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ANNUAL MEETING 2023
APRIL 14-19 • #AACR23

GLIMMER-01: Initial results for dose escalation of a phase 1/2 trial demonstrating proof of mechanism of a novel, first-in-class bi-sialidase (E-602) in solid tumors

Jason J. Luke MD, Melissa Johnson MD, Anthony Tolcher MD, Christopher T. Chen MD, Tong Dai MD, Brendan D. Curti MD, Anthony B. El-Khoueiry MD, Mario Sznol MD, Brian S. Henick MD, Christine Horak PhD, Pushpa Jayaraman PhD, Christopher B. Cole MD PhD, Dawn Wilson, Lizhi Cao PhD, Jenny Che PhD, Li Peng PhD, David Feltquate MD PhD, Deanne Lathers PhD, Manish R. Sharma MD

PALLEON® PHARMACEUTICALS

Disclosures past 3 years

- **Updated disclosures available at:** https://www.linkedin.com/in/jason-luke-11a38910/
- **DSMB:** Abbvie, Agenus, Immutep, Evaxion
- **Scientific Advisory Board:** (no stock) 7 Hills, Affivant, BioCytics, Bright Peak, Exo, Fstar, Inzen, RefleXion, Xilio (stock) Actym, Alphamab Oncology, Arch Oncology, Duke Street Bio, Kanaph, Mavu, NeoTx, Onc.AI, OncoNano, physIQ, Pyxis, Saros, STipe, Tempest
- **Consultancy with compensation:** Abbvie, Agenus, Alnylam, AstraZeneca, Atomwise, Bayer, Bristol-Myers Squibb, Castle, Checkmate, Codiak, Crown, Cugene, Curadev, Day One, Eisai, EMD Serono, Endeavor, Flame, G1 Therapeutics, Genentech, Gilead, Glenmark, HotSpot, Kadmon, KSQ, Janssen, Ikena, Inzen, Immatics, Immunocore, Incyte, Instil, IO Biotech, Macrogenics, Merck, Mersana, Nektar, Novartis, Partner, Pfizer, Pioneering Medicines, PsiOxus, Regeneron, Replimmune, Ribon, Roivant, Servier, STINGthera, Synlogic, Synthekine
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- **Patents:** (both provisional) Serial #15/612,657 (Cancer Immunotherapy), PCT/US18/36052 (Microbiome Biomarkers for Anti-PD-1/PD-L1 Responsiveness: Diagnostic, Prognostic and Therapeutic Uses Thereof)

Current as of March 17th, 2023

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@jasonlukemd

Siglecs are a large family of sialoglycan-sensing ITIM-containing checkpoint receptors (Glyco-Immune Checkpoints)

