



# Jefferies 2019 London Healthcare Conference

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Chief R&D Officer  
November 20, 2019

*This presentation includes forward-looking statements regarding Nektar's proprietary drug candidates, the timing of the start and conclusion of ongoing or planned clinical trials, the timing and outcome of regulatory decisions, and future availability of clinical trial data. Actual results could differ materially and these statements are subject to important risks detailed in Nektar's filings with the SEC including the Form 10-Q filed on November 7, 2019. Nektar undertakes no obligation to update forward-looking statements as a result of new information or otherwise.*

# Focus of Nektar Pipeline

## Immuno-oncology

Target the innate and adaptive immune system

**Bempegaldesleukin (NKTR-214)**

(Co-Develop and Co-Promote)

CD122-preferential IL-2 Pathway Agonist

- Multiple Solid Tumors
- *In Phase 3 Studies*



Bristol-Myers Squibb

**NEKTAR**

**NKTR-262 (Wholly-Owned)**

TLR 7/8 Agonist

- Multiple Solid Tumors
- *Phase 1/2 study ongoing*

**NKTR-255 (Wholly-Owned)**

IL-15 Receptor Agonist

*Phase 1 First-in-Human Study in NHL and MM Initiated Oct 2019*

## Immunology

Harness the immune system to fight auto-immune disease

**NKTR-358 (Co-Promote)**

T Regulatory Cell Stimulator

In Phase 1 Studies:

- *MAD in Lupus patients*
- *Phase 1b in Psoriasis patients*
- *Phase 1b in Atopic Dermatitis*

Additional Studies in Other Inflammatory Diseases are Planned

*Lilly*

**NEKTAR**

## Chronic Pain

A next generation opioid molecule

**NKTR-181 (Wholly-Owned)**

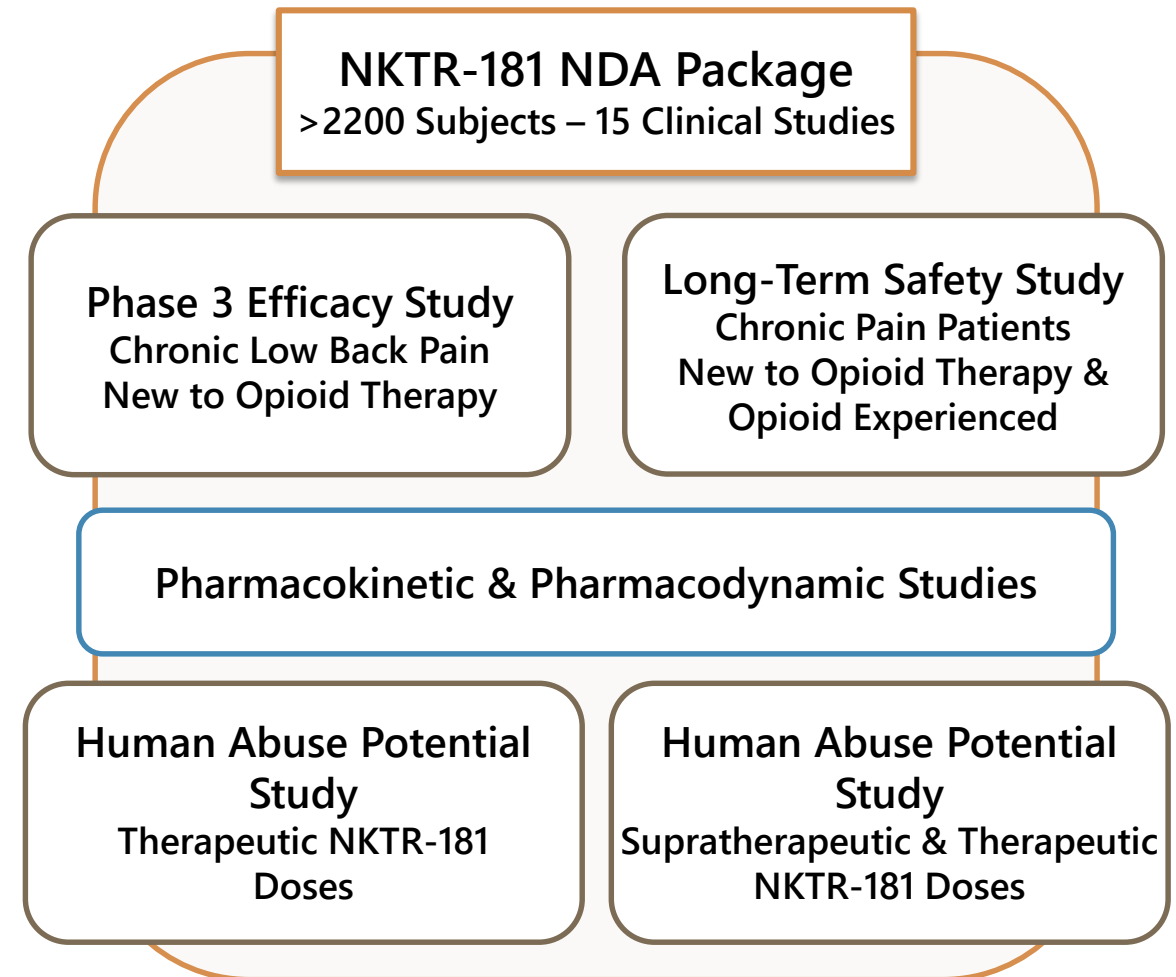
New Opioid Agonist Molecule

- Chronic Low Back Pain

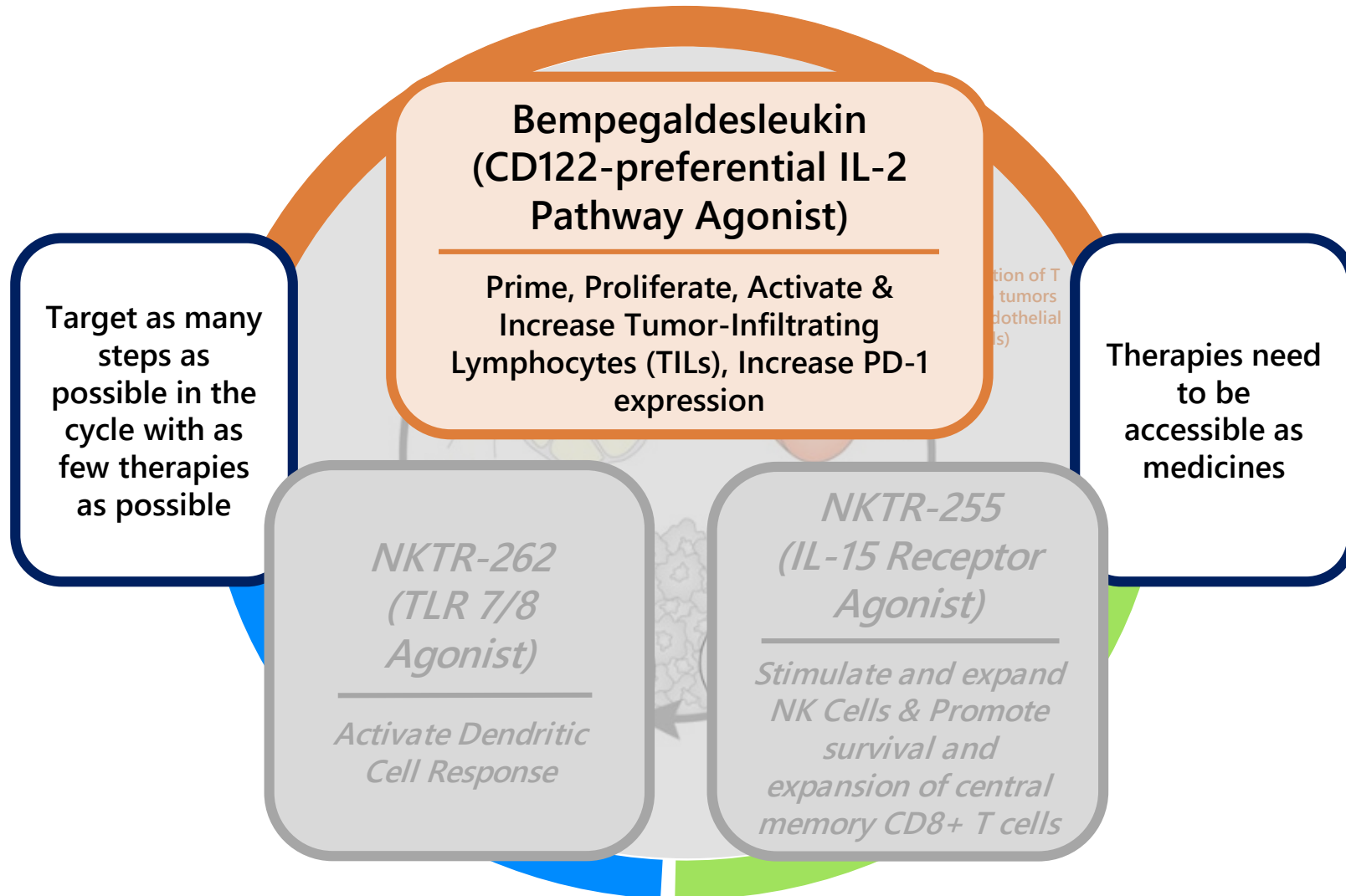
*NDA Filed;  
Awaiting product-specific advisory committee*

# NKTR-181: Potential Novel Therapy for Chronic Low Back Pain Patients

- NKTR-181 designed to separate analgesia from euphoria
- Formed wholly-owned subsidiary to launch NKTR-181 while advancing the regulatory process
  - In the process of securing one or more capital partners to support launch within subsidiary
- In July, Nektar received a General Advice Letter from FDA that stated that it is postponing product-specific advisory committee meetings for opioid analgesics so original PDUFA was missed
- Recently, FDA informed us that they can now re-schedule product-specific advisory committee meetings
  - We now anticipate adcomm for NKTR-181 within the next several months

