



**NEKTAR<sup>®</sup>**

**JP Morgan Healthcare Conference**

**Howard Robin**  
**President & CEO**  
January 9, 2018

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 8, 2017. 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**

**NKTR-214** (Wholly-Owned)

**CD122-Biased Agonist**

- Multiple Solid Tumors

*In Phase 1/2 Trials*

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

**TLR 7/8 Agonist**

- Multiple Solid Tumors

*IND Filed, Phase 1 Dosing to Start Q1 2018*

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

**IL-15 Receptor Agonist**

*IND in 2018*

## Immunology

**Harness the immune system to fight auto-immune disease**

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

**T Regulatory Cell Stimulator**

- Lupus
- Crohn's Disease
- Rheumatoid Arthritis
- Psoriasis

*In Phase 1 Study*

**NEKTAR** *Lilly*

## Chronic Pain & Opioid Epidemic

**Help prevent the next generation of opioid addiction**

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

**New Opioid Agonist Molecule**

- Separates analgesia from euphoria that leads to abuse and addiction
- Moderate to Severe Chronic Pain

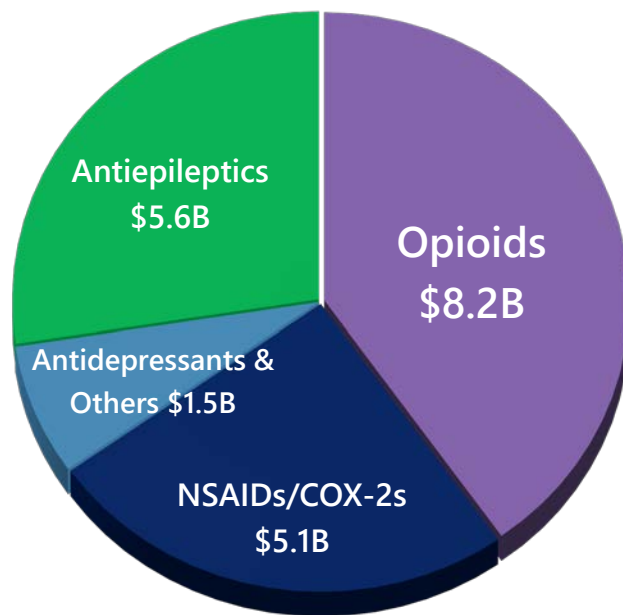
*NDA to be Submitted Q2 2018*

# NKTR-181: A Novel Opioid Poised to Transform the Chronic Pain Market

NKTR-181 brings unique properties to the treatment of chronic pain:

- ▶ Slow rate of entry into CNS separates pain control from euphoria that leads to abuse and addiction
- ▶ Low levels of sedation, dizziness and respiratory depression
- ▶ Targeting C-III or better scheduling
- ▶ Properties are inherent to molecule
- ▶ Received Fast Track Status from FDA
- ▶ Phase 3 program complete
- ▶ NDA submission planned in Q2 2018