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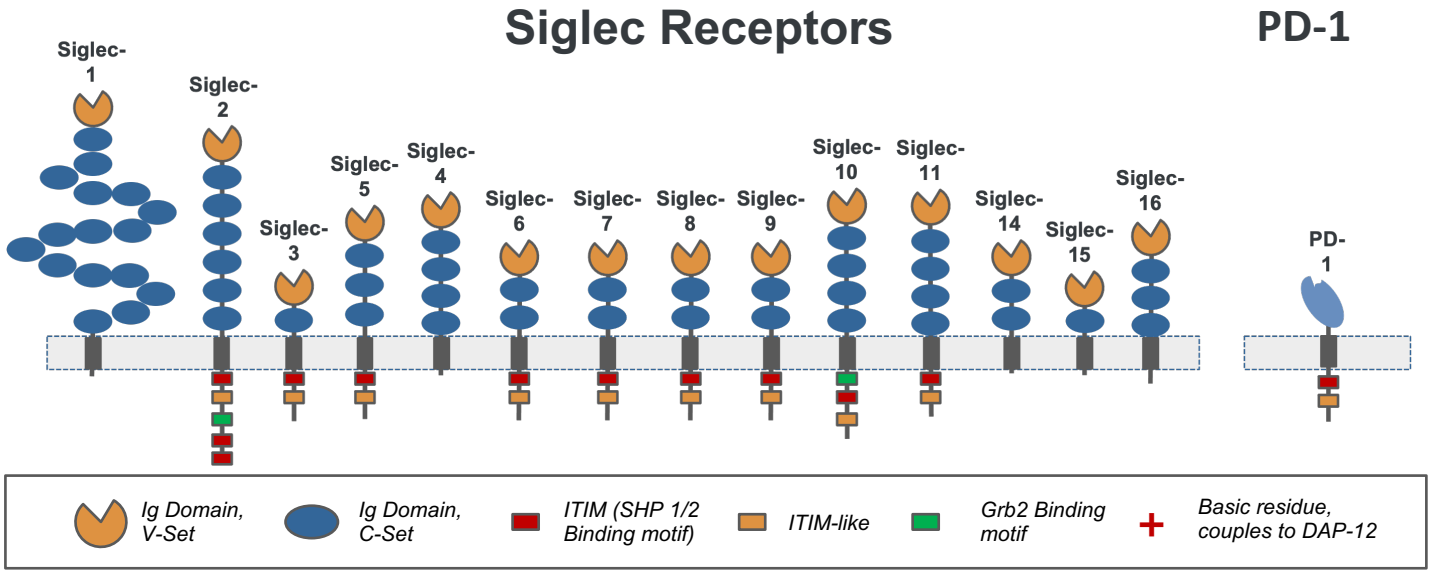
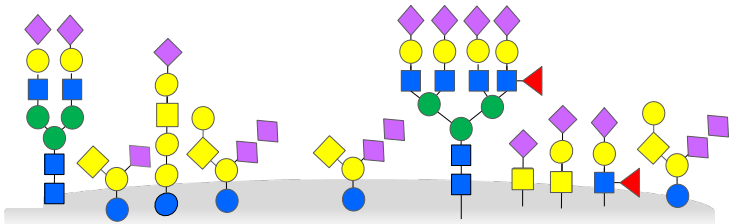


Sialoglycans are the ligands for Siglec receptors

Sialoglycans = glycan (carbohydrate) + sialic acid

- Sialoglycans are glycans that contain a terminal sialic acid and are present on many glycoproteins, glycolipids
- Many tumors are **hypersialylated** relative to healthy tissue
- Exhausted T cells become hypersialylated