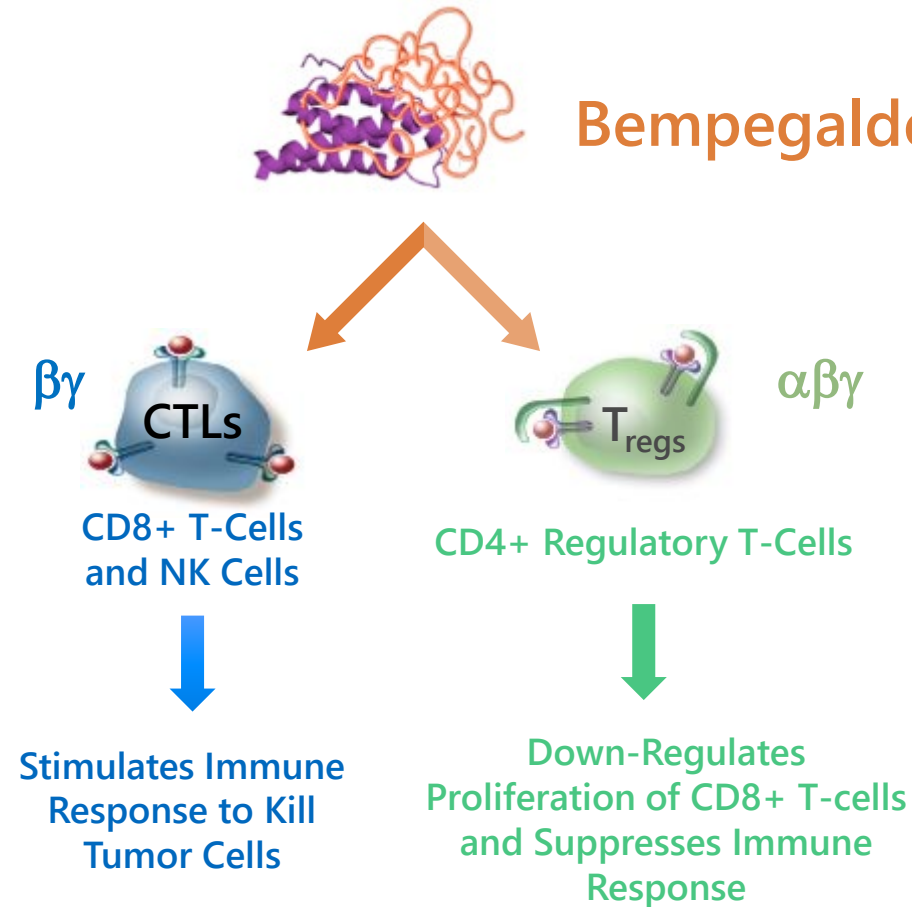


# Nektar's Immuno-Oncology Strategy to Create Therapies that Cover the Immunity Cycle

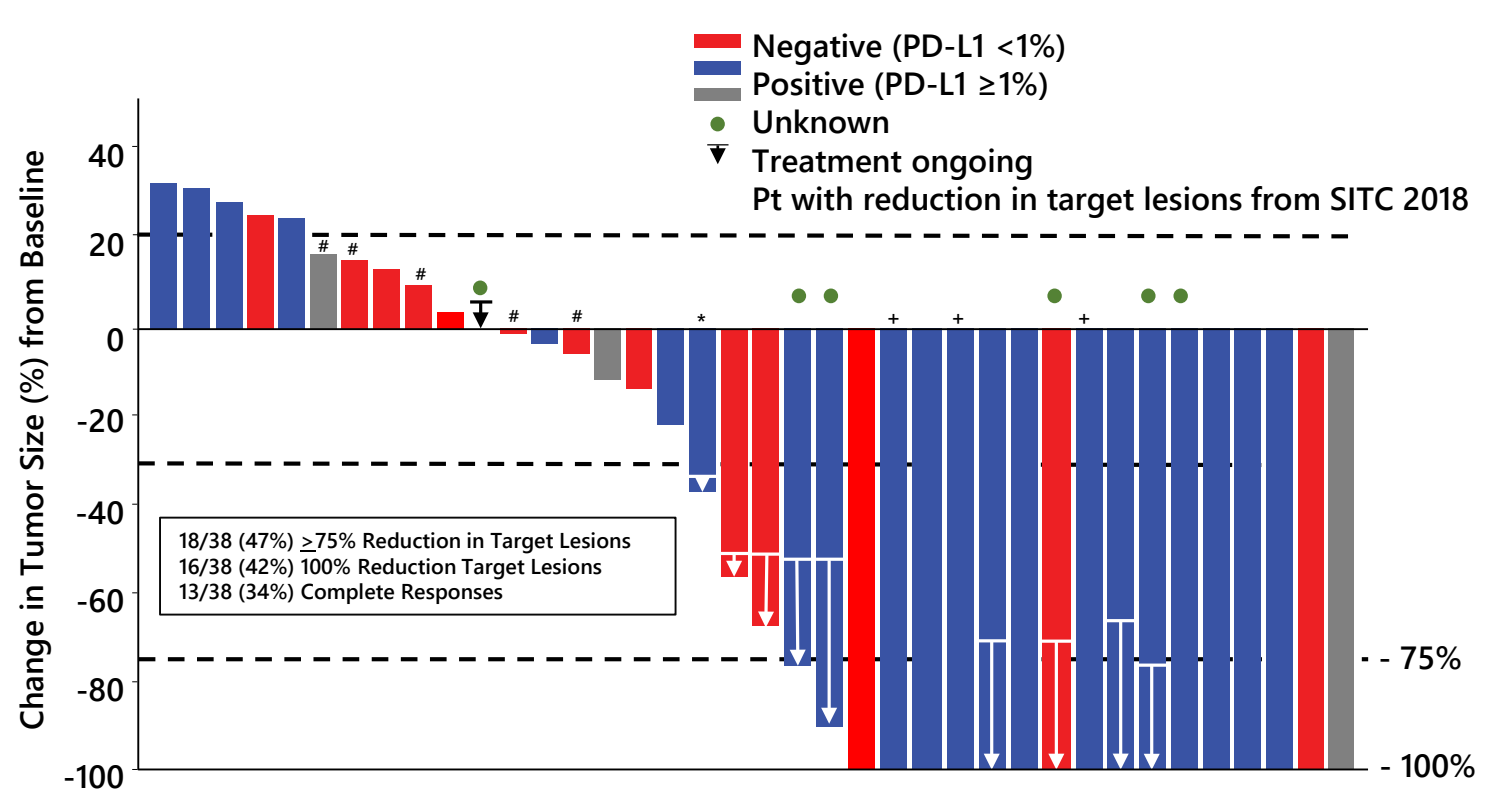


# Bempegaldesleukin: Biasing Action to CD122, or IL-2R Beta, to Stimulate T-Cell Proliferation

- Biases signaling to favor the CD122 receptor (IL-2R $\beta\gamma$  complex) to proliferate CD8+ T cells and NK cells
- Transient binding to the alpha receptor retained to enhance priming in lymph nodes (T cell proliferation to new tumor antigen)
- Prodrug design and receptor bias eliminate over-activation of IL-2 pathway that results in serious safety issues
- Achieves antibody-like dosing schedule in outpatient setting



# SITC 2019: Stage IV IO-Naïve 1L Melanoma Cohort at RP2D Best Overall Response by Independent Radiology



1L Melanoma (n=38 Efficacy Evaluable) At Median 18.6 Months of Follow-up:	Overall Response Rate
Confirmed ORR (CR+PR)	20 (53%)
CR	13 (34%)
PD-L1 negative (n=13)	5 (39%)
PD-L1 positive (n=22)	14 (64%)
PD-L1 unknown (n=3)	1 (33%)
LDH > ULN (n=11)	5 (45%)
Liver metastases (n=10)	5 (50%)
Median Time to Response (mos)	2.0
Median Time to CR (mos)	7.9

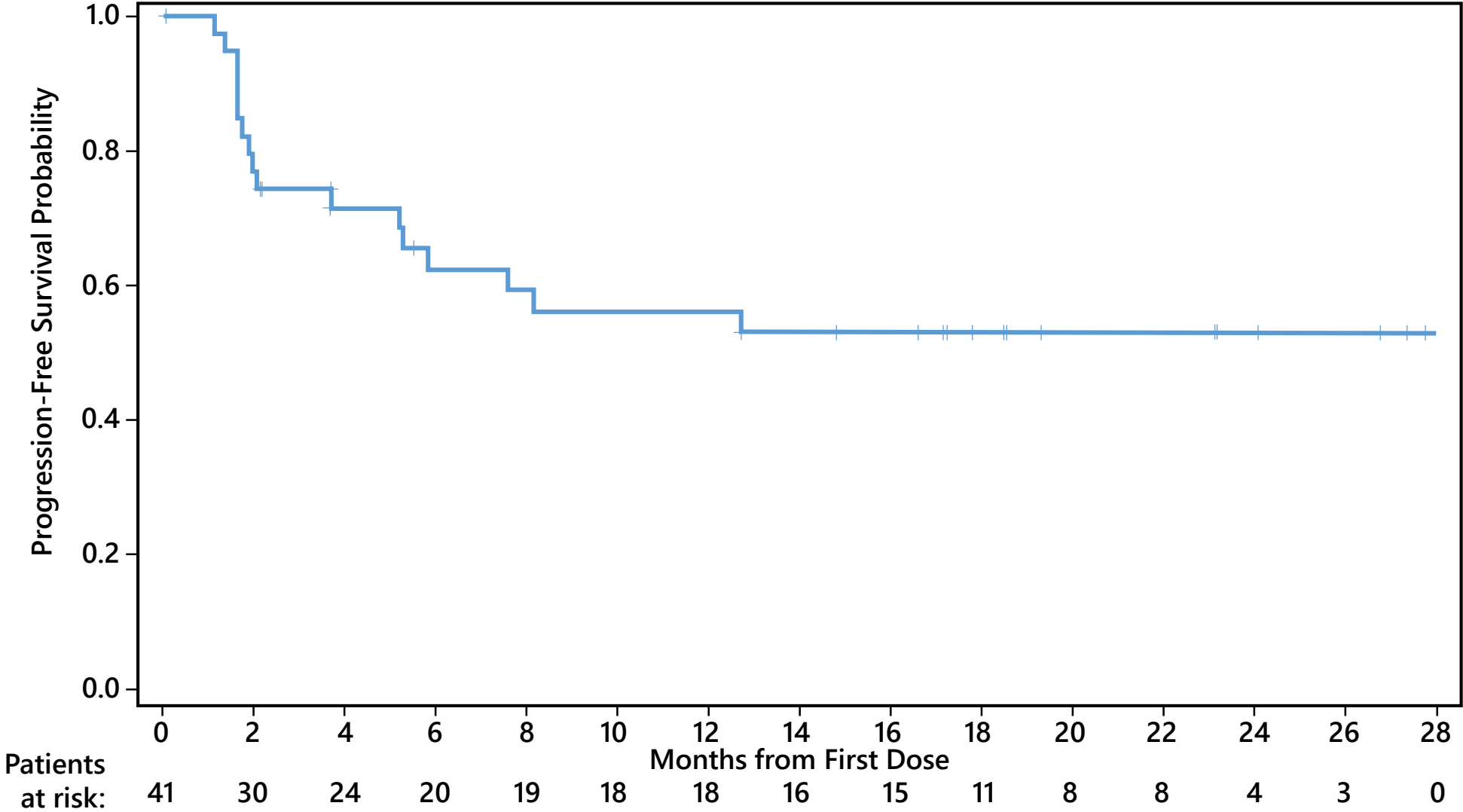
All 5 responders with liver metastases experienced CRs

# Breakthrough Therapy Designation Granted for BEMPEG + NIVO for Patients with Metastatic Melanoma

- ▶ BEMPEG + NIVO received Breakthrough Therapy Designation on July 29th, 2019 from the FDA for patients with previously untreated, unresectable or metastatic melanoma
- ▶ BTD programs receive intensive FDA guidance during drug development and BLA review
  - More frequent meetings, timely advice from FDA
- ▶ BTD programs also receive FDA organizational commitment with a cross-disciplinary project lead
  - More collaborative multidisciplinary process to guide the efficient drug development
- ▶ Advantages of BTD include eligibility for rolling review and Priority Review of BLA

