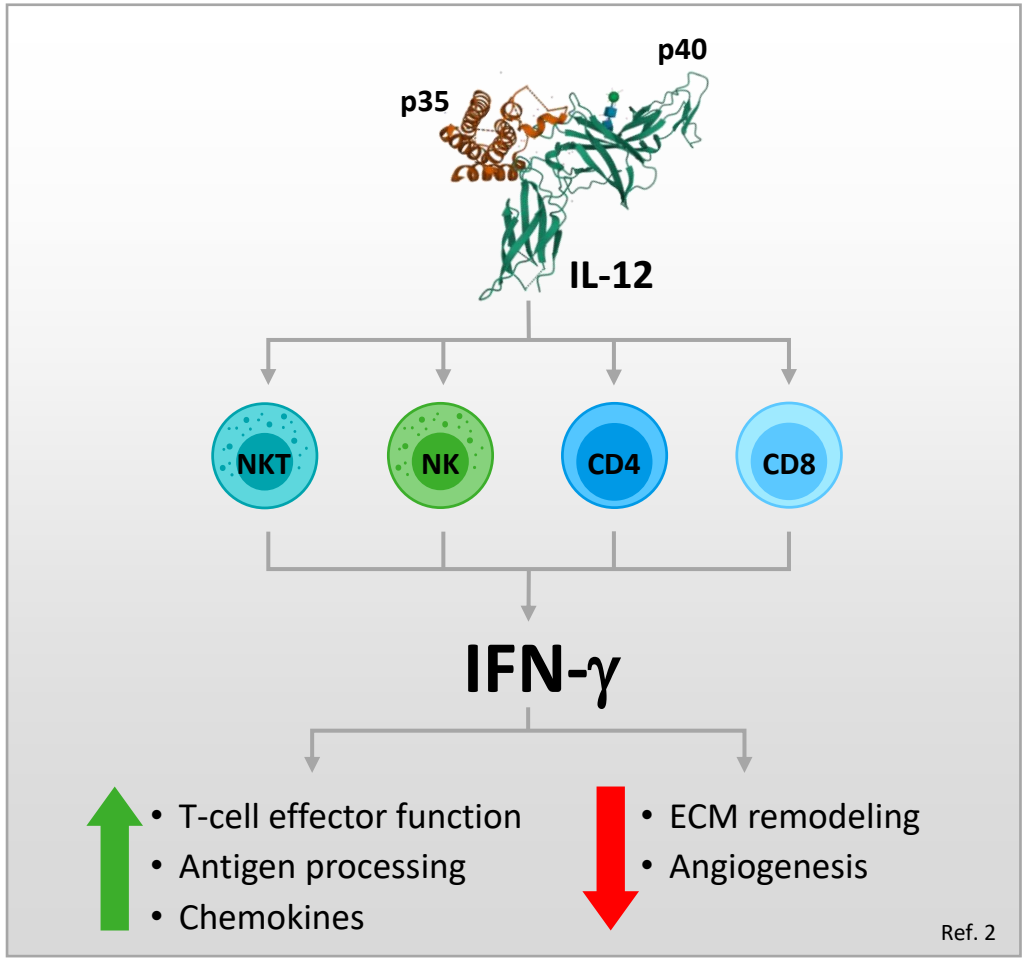


Maximal Resistance with Potency Similar to WT



IL-12 is Recognized as a Highly-Potent Proinflammatory Cytokine But Clinical Utility Has Been Limited by Severe Toxicities

- **Heterodimeric protein consisting of two covalently linked subunits[1]**
  - Individual components, p35 and p40, are inactive
- **Anti-tumor efficacy observed in preclinical studies[2]**
  - Driven by activation of innate and adaptive immune compartments and production of IFN-γ[1]
- **Clinical evaluation limited by narrow therapeutic window[1,2,3]**
  - Severe toxicities associated with systemic exposure to IL-12 leading to a narrow therapeutic index[1,2,3]



NKT = Natural killer T cell, NK = Natural killer cell, CD4 = CD4+ T cell, CD8 = CD8+ T cell

1. Nguyen KG et. al. Cancer Immunotherapy. Front. Immunol. October 15 2020 11:575597
2. Vecchio MD et. al. Clin Cancer Res August 15 2007 (13) (16) 4677-4685
3. Strauss J et. al. Clin Cancer Res January 1 2019 (25) (1) 99-109