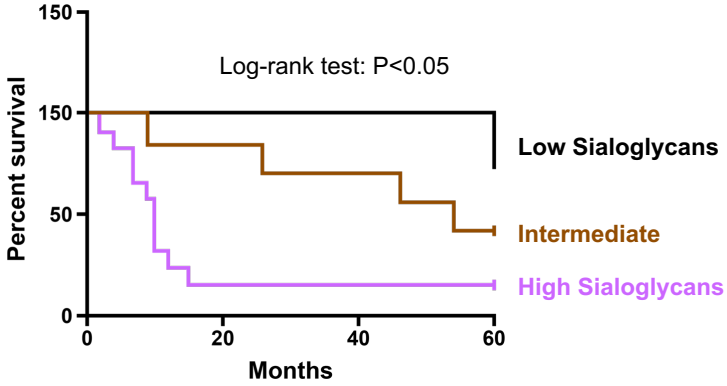


Cell Surface Sialoglycans

Glucose *Galactose* *GlcNAc* *GalNac*
Fucose *Mannose* *Sialic Acid*

Hypersialylation is associated with poor prognosis: Melanoma Example

Survival: High vs. Low Expression of Tumor Surface Sialoglycan GM3 and GD3

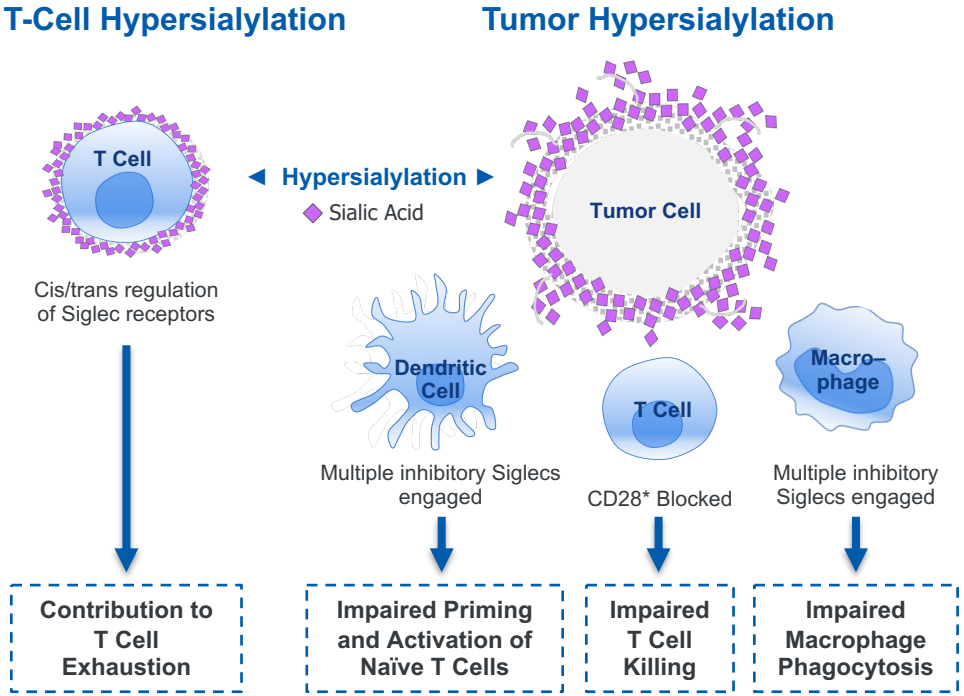


50+ studies in multiple tumor types including lung, colon, breast, melanoma, and others.

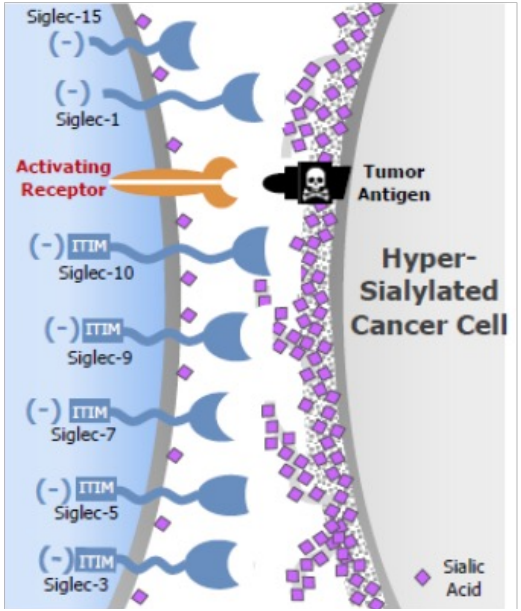
Reviewed in Smith and Bertozzi Nat Rev Drug Disc 2021, Dobie and Skropeta BJC 2021