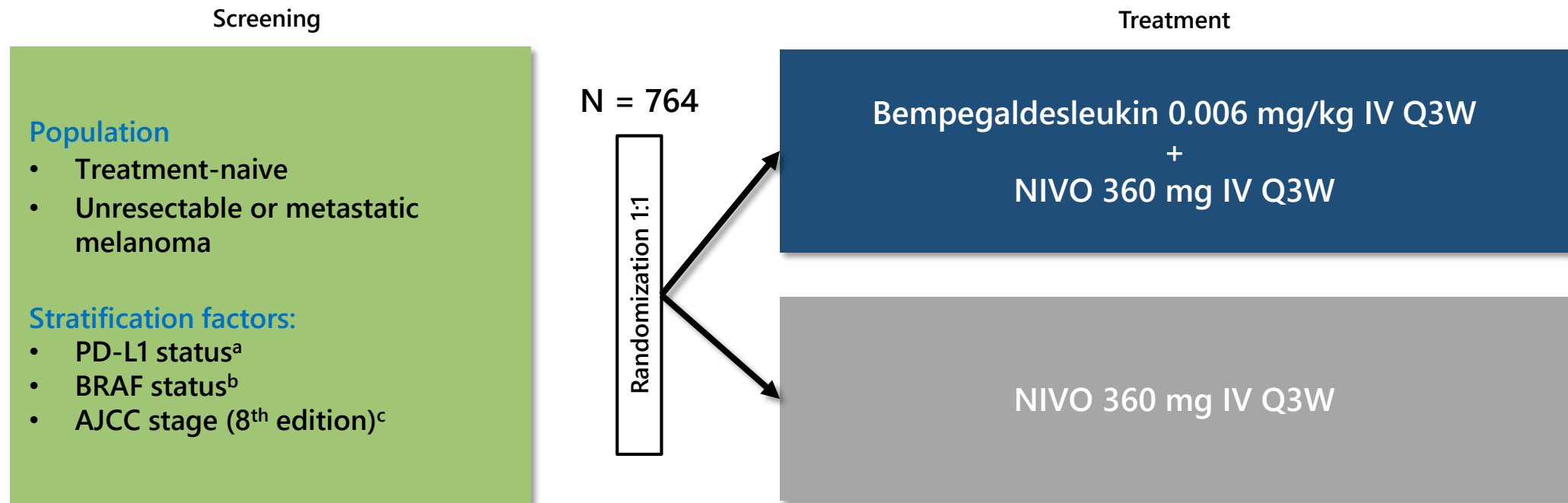


# SITC 2019: mPFS Not Reached for Stage IV IO-Naïve 1L Melanoma Cohort at 18.6 Month Follow-up



# PIVOT IO 001 Phase 3 Study in Patients with Previously Untreated Metastatic Melanoma

A Phase 3, Randomized, Open-Label Study of Bempegaldesleukin (BEMPEG) Plus Nivolumab (NIVO) Versus NIVO Monotherapy in Patients With Previously Untreated, Unresectable or Metastatic Melanoma

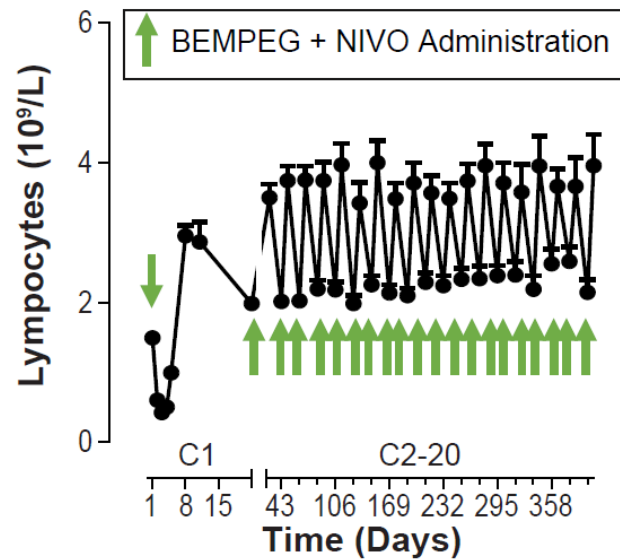


Primary Endpoints: ORR by BICR, PFS by BICR, OS

<sup>a</sup>Tumor cell PD-L1 expression (≥1% or <1%/Indeterminate) determined using 28-8 pharmDx (Dako, an Agilent Technologies, Inc. company, Santa Clara, CA). <sup>b</sup>V600-mutant vs wild-type. <sup>c</sup>M0/M1 any [0] vs M1 any [1], based on the screening imaging and laboratory test results (lactate dehydrogenase level).  
AJCC, American Joint Committee on Cancer; BICR, blinded independent central review; IV, intravenous; NIVO, nivolumab; ORR, overall response rate; OS, overall survival; PD-L1, programmed death ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria In Solid Tumors.

# ASCO 2019: Rapid Activation of the Immune System was Observed with BEMPEG and NIVO

## Increase in Lymphocytes with Every Treatment Cycle\*

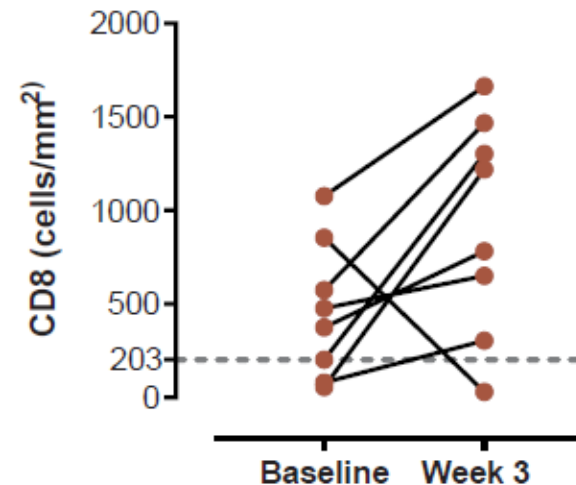


Lymphocyte effects of the BEMPEG + NIVO combination are driven by BEMPEG, as a similar pattern is observed with monotherapy<sup>2</sup>

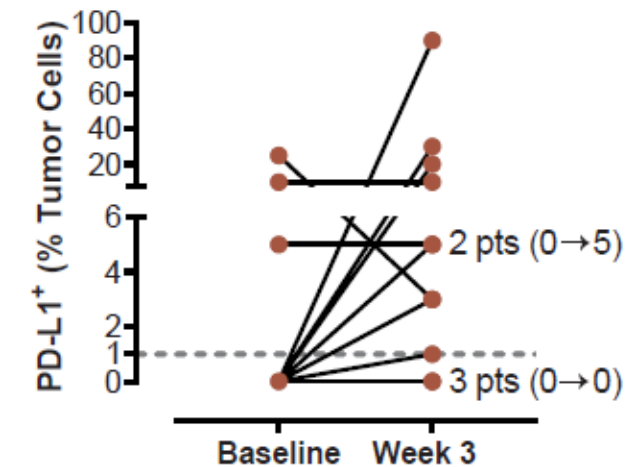
\*Lymphocyte levels were obtained from standard hematology analyses. All efficacy evaluable melanoma (n=38) and mUC (n=27) in the BEMPEG + NIVO combination enrolled in PIVOT-02 (n=65, Mean+SD) were included in the analyses.

## On-Treatment Increase in TIL and PD-L1 Conversion

### Change in CD8 Infiltrate in MEL<sup>3,^</sup>



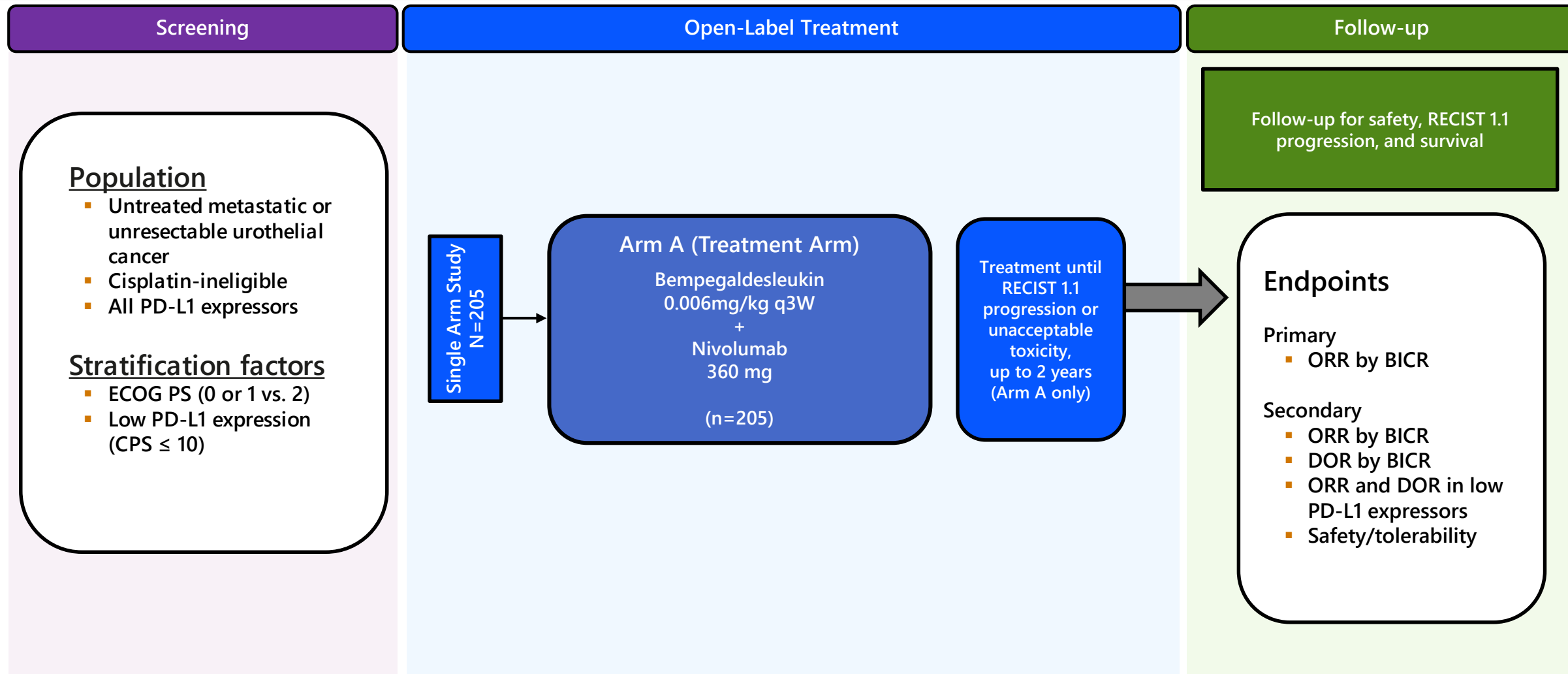
### PD-L1 Conversion in UC<sup>4,#</sup>