**\$20 Billion+  
Global Chronic Pain  
Therapy Market**

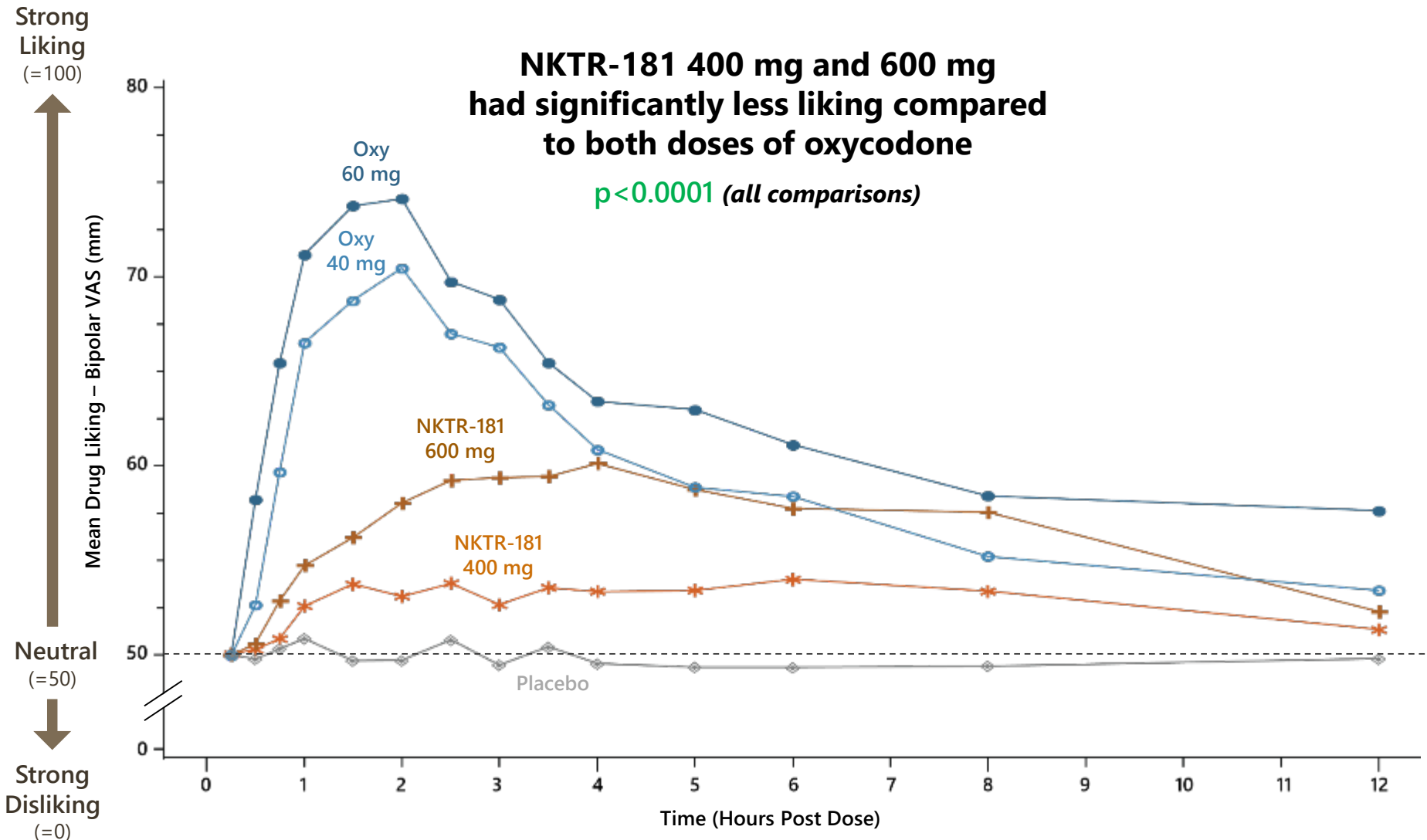


**Chronic pain market includes:**

Chronic back pain  
Osteoarthritis  
Fibromyalgia  
Neuropathic pain

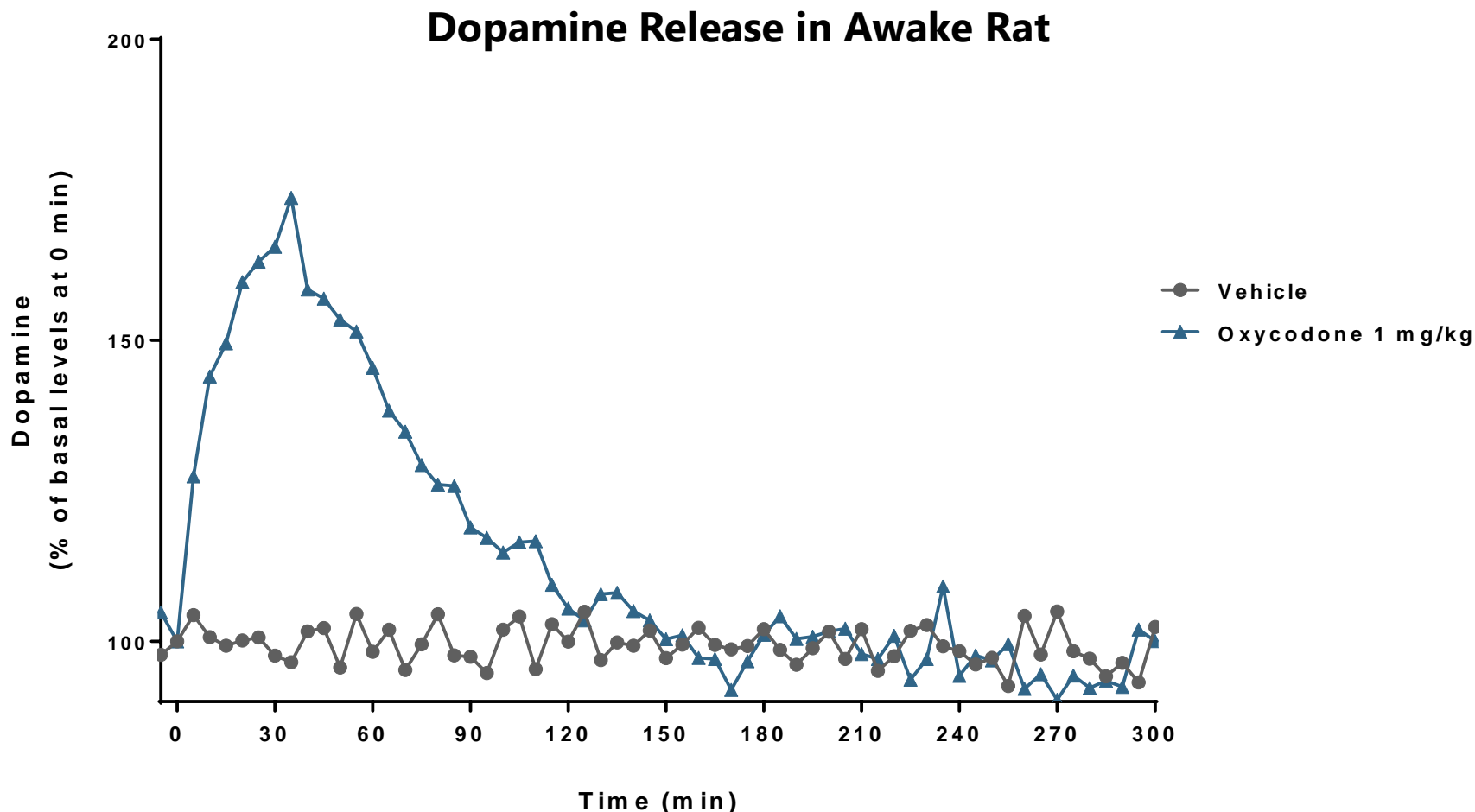
# Drug Liking in Human Abuse Liability Trial

*NKTR-181 Therapeutic Doses Comparison to Oxycodone Therapeutic Doses*



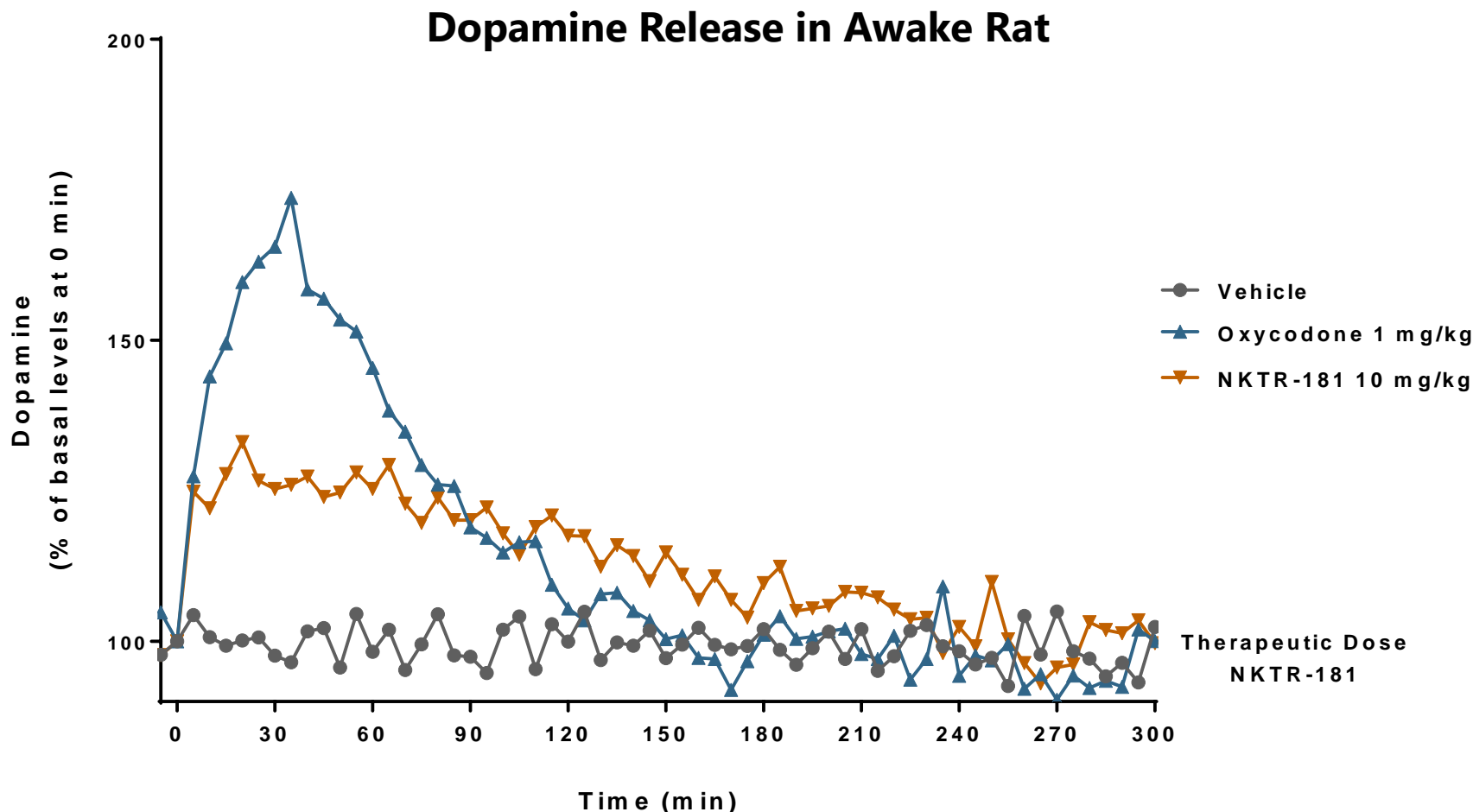
\*The peak liking score for NKTR-181 400 mg oral tablet confirmed the same peak liking score for NKTR-181 400 mg oral solution evaluated in the company's prior HAP study (62.0 vs 62.3\*\*). \*\* Webster et al.; Human Abuse Potential of the New Opioid Analgesic Molecule NKTR-181 Compared with Oxycodone. Pain Med 2017 pnw344. doi: 10.1093/pm/pnw344

# CNS Dopamine Release in Preclinical Studies Shows Marked Difference to Oxycodone



Mean, N=7/group  
Compounds given IV  
Dopamine levels measured from nucleus accumbens using microdialysis  
Source: Nektar internal data

# CNS Dopamine Release in Preclinical Studies Shows Marked Difference to Oxycodone



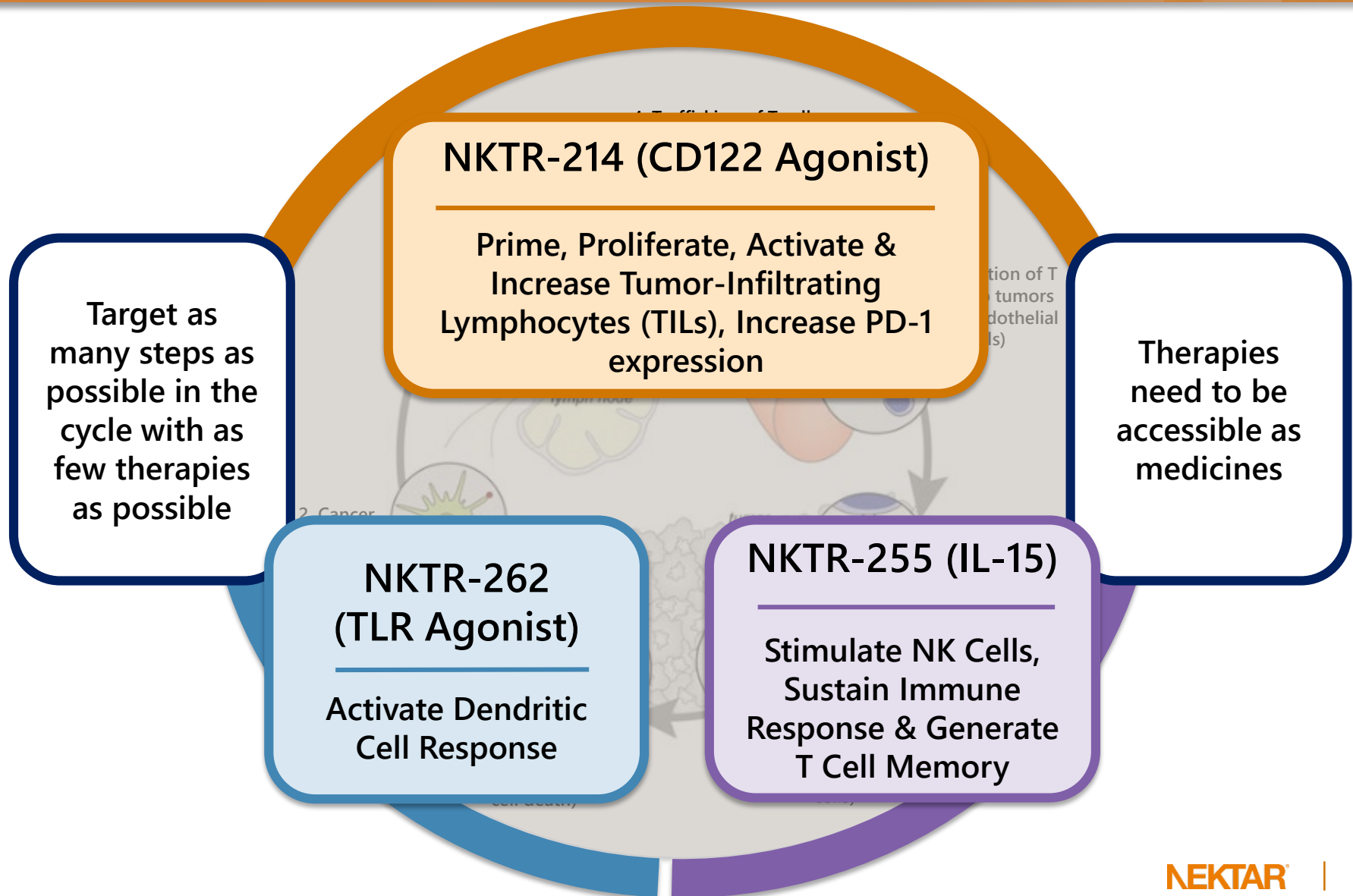
Mean, N=7/group  
Compounds given IV  
Dopamine levels measured from nucleus accumbens using microdialysis  
Source: Nektar internal data