Sialoglycans promote tumor immune evasion

Hypersialylation of both immune cells and tumors enables immune evasion



Redundancy in Siglec-Sialoglycan axis makes targeting Siglecs difficult



Sialic Acid

Gray et al. Nat Chem Biol 2020
Reviewed in Duan and Paulson Ann Rev Immunol 2020

230102GA

E-602: Desialylation as a Cancer Therapy

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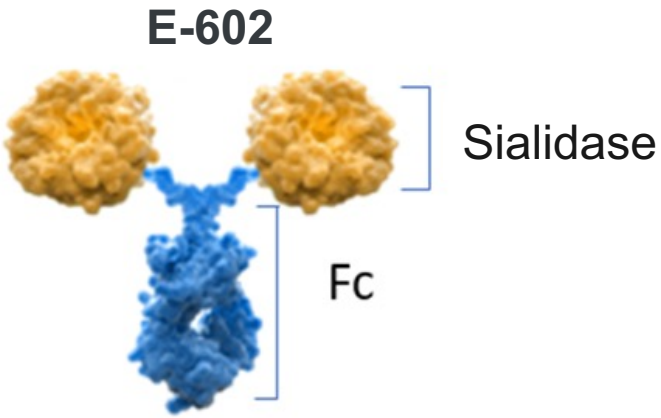
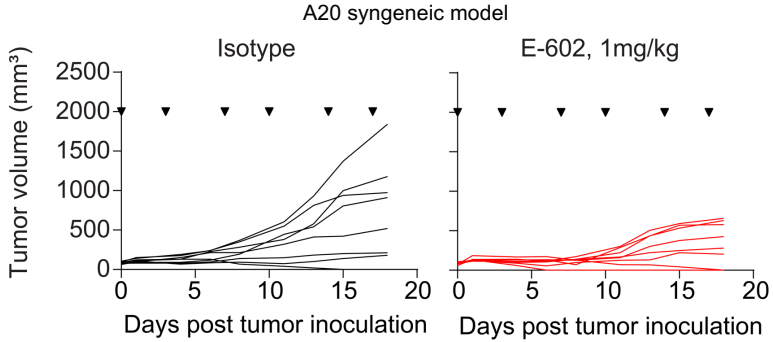
E-602 is a first-in-class fusion protein of engineered human sialidase and a human IgG1 Fc region

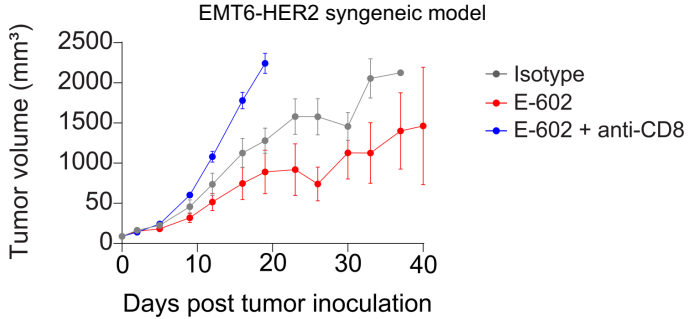


- E-602 preclinical studies demonstrated augmentation of immune function
  - Augments antigen-specific priming
  - Promotes activation of T cells
  - Restores function of exhausted-like T cells

Single agent antitumor activity *in vivo**



E-602-mediated anti-tumor activity depends on CD8 T cells



*Other preclinical models with demonstrated efficacy for EAGLE bi-sialidase molecules include B16, CT26, MC38

Glycan-Mediated Immune Regulation With a Bi-Sialidase Fusion Protein (GLIMMER-01)

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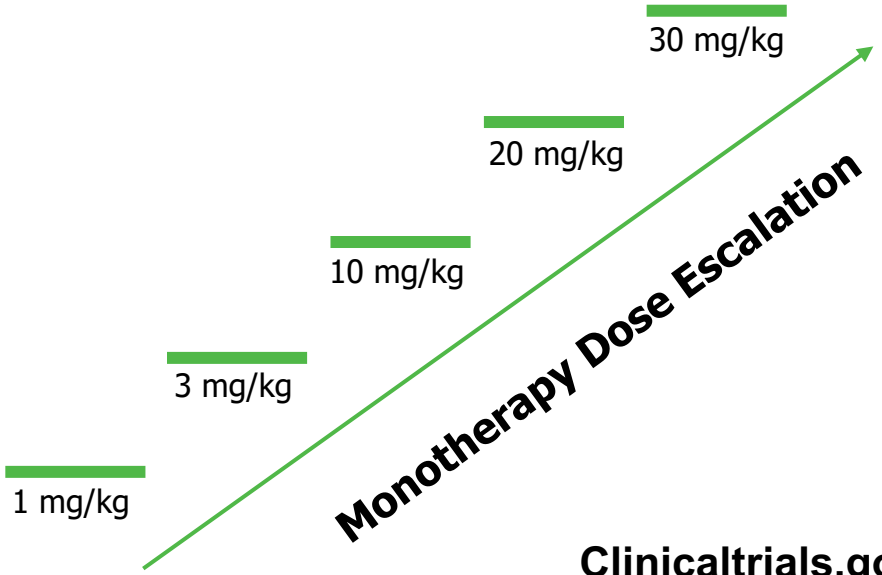
Phase 1 Study Schema