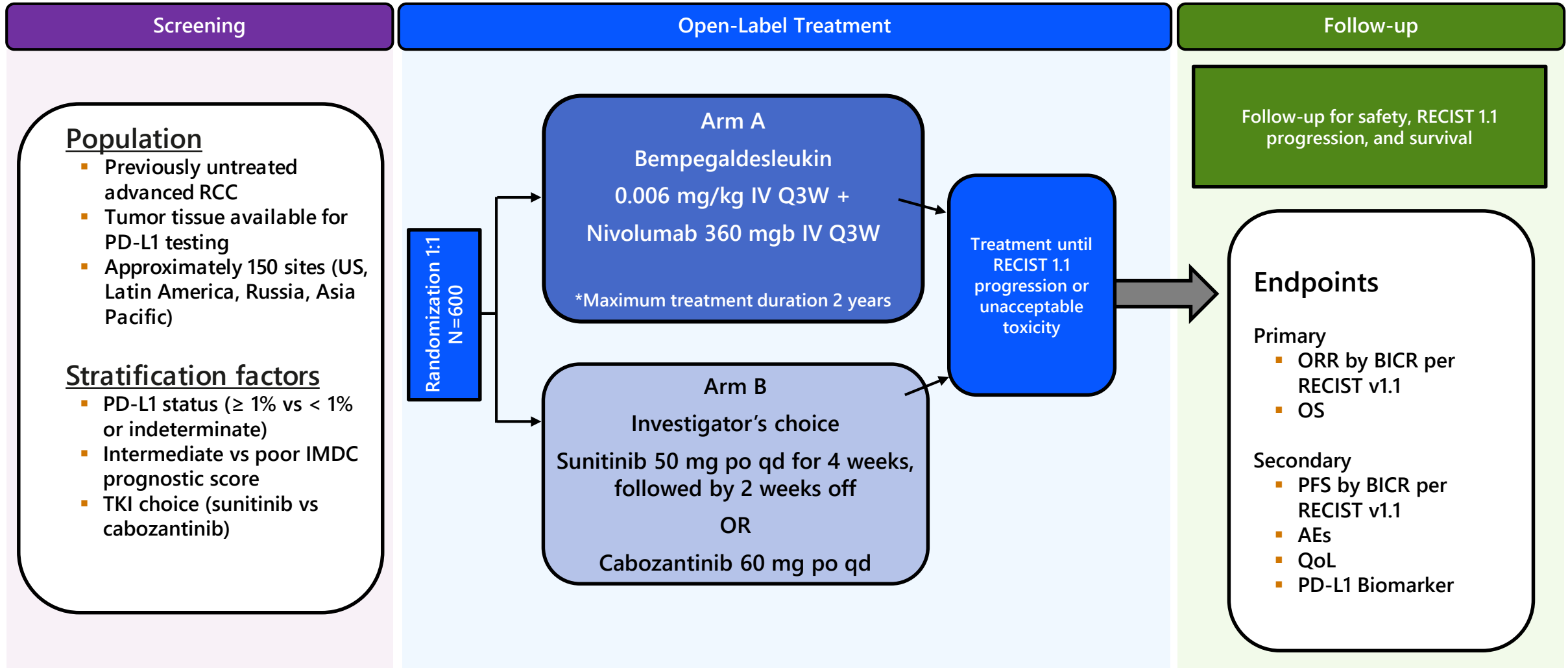
<sup>^</sup>IHC for CD8 was obtained by standard methods. All patients with first-line melanoma (1L MEL) with matched Baseline and Week 3 biopsy (n=8) were included in the analyses.

<sup>#</sup>All patients with 1L urothelial carcinoma (UC) with matched Baseline and Week 3 biopsy (n=13) at time of data cut were included and assessed for PD-L1 expression (DAKO PD-L1 IHC 28-8 pharmDx).

# PIVOT-10: Ongoing Phase 2 1L Metastatic Cis-ineligible Bladder Cancer Trial



# Ongoing Phase 3 Study in 1L Advanced Renal Cell Carcinoma Patients Trial



# Additional Clinical Collaborations for Bempegaldesleukin



Phase 1b/2  
SCCHN & mCRPC

- Nektar and Pfizer collaboration to evaluate bempegaldesleukin with several combination regimens in Pfizer's oncology portfolio including: avelumab, talazoparib & enzalutamide
- Pfizer will serve as the sponsor for the Phase 1b/2 trials



Phase 1  
Head & Neck SCC

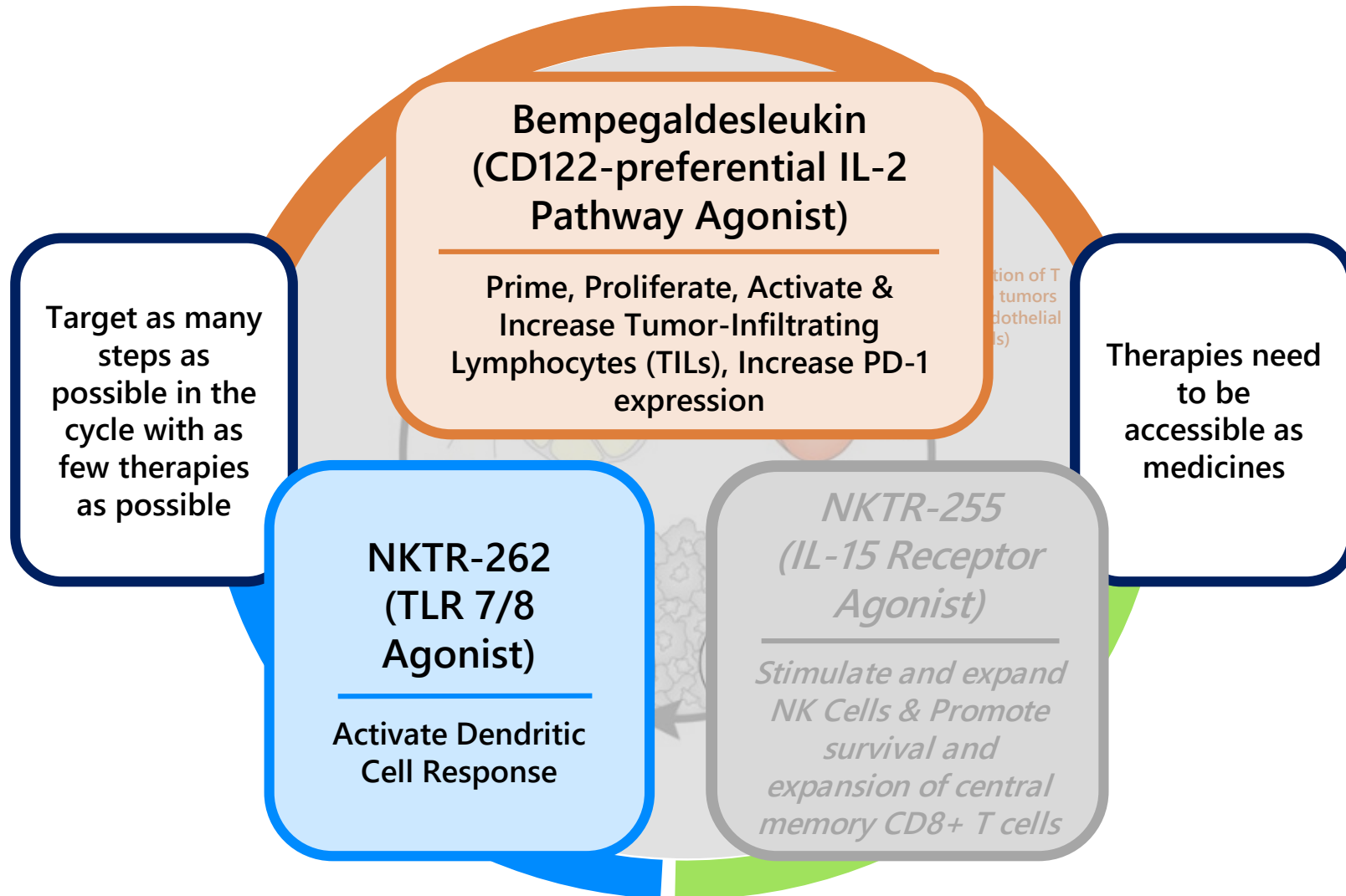
- Vaccibody and Nektar collaborating on combining bempegaldesleukin with VB10.NEO, a personalized cancer neoantigen vaccine
- Proof-of-concept study evaluating vaccine-specific immune-response markers in 2L head and neck cancer



Phase 1  
Pancreatic Cancer

- BioXcel, Nektar and Pfizer collaborating on combining bempegaldesleukin with BXCL701, a small molecule immune-modulator, DPP 8/9 and FAP inhibitor and a checkpoint inhibitor
- Phase 1 study underway in patients with 2L pancreatic cancer

# Nektar's Immuno-Oncology Strategy to Create Therapies that Cover the Immunity Cycle

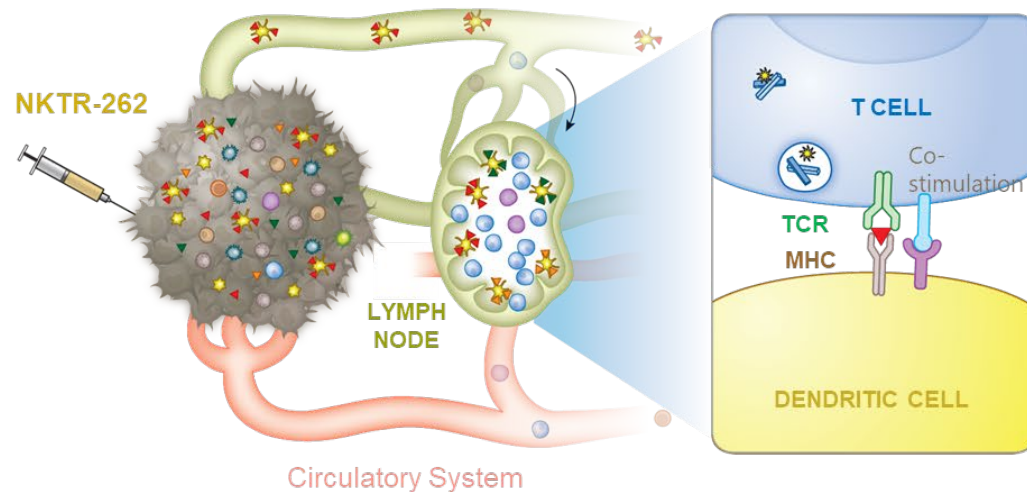




# NKTR-262 plus Bempegaldesleukin: Targeting the Innate and Adaptive Immune Response

## PRIMING with NKTR-262

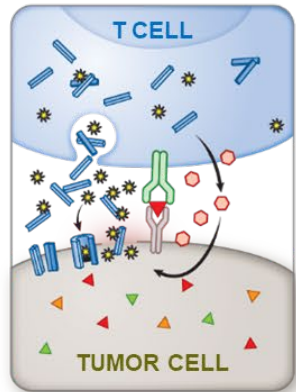
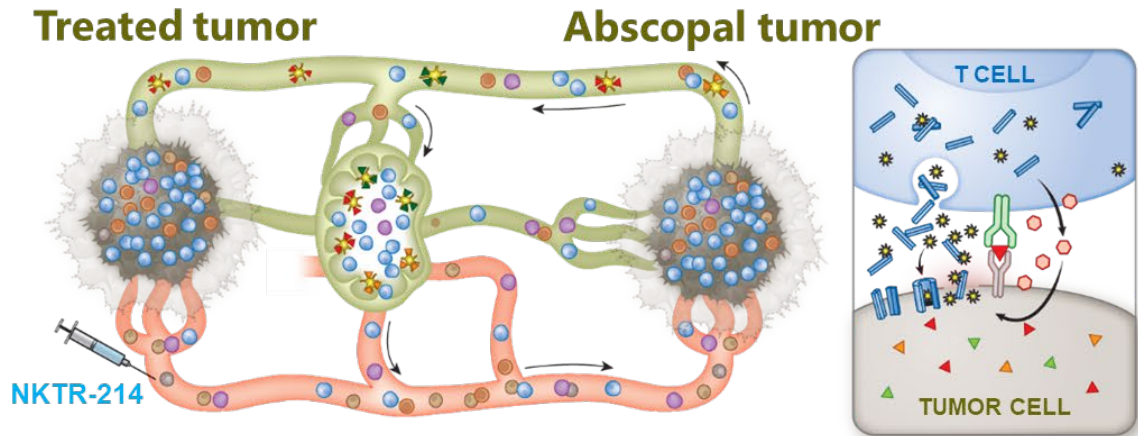
Enhanced antigen presentation  
and T cell priming in lymph node