# NKTR-181: NDA Submission & Timeline

- ▶ Pre-NDA meeting scheduled in Q1 2018
- ▶ NDA submission planned in Q2 2018 with extensive efficacy and safety clinical data package:
  - 600-patient efficacy study in patients with chronic pain who are new to opioid therapy
  - 630-patient long-term 52-week safety and efficacy trial in patients who are new to opioid therapy as well as those who are experienced with opioid therapy
  - PK and PD studies in over 450 healthy subjects (therapeutic and supratherapeutic NKTR-181 doses)
  - Human abuse potential study of therapeutic and supratherapeutic NKTR-181 doses in recreational drug users (tablets)
  - Human abuse potential study of therapeutic NKTR-181 doses in recreational drug users (solution)
- ▶ Plans to commercialize with partner

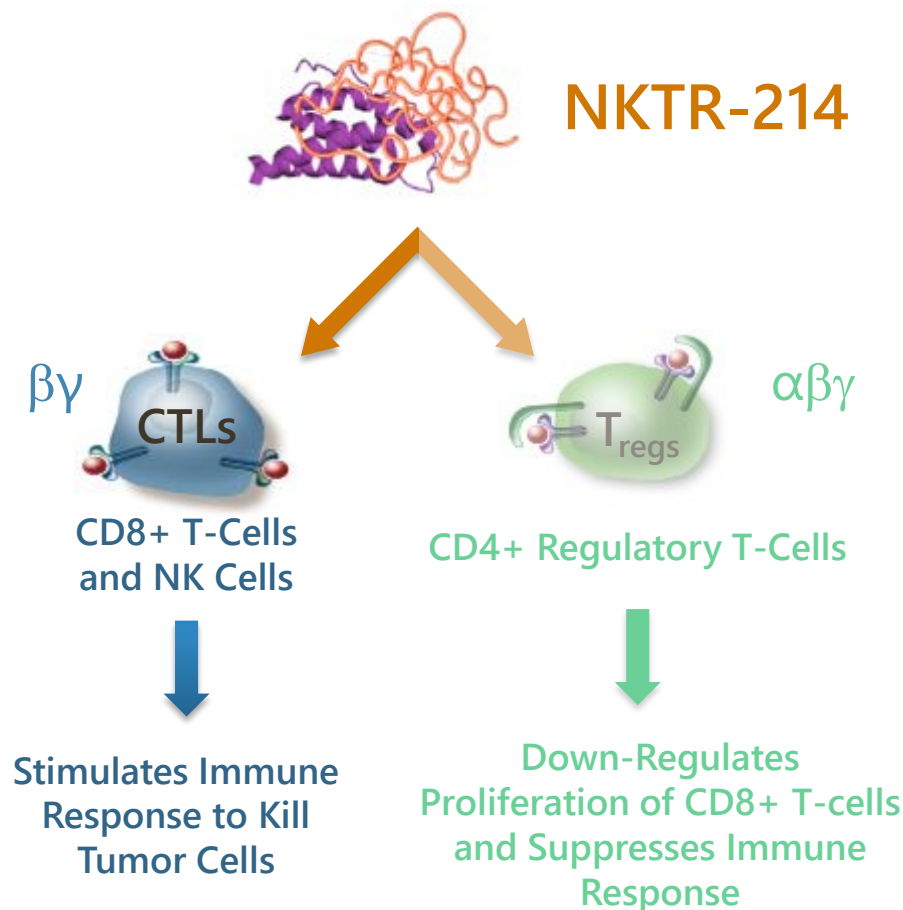


# Nektar's Immuno-Oncology Strategy to Create Therapies that Cover the Immunity Cycle



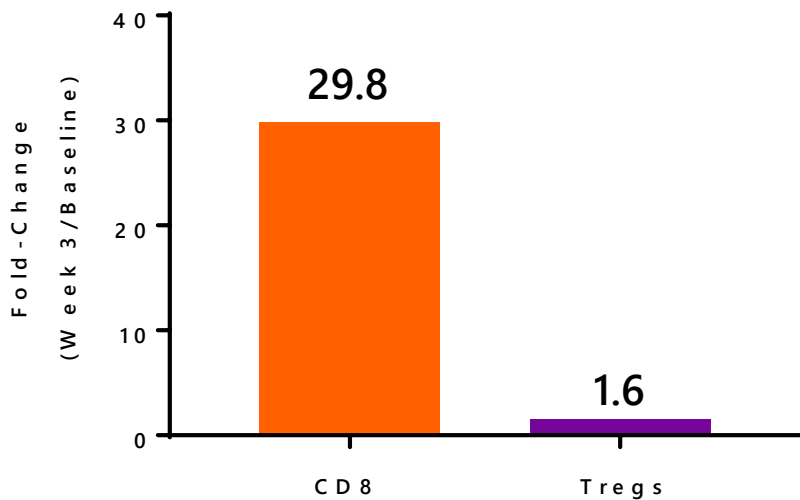
# NKTR-214: Biasing Action to CD 122, or IL-2R Beta, to Stimulate T-Cell Production

- ▶ Biases signaling to favor the CD122 Receptor (IL-2R $\beta\gamma$  complex)
- ▶ Eliminates over-activation of IL-2 pathway that results in serious safety issues
- ▶ Achieves antibody-like dosing schedule in outpatient setting



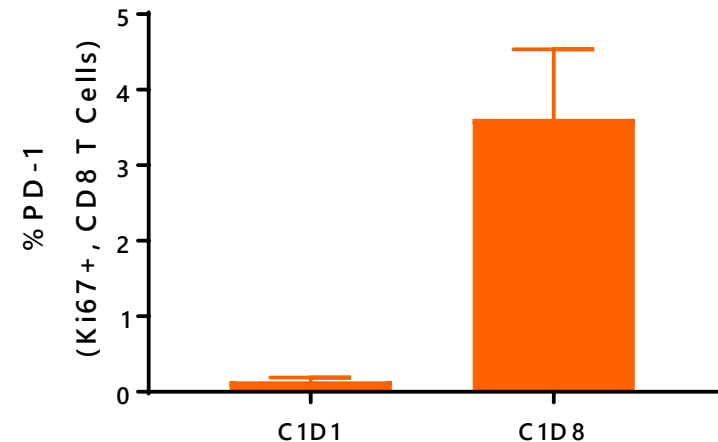
# NKTR-214 Selectively Grows T Cells and Increases PD-1 Expression in Cancer Patients

## Increased T cell Populations in Tumor



Fold Change Expressed as Week 3 / Pre-Dose

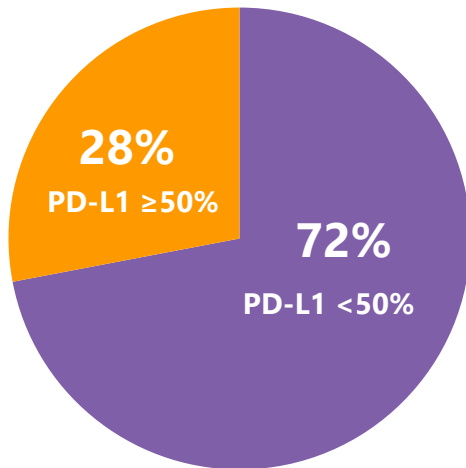
## Increased PD-1 Expression on CD8 T Cells