- Modified 3+3 dose escalation
- Backfill of up to 15 patients permitted
- E-602 administered IV once weekly
- Pre- and post-treatment biopsies optional
- Tumor types included have high sialylation in previous tumor surveys
  - Eligible tumor types include: ovarian, melanoma, NSCLC, breast, CRC, gastric/EGJ, pancreatic, urothelial, head and neck

Clinicaltrials.gov: NCT05259696

Baseline Characteristics

Number of Patients Treated Per Dose Level

Dose Level	Dose Escalation	Backfill
1 mg/kg	n = 5	Not applicable
3 mg/kg	n = 4	Not applicable
10 mg/kg	n = 5	n = 4
20 mg/kg	n = 6	n = 9
30 mg/kg	n = 7	n=5; Ongoing

Baseline Patient Characteristics

- Median Age: 58 years (Range 34 – 75)
- Female: 22 / 40 (55%)
- ECOG PS of 1: 28 / 40 (70%)
- Frequency of Baseline Tumor Hypersialylation: 13 / 19 (68%)*

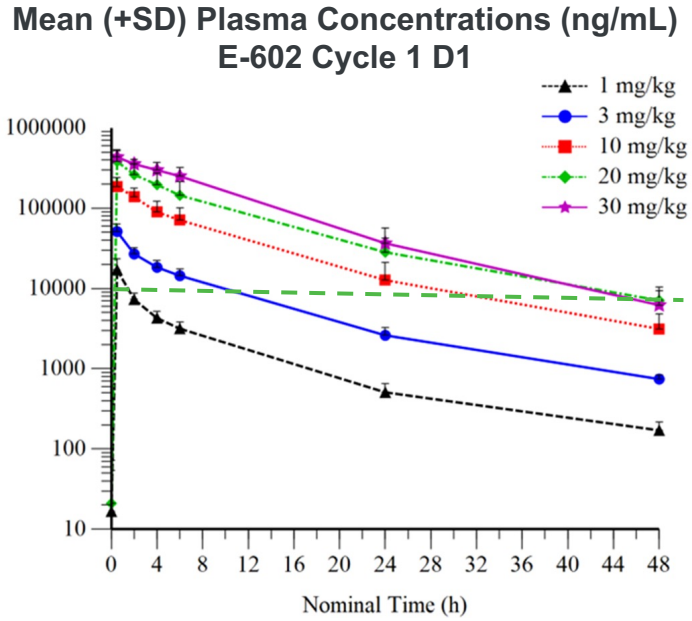
Tumor Type	Tumor Type (N=40), n (%)	Prior Treatment Lines (Mean, Range)	Prior PD(L)-1 Therapy
Colorectal	21 (52.5%)	4.4 (2-9)	14%
Pancreatic	10 (25%)	3.3 (1-5)	0%
NSCLC	3 (7.5%)	3 (2-4)	100%
Ovarian	2 (5.0%)	7 (5-9)	50%
EGJ	1 (2.5%)	2	100%
Gastric	1 (2.5%)	5	100%
Head and Neck	1 (2.5%)	4	100%
Melanoma	1 (2.5%)	2	100%