**NKTR-262  
treated tumor**

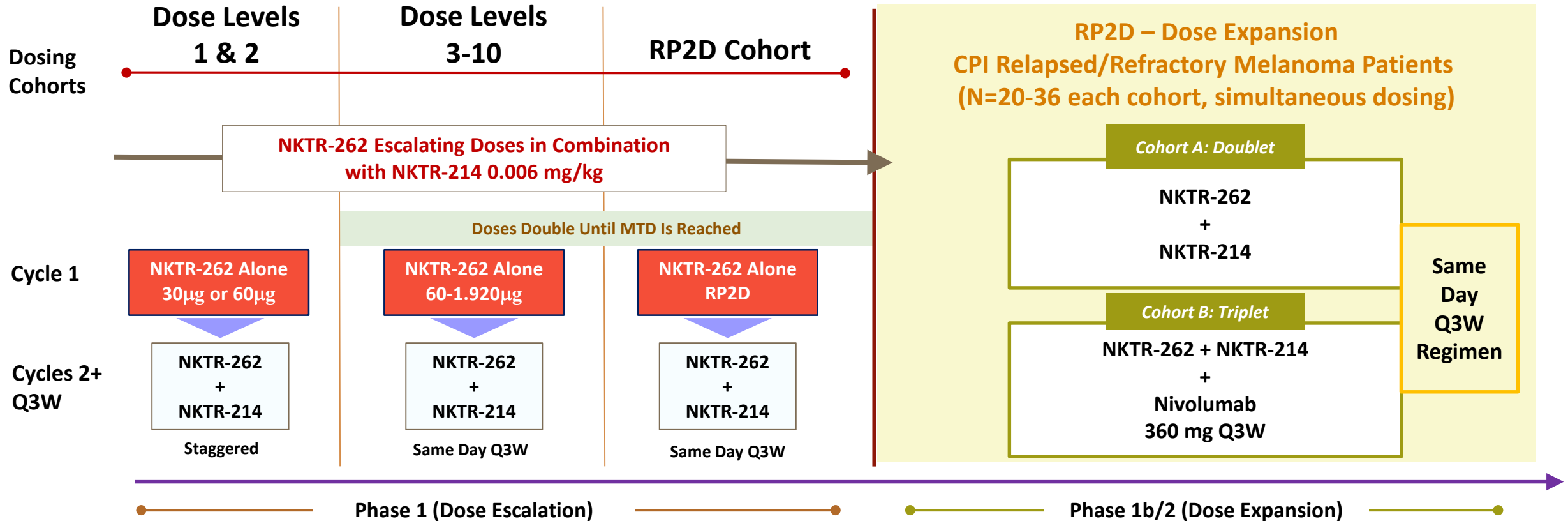
## BOOSTING with bempegaldesleukin

Expansion of circulatory antitumor  
CD8 T cells and tumor infiltration





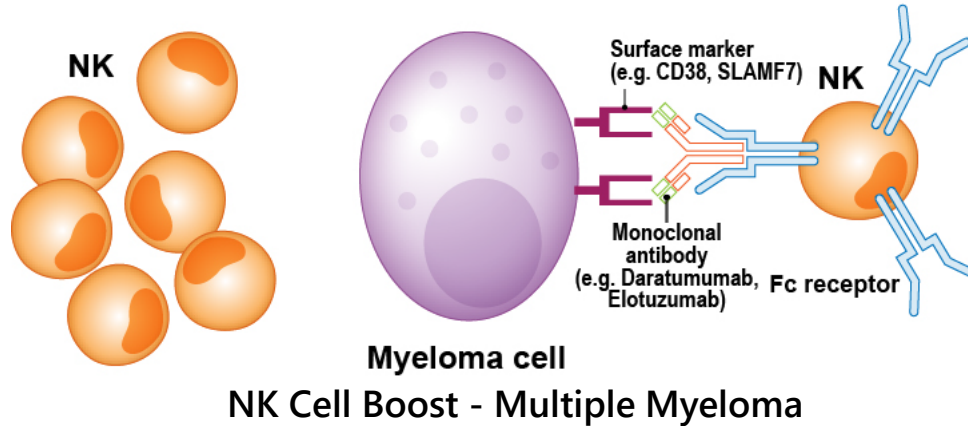
# NKTR-262 REVEAL Phase 1/2 Study Design



# NKTR-255: Advantages of Harnessing the IL-15 Pathway & Opportunity in Cancer Immune Therapy

**NKTR-255**

## Boost NK cell numbers and function

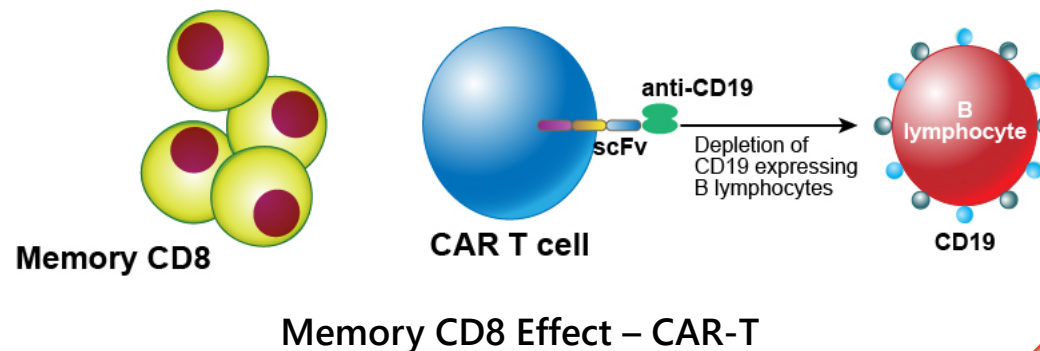


## Enhancement of ADCC Antibodies

Daratumumab  
Elotuzumab  
Anti-BCMA

Potential to combine with any targeted antibody that utilizes an ADCC MOA

## Increase duration of response for CAR-T and cellular therapies



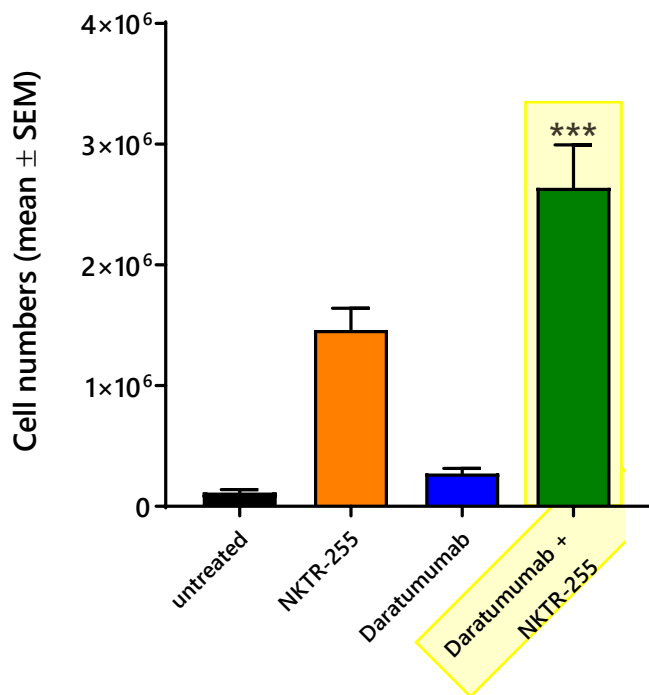
## Enhancement of CAR-T

CD19 CAR-T  
BCMA CAR-T  
CD38 CAR-T

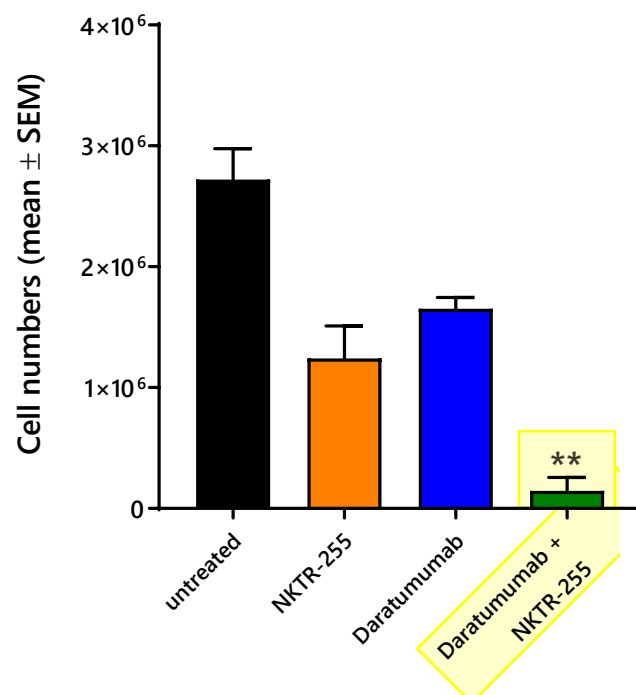
Potential to expand into other hematological and solid tumor CAR-T and cellular therapies

# NKTR-255 Combined with Daratumumab Effectively Depletes Lymphoma Cells in the Bone Marrow Tissue by Enhancing NK Cells

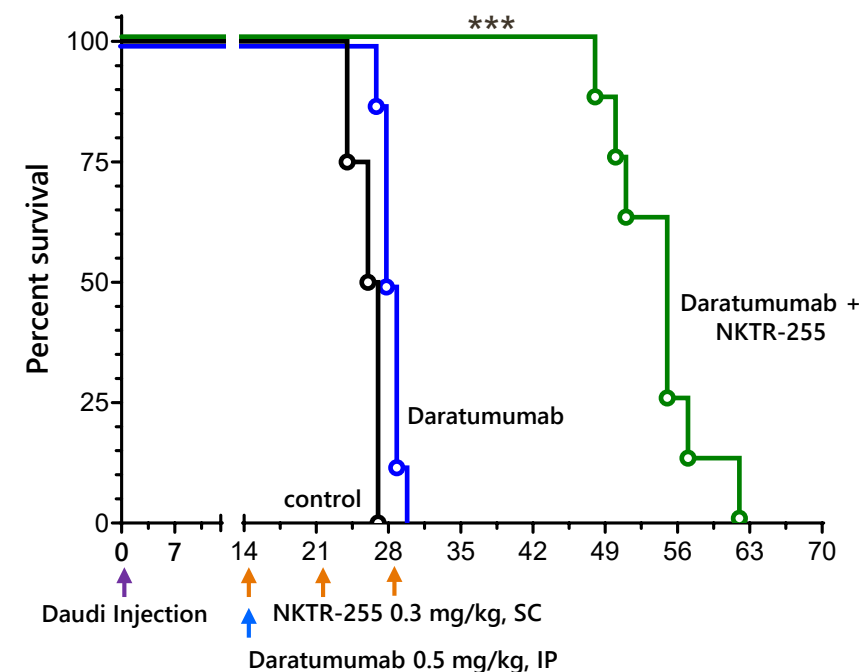
NK Cell Count  
in Bone Marrow#



Human Lymphoma Cell Count  
In Mouse Bone Marrow



Human B Cell Lymphoma Model  
Survival



SCID mice (N=6/group) inoculated with Daudi B cell lymphoma cells were treated with single dose of daratumumab (14 days after inoculation) and two doses of NKTR-255 (14 and 21 days after inoculation). Lymphoma depletion, NK cell expansion and activation in the bone marrow assessed three days after the second NKTR-255 dose (day 24) by flow cytometry.