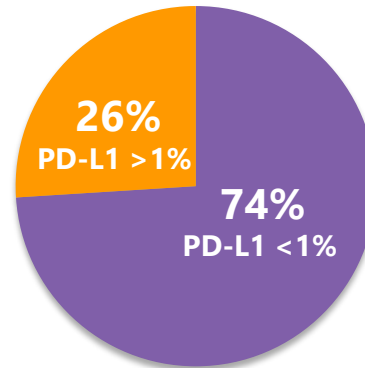
26x Average Fold Increase in PD-1 Expression over Baseline

# Majority of Patients Have PD-L1 Negative Tumors and Don't Benefit from Existing Checkpoint Inhibitors

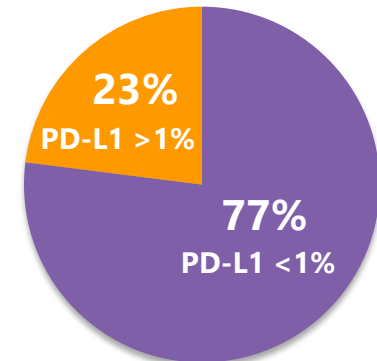
**NSCLC  
Stage IV**  
1L: 175K



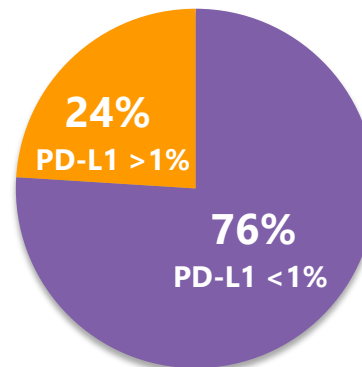
**RCC  
Stage IV**  
1L: 45K



**Melanoma  
Stage IV\***  
1L: 20K



**Urothelial  
Stage IV\*\***  
1L: 21K



**Triple Negative Breast  
Stage IV**  
1L: 19K

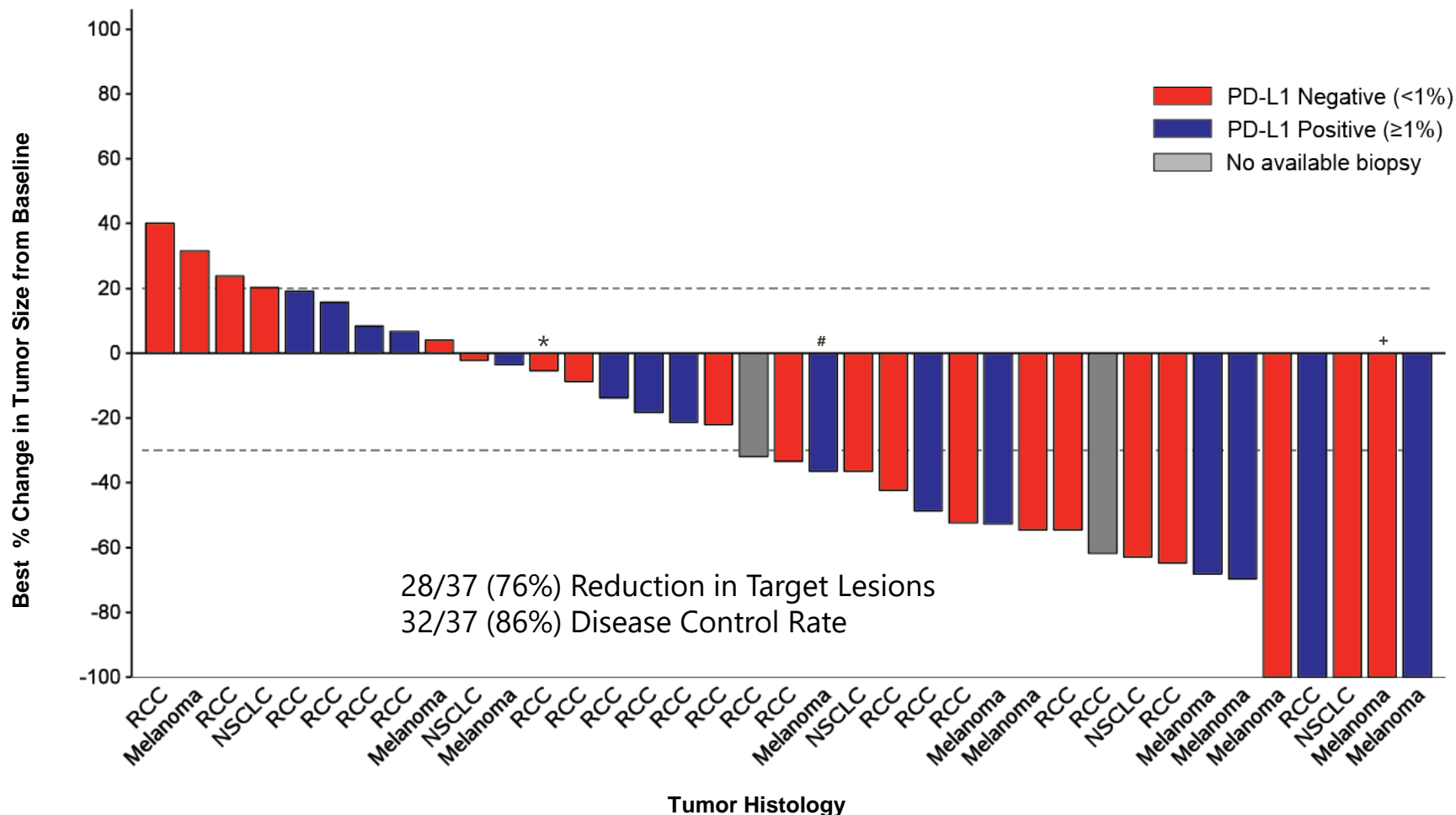


\*Includes Stage III unresectable

\*\*Cisplatin eligible + cisplatin ineligible (SOC refused)

Source: DRG Disease Landscape: Forecast Nov/Dec 2017 (1L Incidence Treated US, EU-5 and Japan)

# NKTR-214 + Opdivo® Shows Tumor Reduction for Both PD-L1 Negative and Positive Patients (N=37)



\* Best overall response is PD (SD for target lesions, PD per non-target lesions)

# Best overall response is SD (PR for target lesions, PD per new lesion at confirmatory scan)

+ Best overall response is PR (CR for target lesions, non-target lesions still present)

Data are shown for patients with post-baseline scans that included assessment of target lesions.

One patient discontinued from study due to clinical progression before the first post-baseline tumor assessment

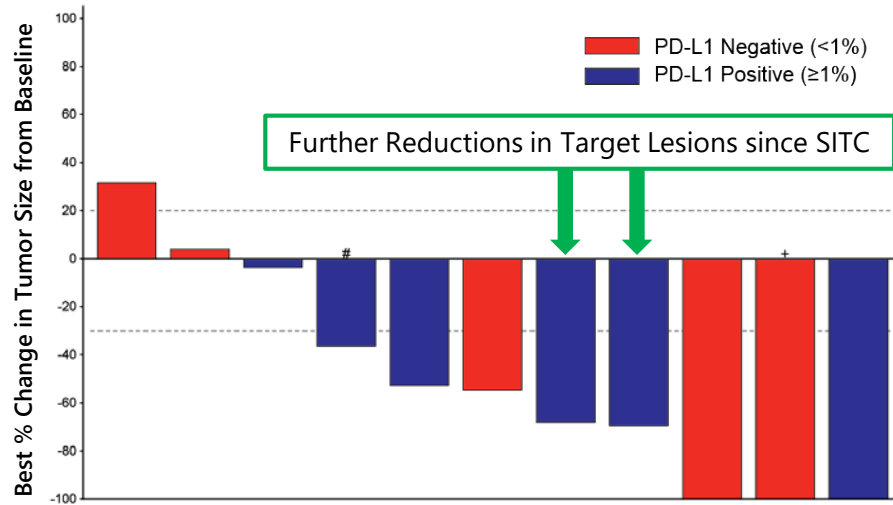
Source: SITC 2017 and Company data; Data as of December 20, 2017