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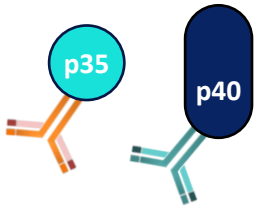
Mural's Approach: Tumor Site-Specific Assembly of Functional IL-12 Designed to Limit Systemic IL-12 Exposure

Build functional IL-12 in the tumor with goals of avoiding toxicity associated with systemic exposure and maximizing the IL-12 therapeutic window

IL-12 subunits are fused to Mural's antibody fragments

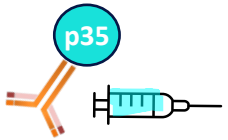
Tumor-targeted IL-12 subunits

Non-targeted engineered inactive subunits

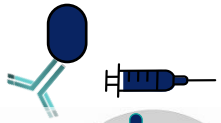


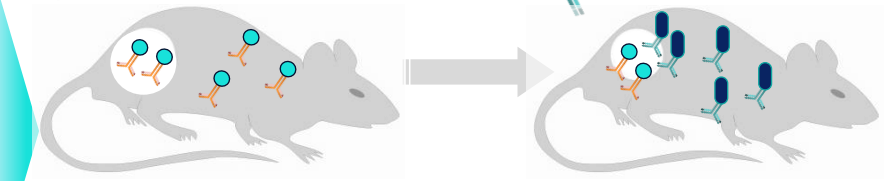
Tumor-targeting Antibody fragments

Treat with targeted **p35 subunit**



Treat with targeted **p40 subunit**



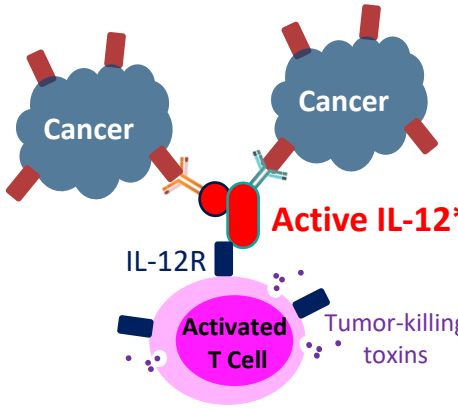


Clearance of systemic p35 subunits from circulation

Results in **active IL-12 in the tumor**

Active IL-12 assembly *in situ*

Cancer cells expressing tumor antigen



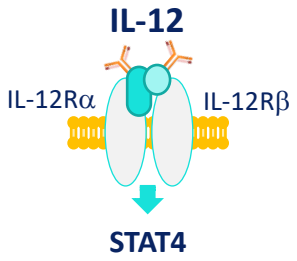
*IL-12 subunits could be both cis- and trans-acting

- Designed to reduce systemic exposure to functional IL-12, thereby potentially reducing associated toxicities
- Targeted accumulation of functional IL-12 in the tumor may improve anti-tumor activity