* As assessed by HYDRA (3/7/9), Palleon's proprietary reagents compatible with IHC

Preliminary Data as of 01-Apr-2023

E-602 target threshold maintained in plasma for >24 hours

- Dose proportional Cmax and AUC from 1 mg/kg to 30 mg/kg
- T1/2β ~20-24 hours
- **Biologically active plasma concentration (10,000 ng/mL) maintained for >24 hours** at dose levels above 10 mg/kg



Threshold for biologically active E-602 plasma concentration (10,000 ng/mL) as estimated from *in vitro* desialylation experiments. Indicated by green dashed line (---)

Preliminary Data as of 10-Feb-2023

E-602 is tolerated at doses up to 30 mg/kg

Frequency of Treatment-Related Adverse Events Occurring in > 1 Patient

Adverse Event N=40 patients	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)
Infusion related reaction	4 (10%)	15 (37.5%)	1 (2.5%)	
Fatigue	2 (5%)	1 (2.5%)		
Lymphocyte count decreased		1 (2.5%)	2 (5%)	
Abdominal pain		2 (5%)		
Myalgia	2 (5%)			
Nausea		2 (5%)		
Tachycardia	2 (5%)			
Vomiting	2 (5%)			

TRAEs in a single patient (n=1): anemia, amylase increased, arthralgia, blood alkaline phosphatase increased, blood TSH increased, chills, constipation, decreased appetite, dehydration, diarrhea, dizziness, dyspepsia, headache, hyperkalemia, hypertension, hyponatremia, hypotension, lipase increased, pruritus, rash maculopapular, rhinitis

- Doses up to 30 mg/kg were tolerated with no dose-limiting toxicities
- Most frequent adverse event was infusion-related reactions at doses ≥10 mg/kg
- Median number of doses administered = 6 (Range: 1 – 15^{+})
- To date, response-evaluable patients have had stable or progressive disease

Preliminary Data as of 01-Apr-2023

E-602 induces sustained, dose-dependent desialylation of peripheral immune cells

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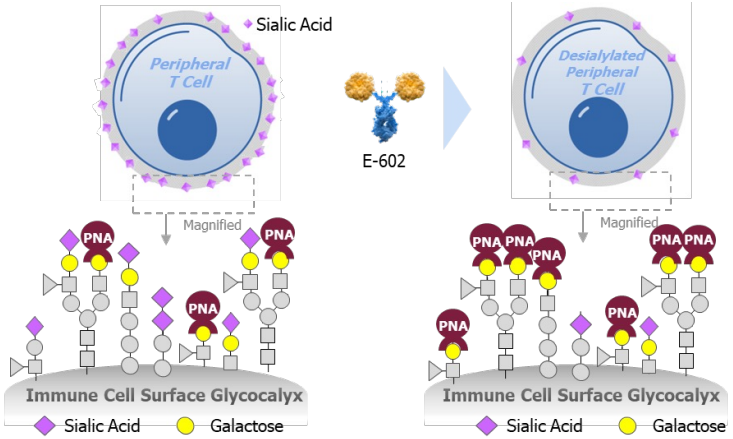
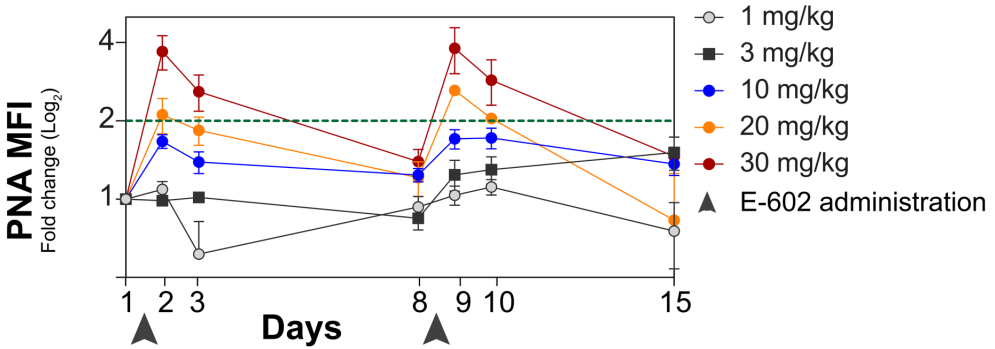
Immune Cell Desialylation