# Stage IV Treatment-Naïve Melanoma Patients (N=11) in PIVOT Dose Escalation

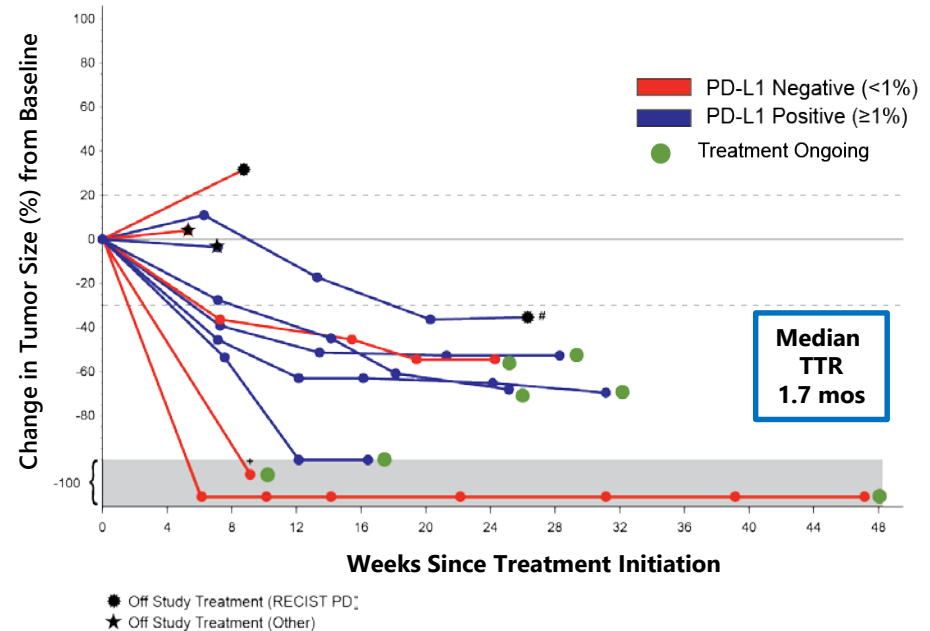
Best Overall Response by RECIST: ORR=7/11 (64%); DCR=10/11 (91%)

Best Overall Response by irRECIST: ORR=8/11 (73%); DCR=10/11 (91%)

## % Change From Baseline in Target Lesions



## % Change in Target Lesions Over Time



ORR is Overall Response Rate

DCR is Disease Control Rate

TTR is Time to Response

+ Best Overall response is PR (CR for target lesions, non-target lesions still present)

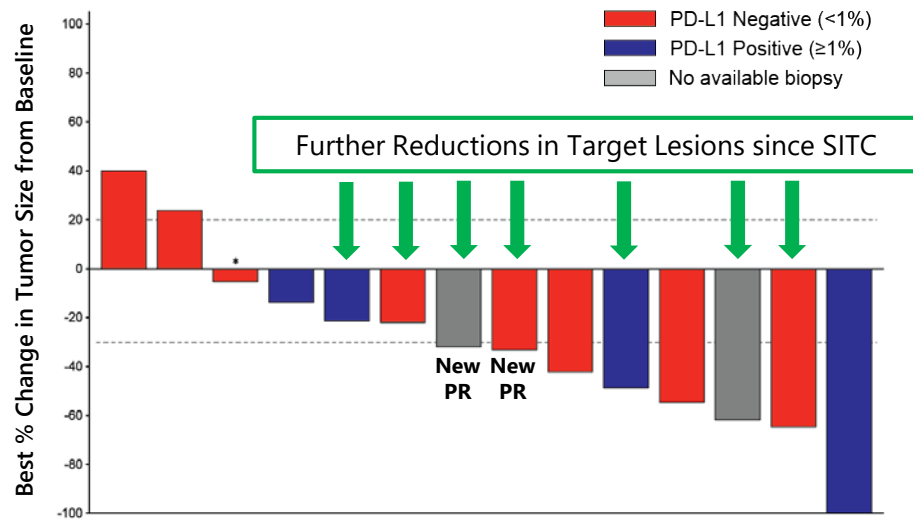
# Best Overall Response is SD (PR for target lesions, PD per new lesion on confirmatory scan)

Source: SITC 2017 and Company data; Data as of December 20, 2017

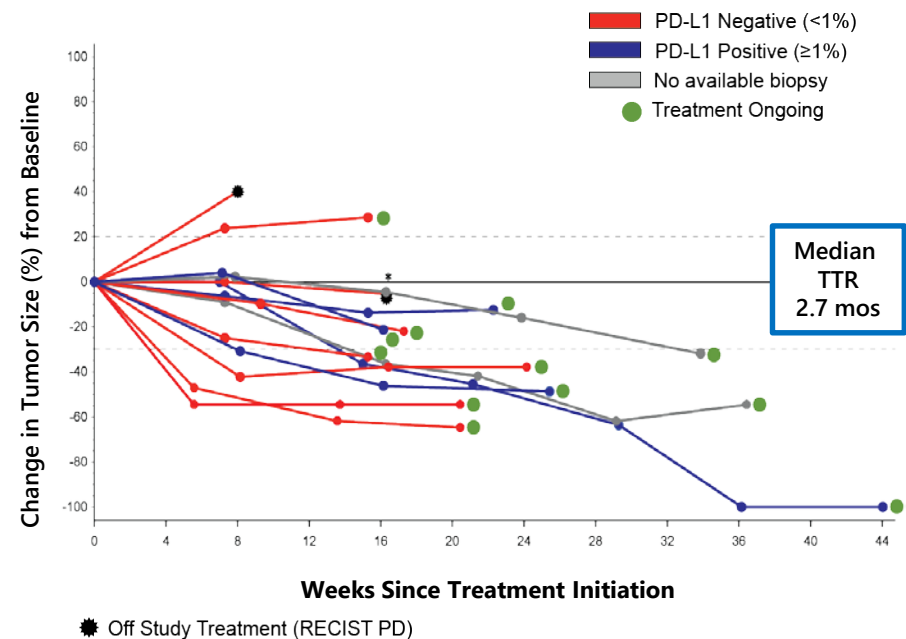
# Stage IV Treatment-Naïve 1L Renal Cell Carcinoma (N=14) in PIVOT Dose Escalation

Best ORR by RECIST : ORR=8/14 (57%); DCR=11/14 (79%)

% Change From Baseline in Target Lesions



% Change in Target Lesions Over Time



ORR is Overall Response Rate

DCR is Disease Control Rate

TTR is Time to Response

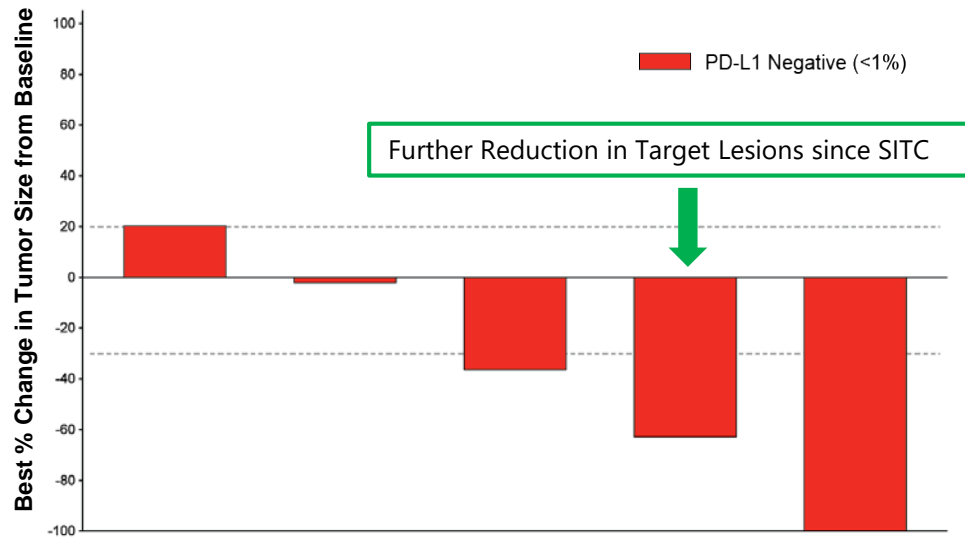
\* Best overall response is PD (SD for target lesions, PD per non-target lesions).