\*\*\* NKTR-255 with daratumumab significantly increases NK cell numbers compared to NKTR-255 and daratumumab single agent (p=0.0026 and p<0.0001, respectively). (One-way ANOVA, Tukey's multiple comparison test)

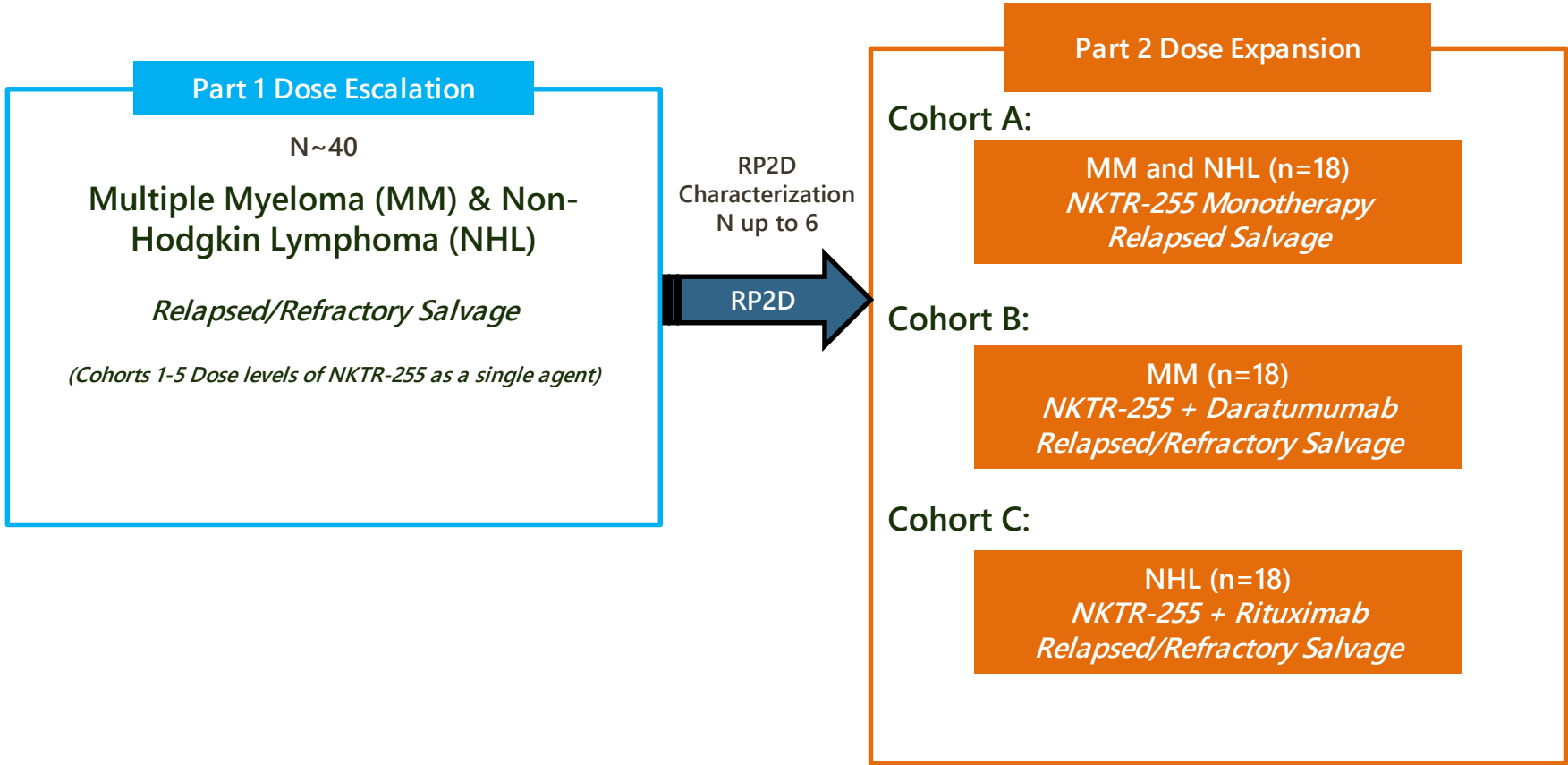
\*\* NKTR-255 with daratumumab significantly improves B cell lymphoma depletion compared to NKTR-255 and daratumumab single agent (p=0.02 and p=0.001, respectively). (One-way ANOVA, Tukey's multiple comparison test).

#Greater than 70% of NK cells in the bone marrow were activated after treatment with NKTR-255 (as measured by Granzyme B) either with or without daratumumab

SCID mice (N=8/group) inoculated intravenously with Daudi B cell lymphoma cells were treated with a single dose of daratumumab (14 days after inoculation) and three doses of NKTR-255 (14, 21 and 28 days after tumor inoculation). Survival of tumor inoculated mice was measured by body condition scoring as endpoint marker.

\*\*\* NKTR-255 combination with daratumumab significantly increases median survival compared to daratumumab single agent treatment (p<0.05, Log-Rank test)

# Ongoing Phase 1 Study of NKTR-255 as Single Agent and in Combo with Daratumumab or Rituximab in Multiple Myeloma and Non-Hodgkin Lymphoma



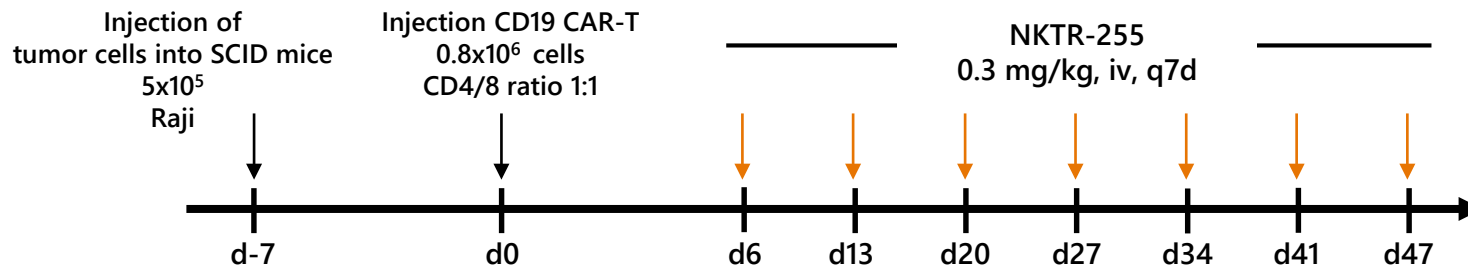
Abbreviations: MM = multiple myeloma; NHL = non-Hodgkin lymphoma; RP2D = recommended Phase 2 dose  
No intra-patient dose escalation will be conducted in any cohort.  
The dose-limiting toxicity (DLT) window for NKTR-255 single agent is 21 days following the initial dose of NKTR-255.

# Research Collaboration with Janssen to Evaluate NKTR-255 in Oncology

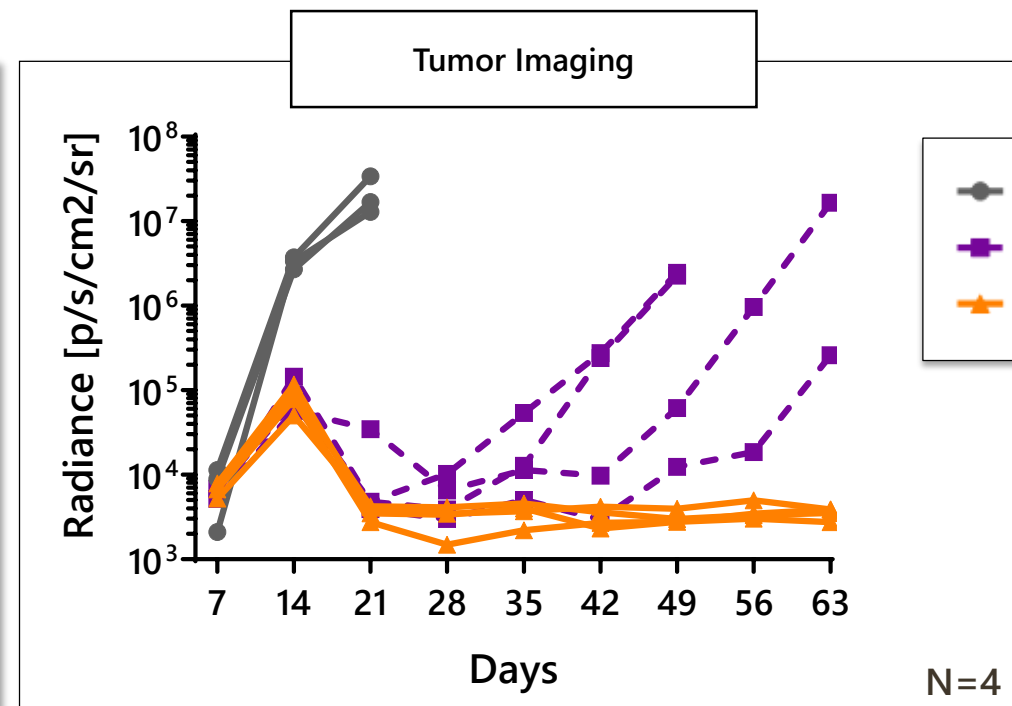
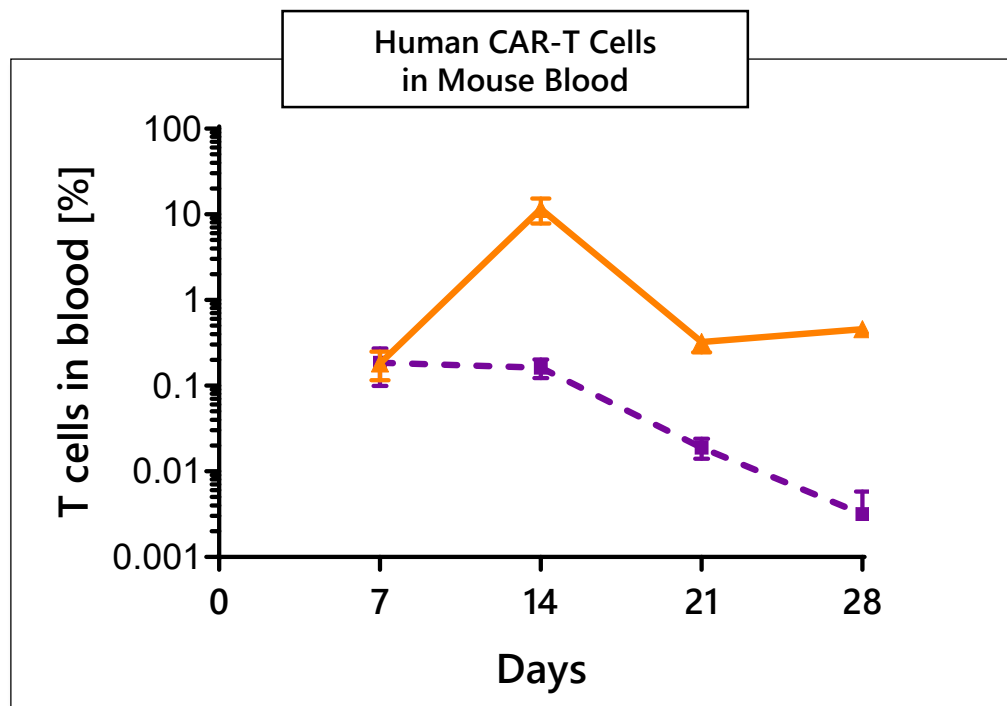
- Janssen to test NKTR-255 in preclinical research studies with therapies in Janssen's oncology portfolio
- Janssen responsible for the costs of the preclinical studies
- Nektar will contribute NKTR-255 for the studies and cover the supply cost of its drug candidate
- Nektar and Janssen will each maintain global commercial rights to their respective drug candidates