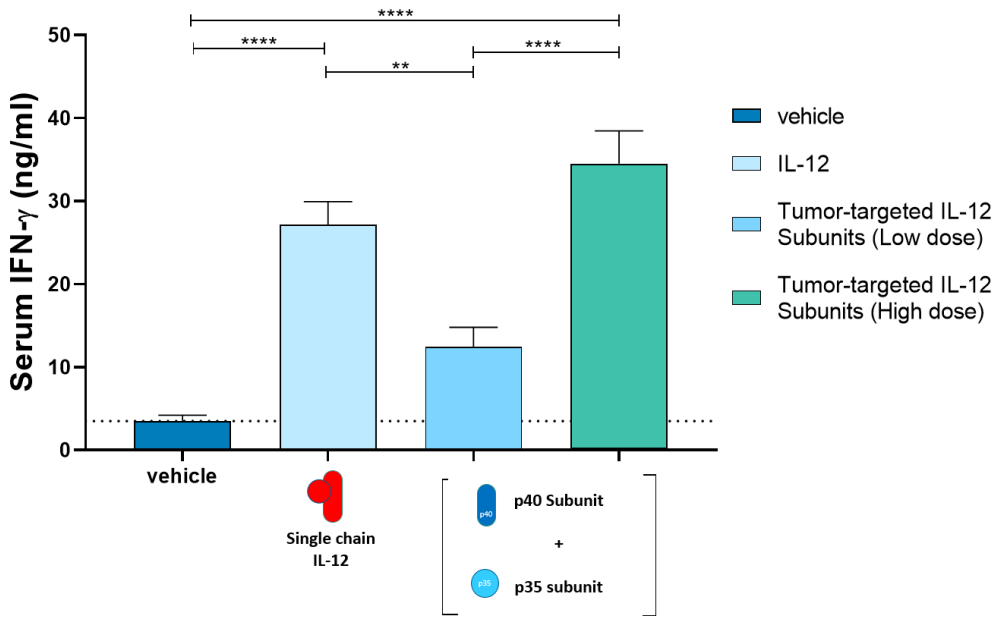
MURAL ONCOLOGY

Tumor-Targeted Split IL-12 Program Design

The potential of IL-12	• A highly potent proinflammatory cytokine that has demonstrated preclinical efficacy and clinical activity [3] when delivered intratumorally • Clinical activity observed in ovarian, melanoma, RCC, and pancreatic tumors [1,2]
Key anti-tumor mechanisms of IL-12	• Drives pro-inflammatory responses at the tumor site through potent activation of innate and adaptive immune cells
Technical challenge of systemic delivery of IL-12	• Limited rhIL-12 clinical utility due to severe toxicities where tolerable systemic dosing regimens are not efficacious
Mural Oncology protein engineering solution	• Separate inactive tumor-targeted IL-12 subunits designed to assemble and activate within the tumor with the potential to avoid toxicity associated with systemic exposure



Sequential Administration of Split IL-12 Subunits Resulted in Dose-Dependent PD Response in PBMC Humanized NCG Mouse Model



1. Nguyen KG et. al. Cancer Immunotherapy. Front. Immunol. October 15 2020 11:575597.
2. Vecchio MD et. al. Clin Cancer Res August 15 2007 (13) (16) 4677-4685. 3.Strauss J et. al. Clin Cancer Res January 1 2019 (25) (1) 99-109.
3. Clinical activity based on third party data

Source: Company internal data on file

Abbrev: **rhIL-12**: recombinant human IL-12; **GLP:** good laboratory practice

MURAL ONCOLOGY

SECTION 4:

FINANCIAL OVERVIEW

Mural Oncology Carve-Out Financials

- Mural Oncology is expected to have $200M - $300M of cash on the balance sheet upon separation
- Key milestones
  - Candidate nominations for IL-18 and IL-12 expected in 2024
  - PROC top-line data readout expected 1Q 2025[1]
  - Mucosal melanoma top-line data readout expected 1Q 2025[1]

(in millions)	Year Ended December 31, 2022	Year Ended December 31, 2021
Operating Expenses		
External R&D Expenses:		
Total Nemvaleukin Spend	77.8	80.1
Early Discovery and Other External R&D Spend	20.2	16.1
Total External R&D Expenses	98.0	96.2
Internal R&D Expenses	69.2	63.6
Total Research and Development Expenses	167.2	159.8
General and Administrative	17.7	15.5
Total Operating Expenses	**184.9**	**175.4**
Operating Loss	**(184.9)**	**(175.4)**
Income Tax Provision	4.9	0.1
Net Loss and Comprehensive Loss	**$(189.8)**	**$(175.4)**

1. Subject to patient enrollment

Mural Oncology - Highlights

Mural Oncology

1. **Mural Oncology is the oncology business of Alkermes plc**; Mural Oncology is expected to be separated into a new, independent publicly traded company via a spin-off in 4Q 2023. Two key data readouts anticipated within 18 months
2. **Portfolio of novel, investigational cytokines** engineered to optimize the "known knowns" of native interleukins – retain their high potency while potentially overcoming their low tolerability
3. **Nemvaleukin is an intrinsically active, stable fusion protein which does not degrade into native-IL-2** and is designed to selectively bind to the intermediate-affinity IL-2 receptor, enabling a potentially enhanced therapeutic window
4. **Nemvaleukin has generated compelling clinical data to date,** with durable responses[1] in monotherapy and in PD-1 combination across a range of tumor types. Exploring alternative dosing regimens. ARTISTRY-6 and ARTISTRY-7 readouts expected in 1Q 2025[2]
5. **IL-18 and IL-12 programs in preclinical development** with potentially differentiated therapeutic properties and leveraging advanced protein engineering capabilities. Candidate nominations expected in 2024

1. Durable response defined as a response with a duration that exceeds the response generally observed with standard of care treatment; in the context of high unmet disease states such as mucosal melanoma and platinum-resistant ovarian cancer ("PROC"), a response that exceeds six months is considered durable
2. Subject to patient enrollment

Abbrev.: **IL-2:** interleukin-2: **IL-12:** interleukin-12; **IL-18:** interleukin-18

MURAL ONCOLOGY

THANK YOU!

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