Source: SITC 2017 and Company data; Data as of December 20, 2017

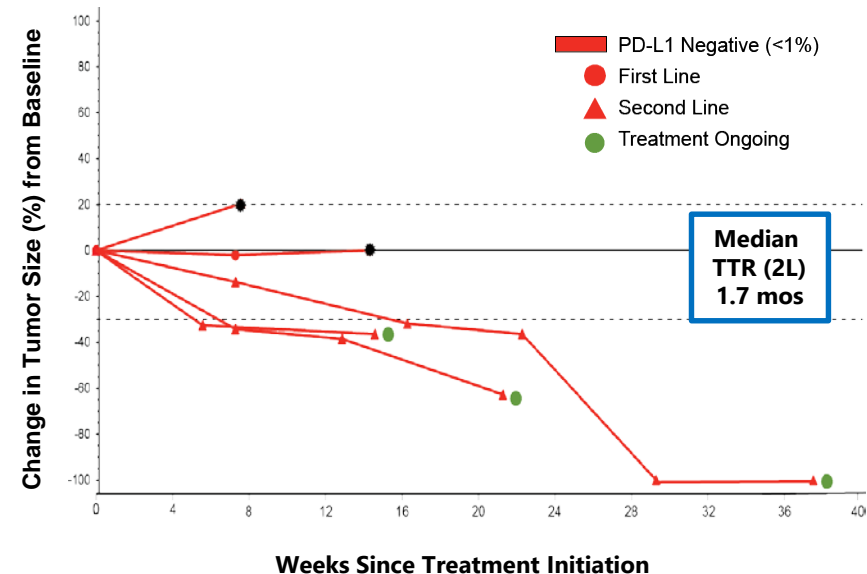
# Stage IV IO-Naïve PD-L1 Negative NSCLC 1L and 2L (N=5) in PIVOT Dose-Escalation

Best Overall Response by RECIST (2L): ORR=3/4 (75%); DCR=3/4 (75%)

% Change From Baseline in Target Lesions



% Change in Target Lesions Over Time



● Off Study Treatment (RECIST PD)



# Key Takeaways from PIVOT Dose-Escalation Study of NKTR-214 with OPDIVO®

## Efficacy

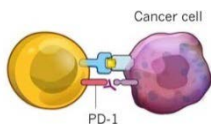
- Compelling ORR and DCR in both PD-L1 negative and PD-L1 positive patients
- Majority of responses occurred within the first 2 months of treatment and deepened over time
- Complete responses were observed in every tumor type
- All patients with responses continue on treatment
- No evidence of T cell anergy observed

## Safety and Tolerability

- Convenient, outpatient dosing schedule once every 3 weeks
- No treatment study discontinuations from treatment-related adverse events
- No treatment related deaths
- Most common side effects were flu like symptoms that were predictable, short lived and easily managed
- No grade 3 or higher immune-related adverse events at recommended phase 2 dose and below

# NKTR-214: Development Program in 2018

## Checkpoint Inhibitors

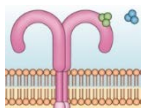


Ongoing PIVOT Study of NKTR-214 with Opdivo® in Melanoma, RCC, NSCLC, Bladder and TNBC (Nektar & Bristol-Myers Squibb)

Ongoing PROPEL Study of NKTR-214 with Keytruda® or Tecentriq® (Nektar)

Ongoing IST in Sarcoma with NKTR-214 with Opdivo® at MSK and MD Anderson (Nektar & Bristol-Myers Squibb)

## TLR Agonist



Phase 1 trial NKTR-214 with NKTR-262 (IND Filed YE2017, Dosing Q12018)

## Cell Therapies

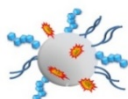


Ongoing IST of NKTR-214 with Endogenous T Cell regimen in NSCLC patients (MD Anderson)

## Small Molecules

Preclinical studies underway with 5 clinical compounds with Takeda in liquid and solid tumors

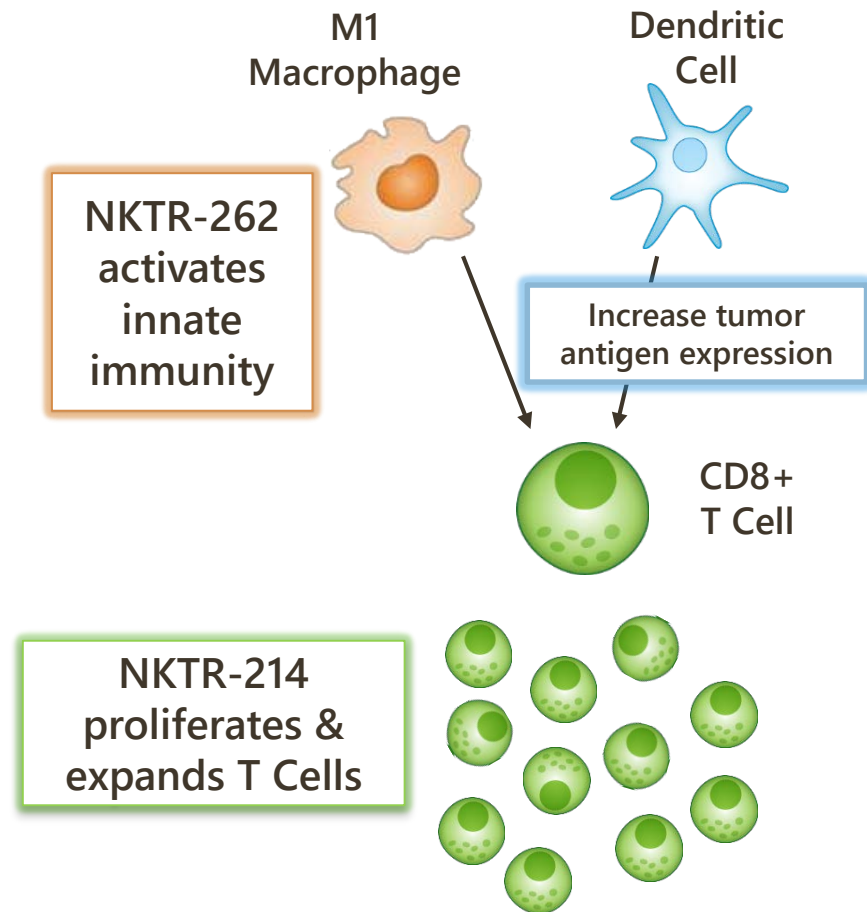
## Vaccines



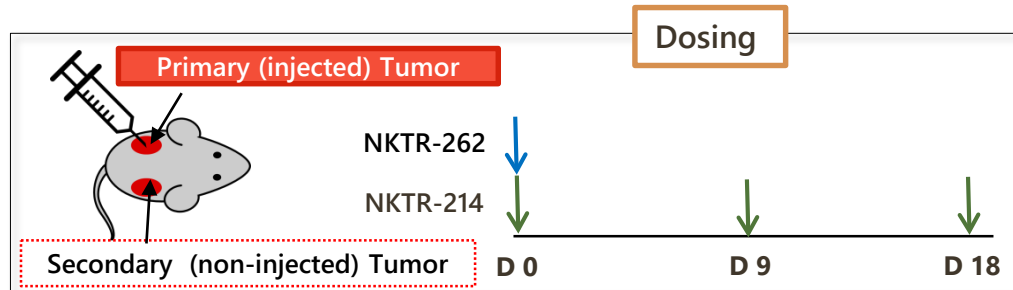
Preclinical studies underway with vaccines

# NKTR-262: A Unique Intratumoral TLR Agonist to Target the Innate Immune Response

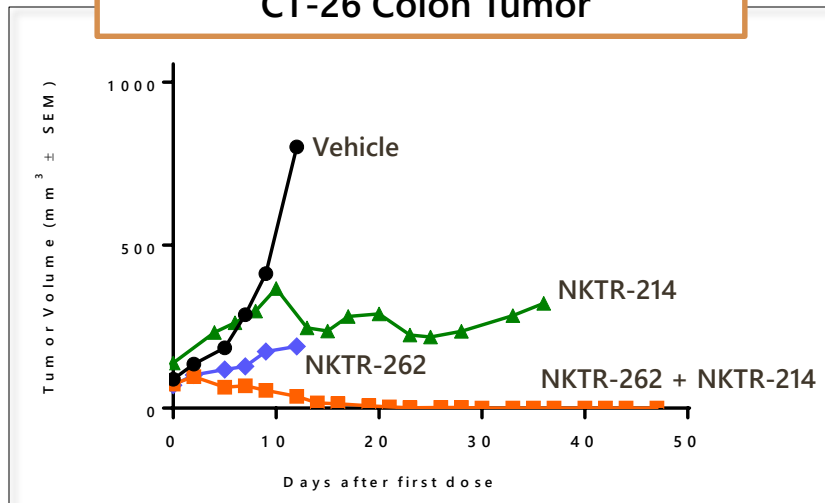
- ▶ **Activates myeloid cell response and increases tumor antigen presentation**
  - Overcomes tumor-suppressing micro-environment by mimicking local infection
- ▶ **NKTR-262 designed to be synergistic with NKTR-214 and is a novel, wholly-owned I-O combination for Nektar**
- ▶ **Nektar technology optimizes abscopal anti-tumor effects with minimal systemic exposure**
- ▶ **IND Filed End of 2017**
- ▶ **Phase 1 Dosing To Start in Q1 2018**