- Desialylation of immune cells by E-602 can be measured using the lectin reagent PNA (binds to galactose)
- Prespecified on-target engagement: **Doubling (2X) of PNA signal on peripheral T cells** which correlated with peripheral desialylation and preclinical anti-tumor activity



CD8+ T cells

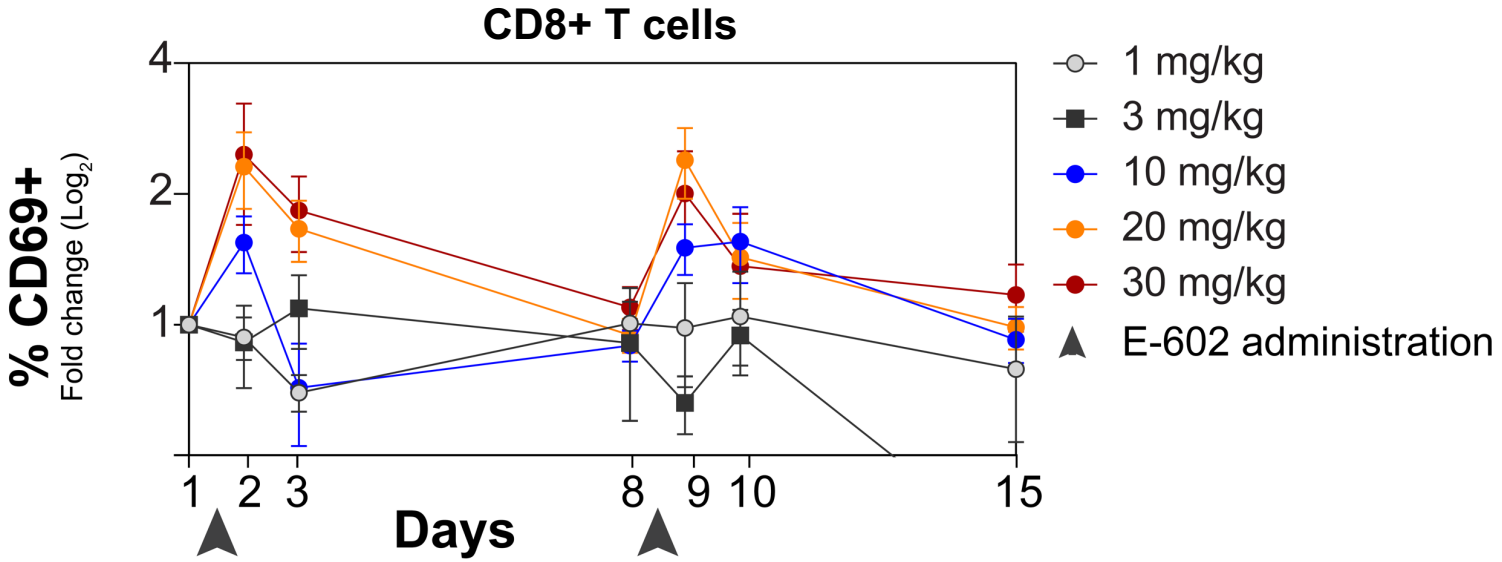


- At 10, 20, and 30 mg/kg, peripheral CD8+ T cells showed sustained biologically meaningful levels of desialylation (≥two-fold PNA increase) 24-48 hours post E-602 treatment
- Similar increases seen in CD4+ T, NK, monocyte populations