# NKTR-255 Enhances CAR-T Therapy: Research Collaboration with Fred Hutchinson Cancer Center



- Model of Diffuse Large B Cell Lymphoma
- End points are tumor imaging and CAR-T level in blood

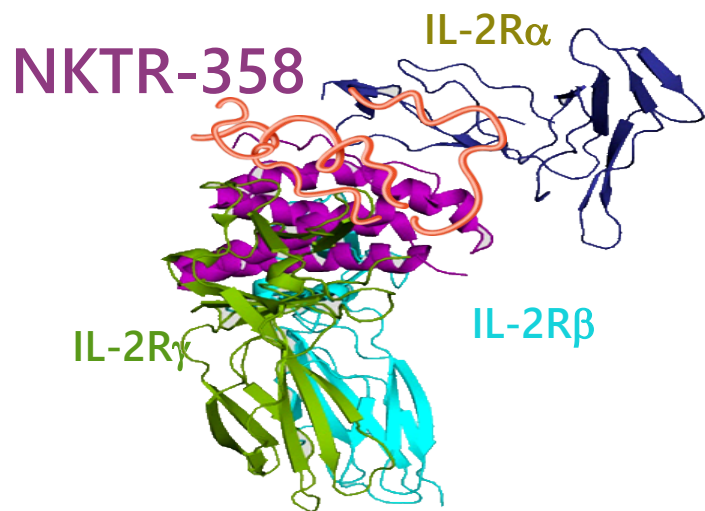


# Research Collaboration with Gilead to Evaluate NKTR-255 in Virology

- Gilead to explore combination of NKTR-255 with antiviral therapies in the Gilead portfolio
- Gilead will conduct preclinical studies and be responsible for 100% of cost
- Each company will contribute their respective compounds
- Collaboration is limited to evaluation of NKTR-255 in the field of virology
- Nektar and Gilead will each maintain global commercial rights to their respective drugs and/or drug candidates
- During agreement term, if Nektar chooses to partner NKTR-255 in virology, Gilead has right of first negotiation (specifically excludes the therapeutic area of oncology)



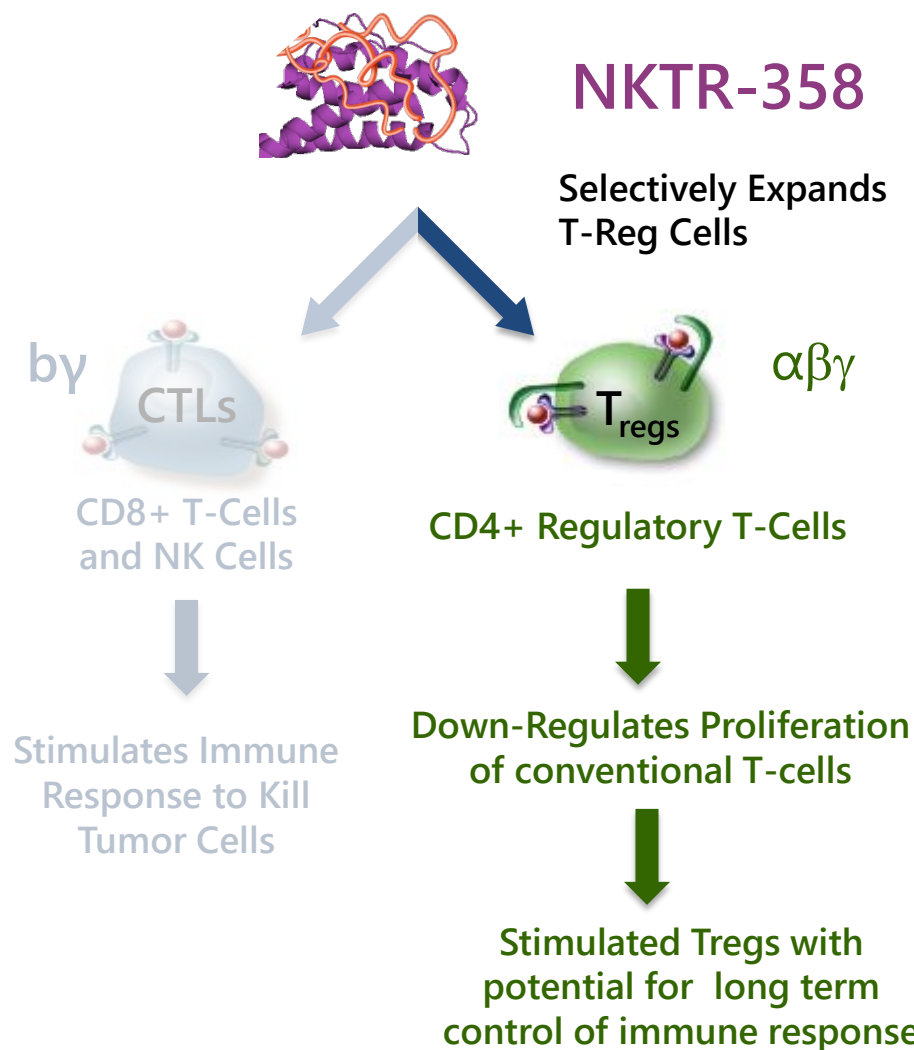
# NKTR-358: Selectively Induces Regulatory T-cells (Tregs) and Their Suppressive Activity



## PEG-conjugation:

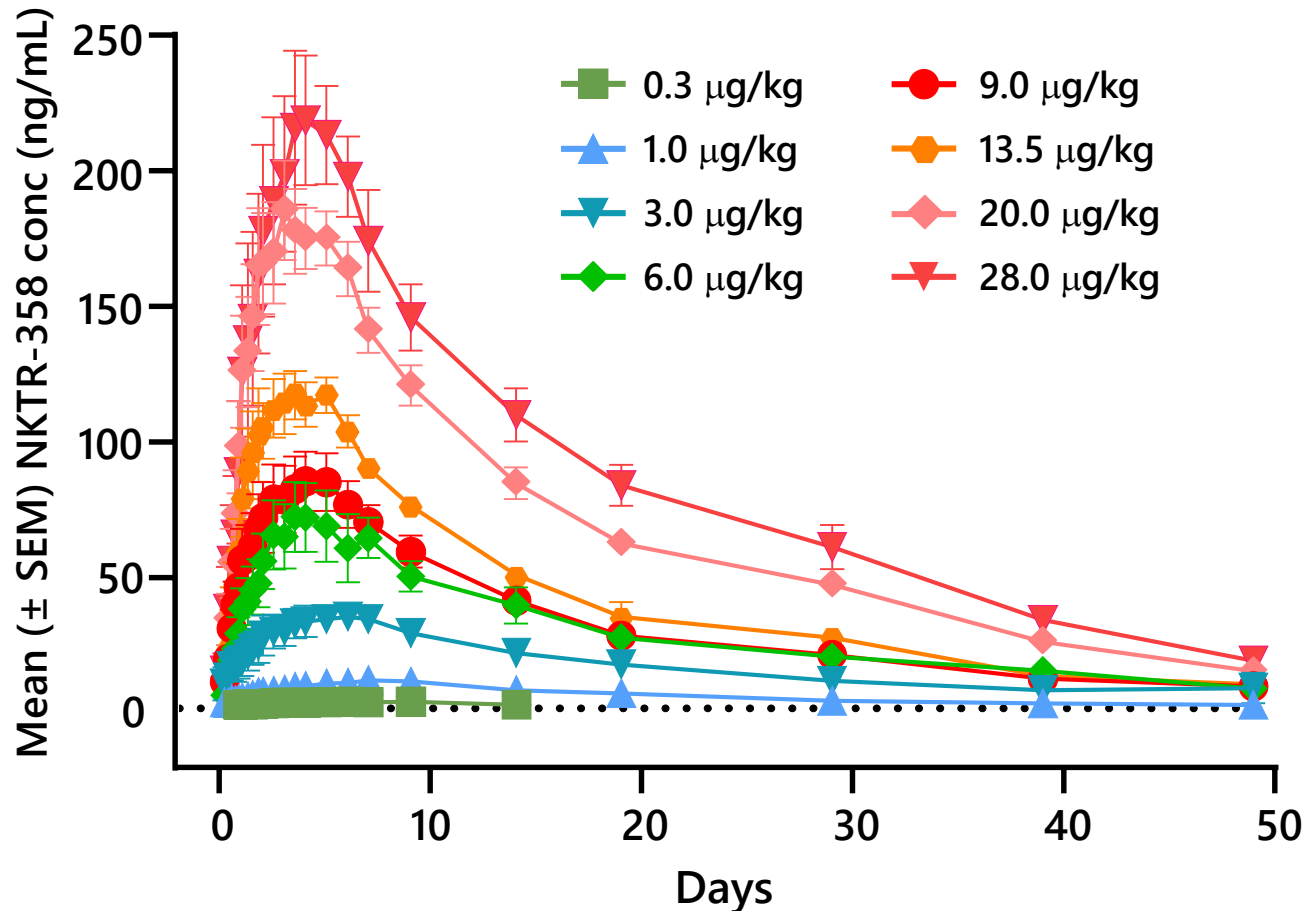
- Alters binding profile of NKTR-358 (vs IL-2) with lower binding affinity to IL-2R $\beta$  and different binding bias for IL-2R $\alpha$  & IL-2R $\beta$
- Imparts selectivity for effect on Tregs over Tcons (vs IL-2)
- Increases half life (vs IL-2)

NKTR-358 has shown activity in animal models of SLE and cutaneous hypersensitivity





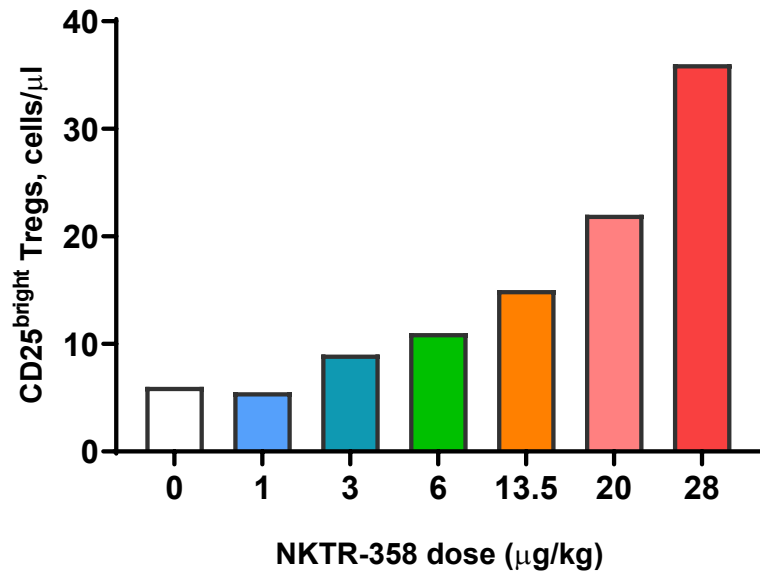
# Phase 1 Single-Ascending Dose Study: NKTR-358 Demonstrates Dose Proportional Pharmacokinetics