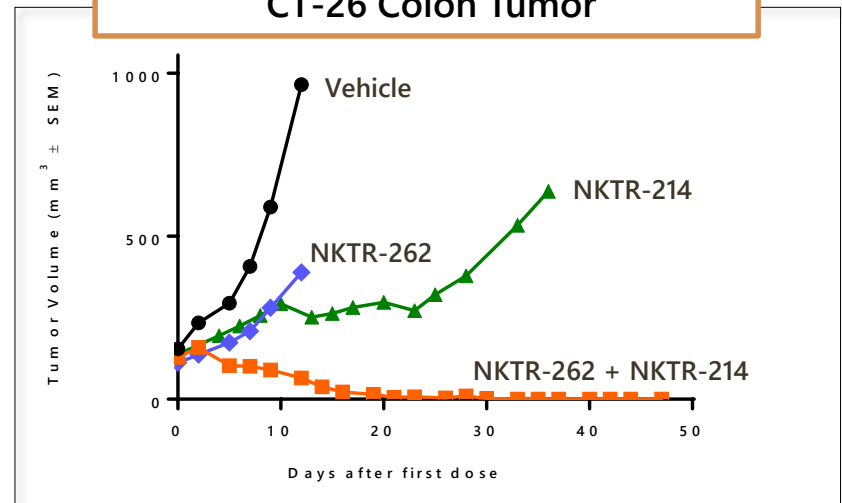
# Complete Regression and Abscopal Effect with Combination of NKTR-262 and NKTR-214



**Primary (injected)  
CT-26 Colon Tumor**

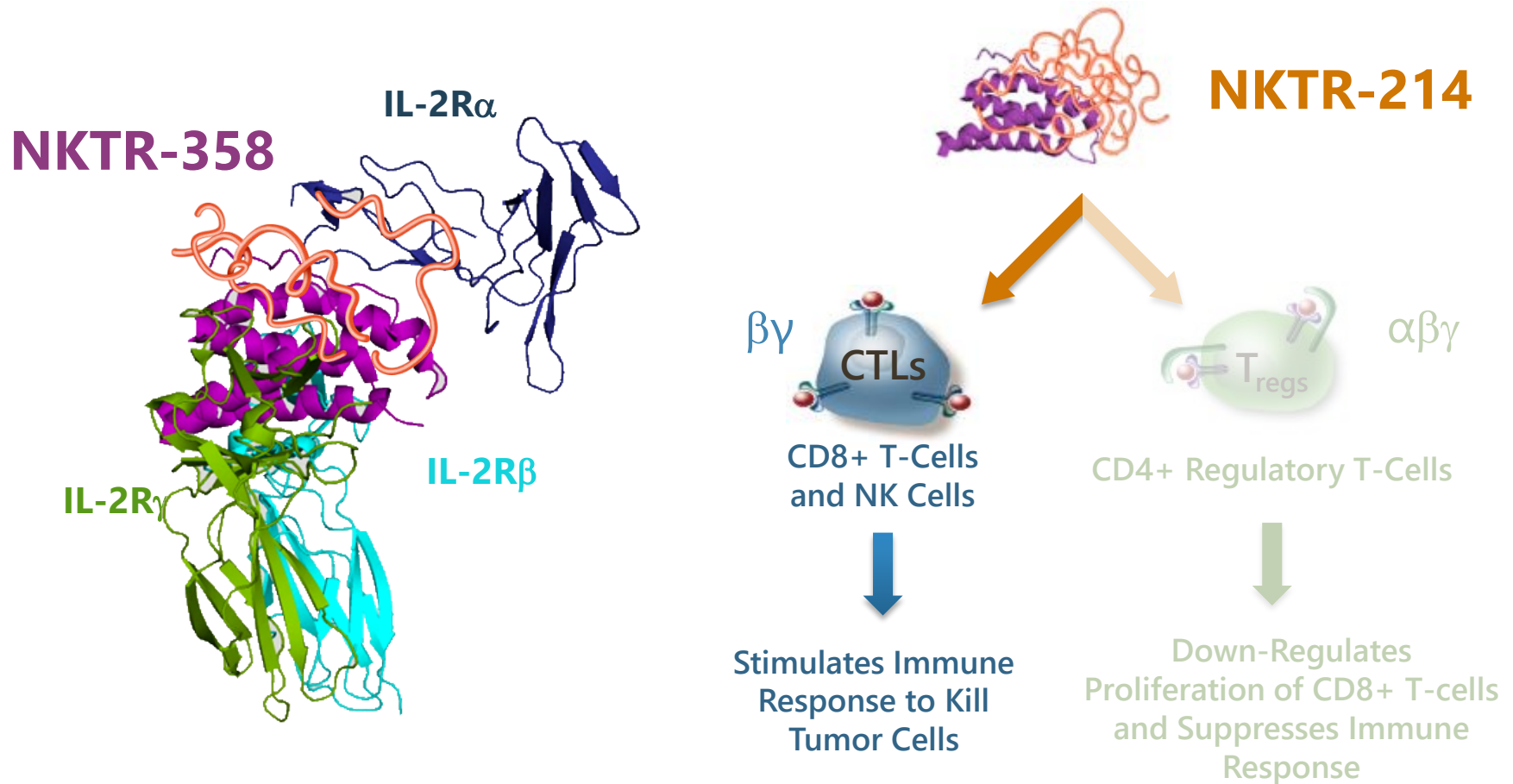


**Secondary (non-injected)  
CT-26 Colon Tumor**

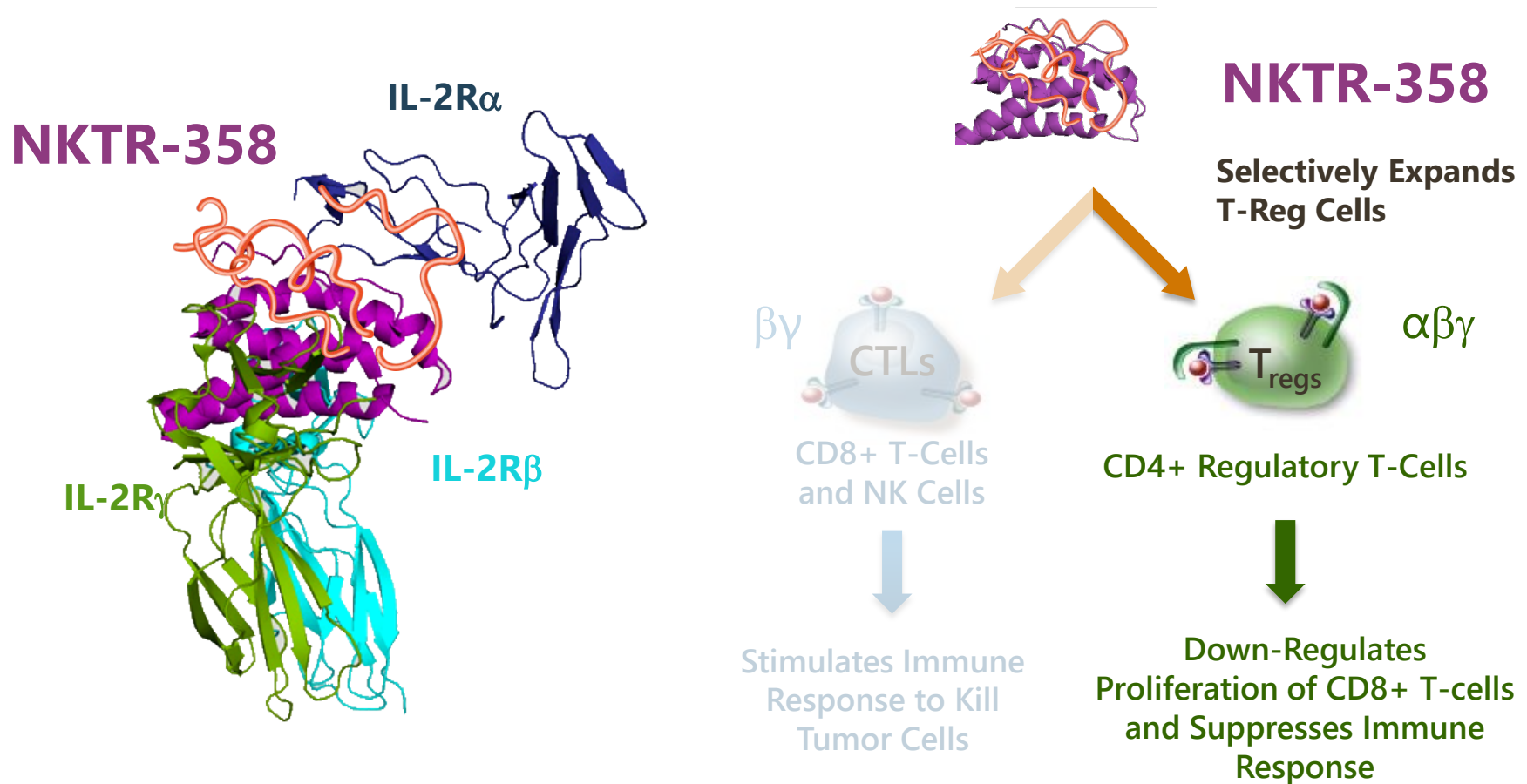


NKTR-262 0.8 mg in 40  $\mu$ L volume given in a single IT dose, NKTR-214 0.8 mg/kg q9dx3 IV; N=10 per group