Preliminary Data as of 01-Feb-2023

Activation of circulating immune cells observed at biologically active doses

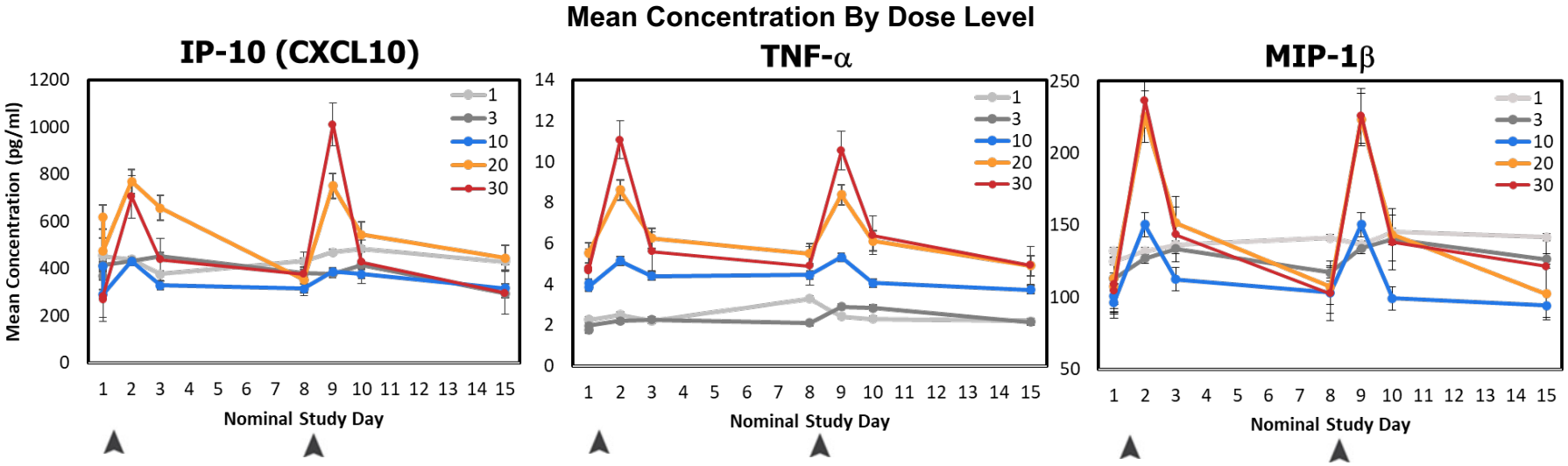
- CD69, a lymphocyte activation marker, was consistently elevated on CD8+ T cells 24-48 hours post treatment at 10, 20, and 30 mg/kg.
- Increased CD69 expression also observed on NK and CD4+ T cells



Preliminary Data as of 01-Feb-2023

Dose dependent increases in peripheral cytokines

- Pro-inflammatory cytokines, IP-10, TNF-α and MIP-1β were consistently elevated in circulation 24-48 hours post treatment
  - IP-10 and TNF-α reflect T_H1 response. Similar degree of IP-10 increase reported with ipi/nivo*
  - MIP-1β is reflective of monocyte activation



*Ribas et al, AACR 2017

Preliminary Data as of 26-Jan-2023

Conclusion: Proof of mechanism established for this novel, first-in-class cancer immunotherapy

- E-602, a first-in-class engineered human sialidase (Neu2)/Fc fusion protein, is tolerated at doses up to 30 mg/kg with no DLTs observed
- On-target, dose dependent desialylation was demonstrated in peripheral immune cells
- Immunomodulatory effects in circulation were observed consistent with preclinical data
- Based on the observed tolerability and pharmacodynamic effects, the Phase 2 portion of the study to evaluate clinical activity of E-602 monotherapy in patients with checkpoint-inhibitor resistant NSCLC and melanoma will proceed as will the Phase 1 portion to evaluate safety in combination with cemiplimab (anti-PD-1)