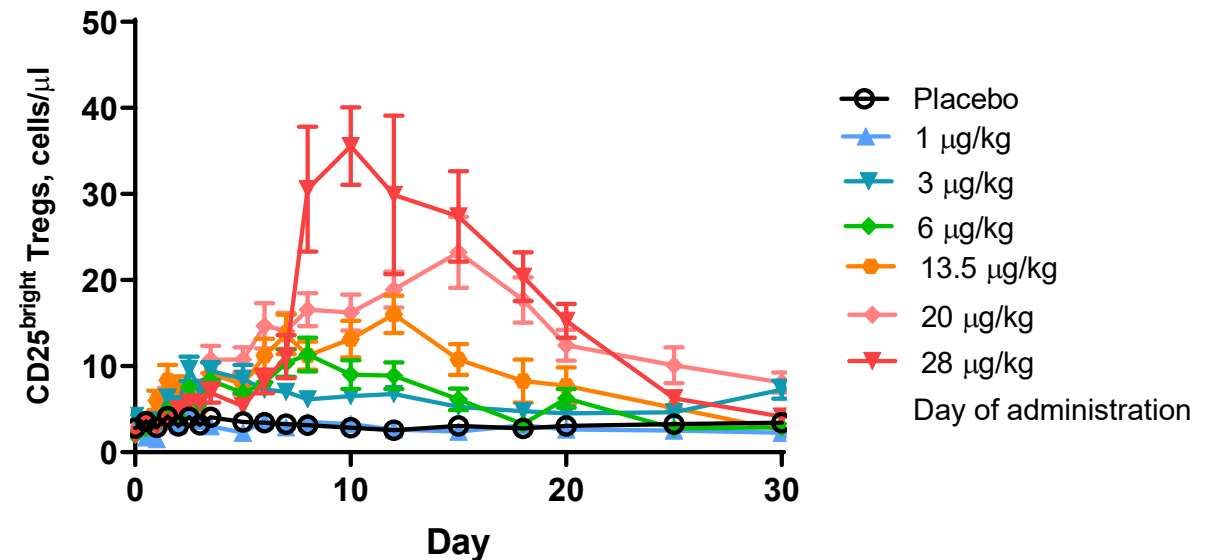
- NKTR-358 C<sub>max</sub> and AUC values exhibited a dose proportional increase
- NKTR-358 concentrations reached maximum levels in 5-7 days
- NKTR-358 has an estimated elimination half-life of 8-11 days vs. the half-life of IL-2 in human serum of ~5-7 minutes

# NKTR-358 Leads to Sustained, Dose-dependent Increases in CD25<sup>bright</sup> Tregs

Median peak effect of CD25<sup>bright</sup> Tregs



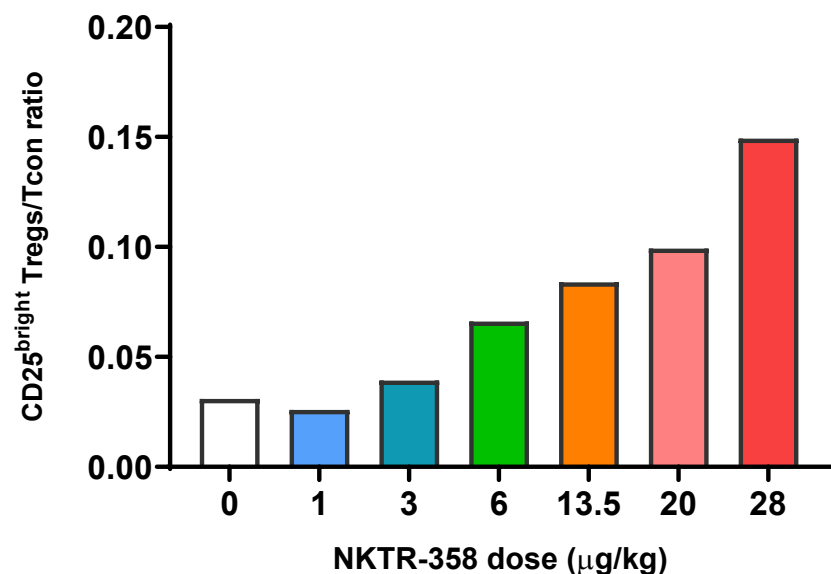
Absolute numbers of CD25<sup>bright</sup> Tregs



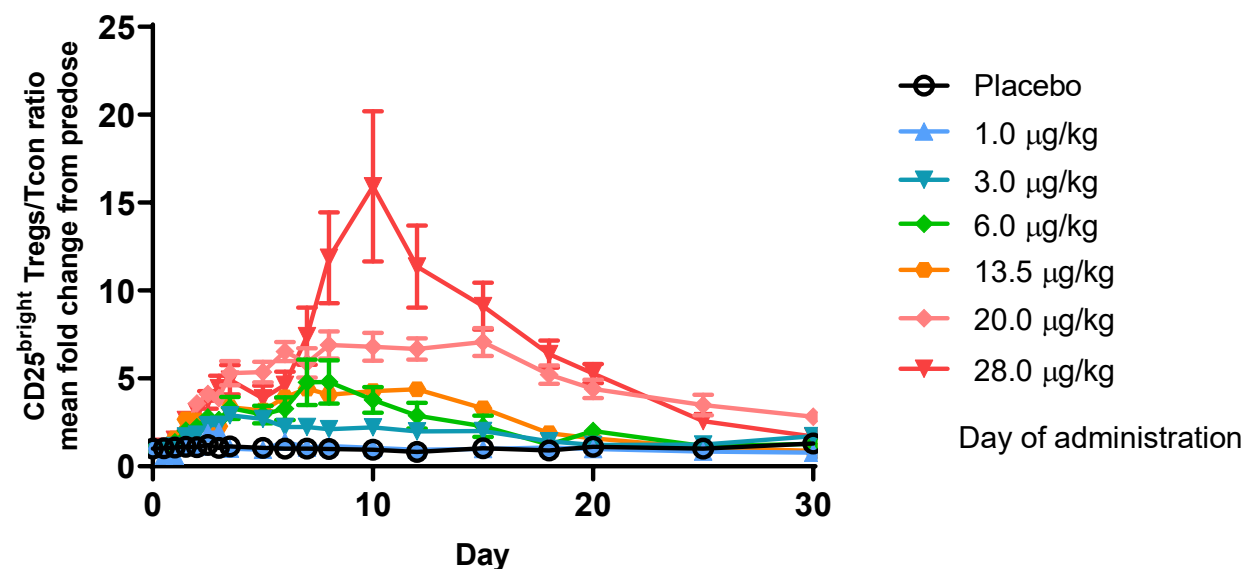
- At 28 μg/kg NKTR-358:
  - 17-fold mean peak increase in numbers of CD25<sup>bright</sup> Tregs above predose value
  - Treg levels peak at Days 10-12 and do not return to baseline until Days 20-25 following administration
- Increase in Treg activation markers ICOS and CTLA4 were observed at doses  $\geq 13.5$  μg/kg

# NKTR-358 Selectively Induces Tregs in a Dose-Dependent Manner

Median peak effect of CD25<sup>bright</sup> Treg/Tcon ratio

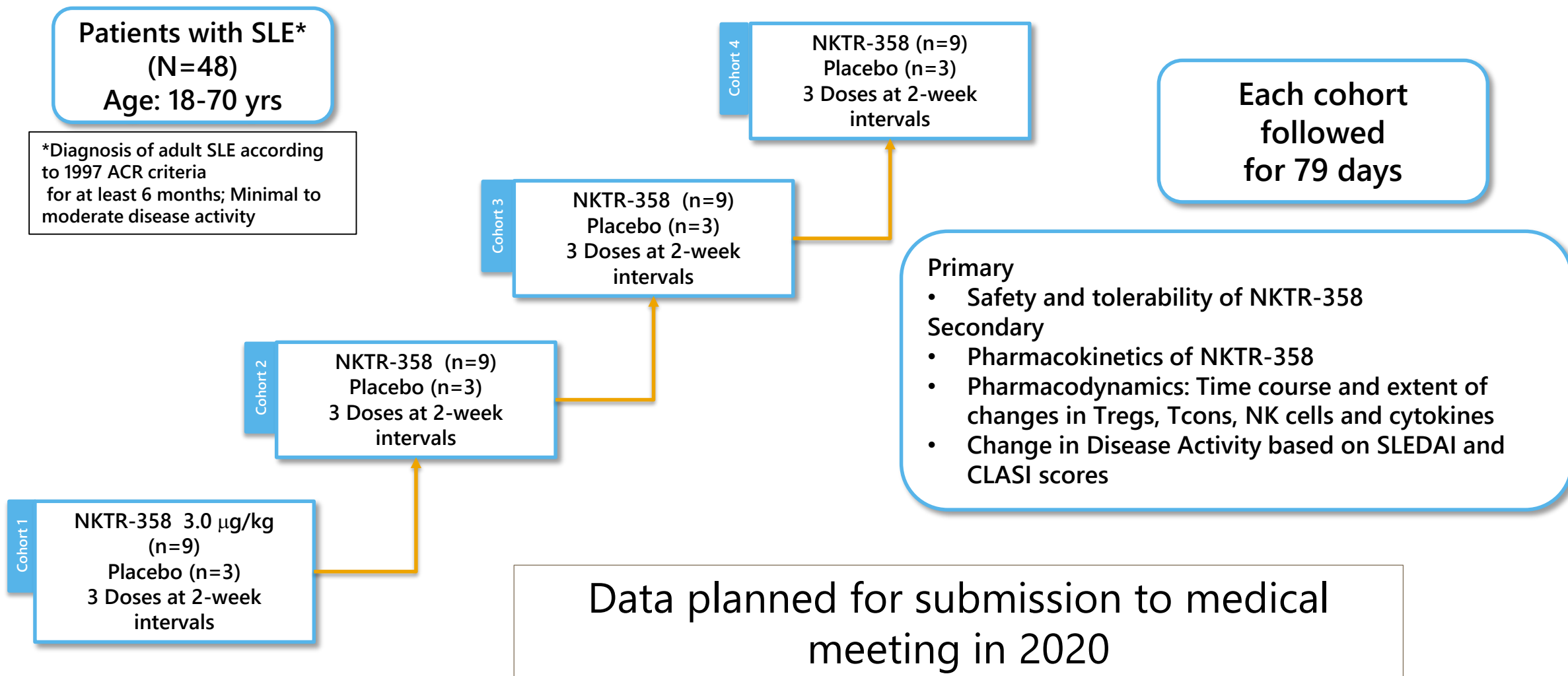


Mean Fold change in CD25<sup>bright</sup> Tregs/Tcon cell ratio



NKTR-358 administration leads to 15-fold increase in mean peak Treg:Tcon ratio over baseline at 28 μg/kg

# Phase 1b Study of Sub-Q Multiple Ascending Doses of NKTR-358 in Patients With Mild to Moderate SLE Disease Activity



# NKTR-358 Program: Next Steps

- Partnership with Lilly to co-develop NKTR-358 announced July 2017
- Two additional Phase 1b studies initiated in Psoriasis and Atopic Dermatitis with targeted recruitment of 40 patients each
- Phase 2 study planned in lupus in 2020
- Additional auto-immune disease state planned in 2020
- Lilly conducting all remaining clinical studies through registrational trials
- Lilly is leading Phase 2 development with the development costs for Nektar capped at 25%



# Focus of Nektar Pipeline

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Lilly

NEKTAR

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