# NKTR-358: A T Regulatory Stimulatory Agent

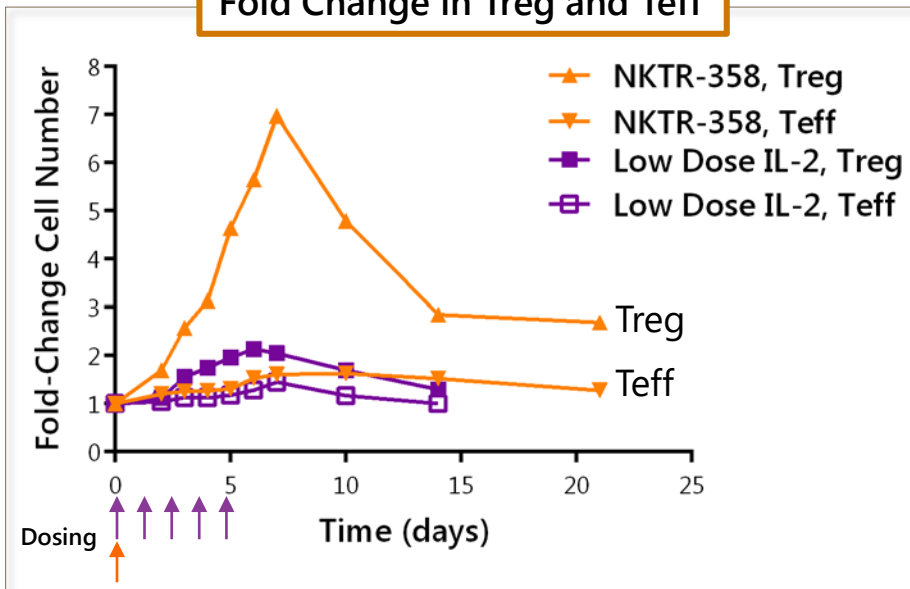


# NKTR-358: Increases T Regulatory Cells and Their Suppressive Activity

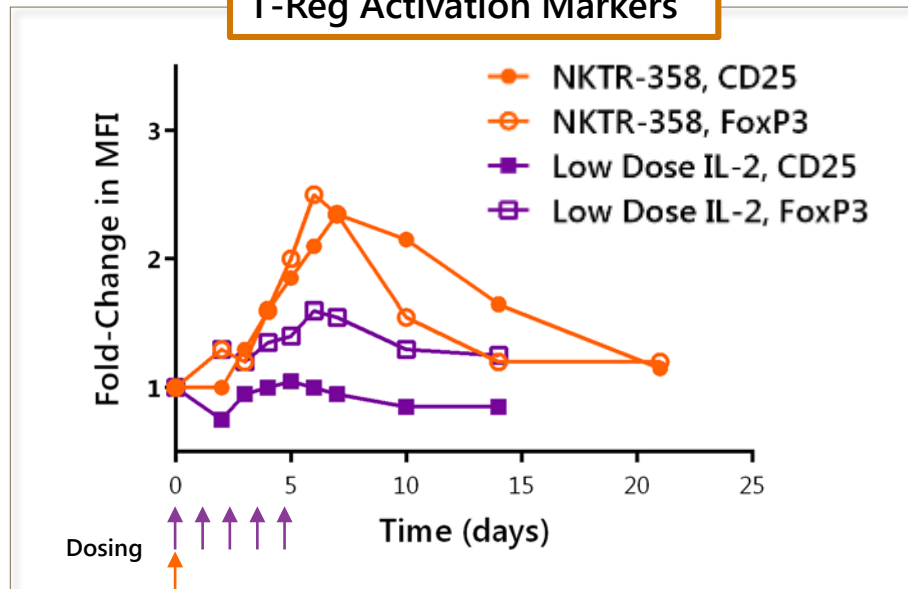


# NKTR-358 is Selective for Enhancing of T-Reg Proliferation and Activation in Non-Human Primates

Fold Change in Treg and Teff



T-Reg Activation Markers



- ▶ Single dose NKTR-358 produced greater Treg expansion than repeat low-dose IL-2
- ▶ In mice, NKTR-358 treatment promotes >30-fold increase in Treg suppressive activity

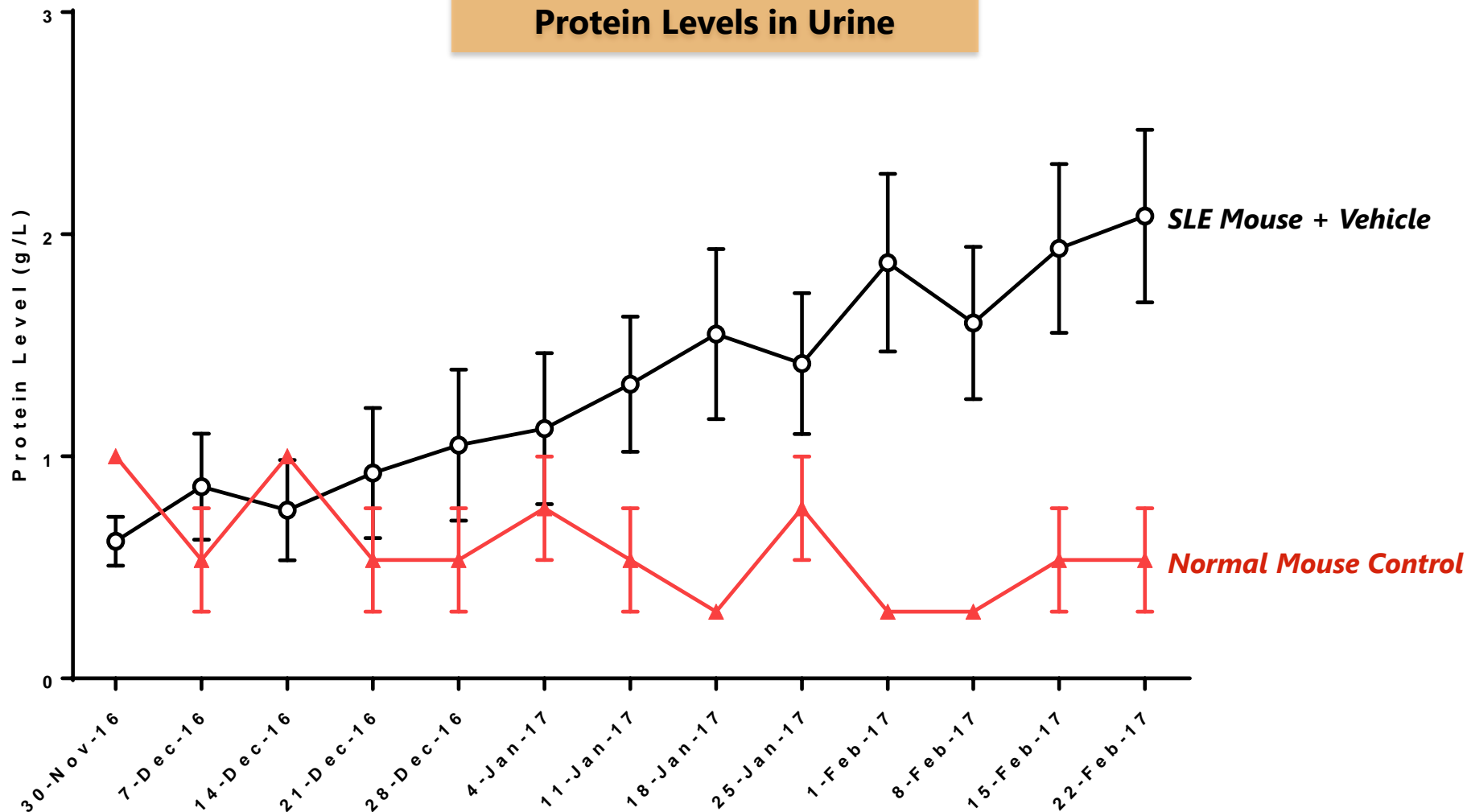
# Second Clinical Study of NKTR-358 to Start in Q1 2018 in Healthy Subjects and Patients with Lupus

- ▶ Ongoing first-in-human study shows multiple-fold increase in T regulatory cells with no increase in CD8+ or NK cells following single doses of NKTR-358
- ▶ No dose-limiting toxicities to-date
- ▶ Full data from Phase 1 single ascending dose study to be presented at medical meeting in 2018
- ▶ Initiating Phase 1 multiple dose ascending study in healthy subjects and patients with lupus in Q1 2018
- ▶ NKTR-358 has potential to be developed as first-in-class resolution therapeutic in lupus, Crohn's disease, rheumatoid arthritis, psoriasis and transplant patients



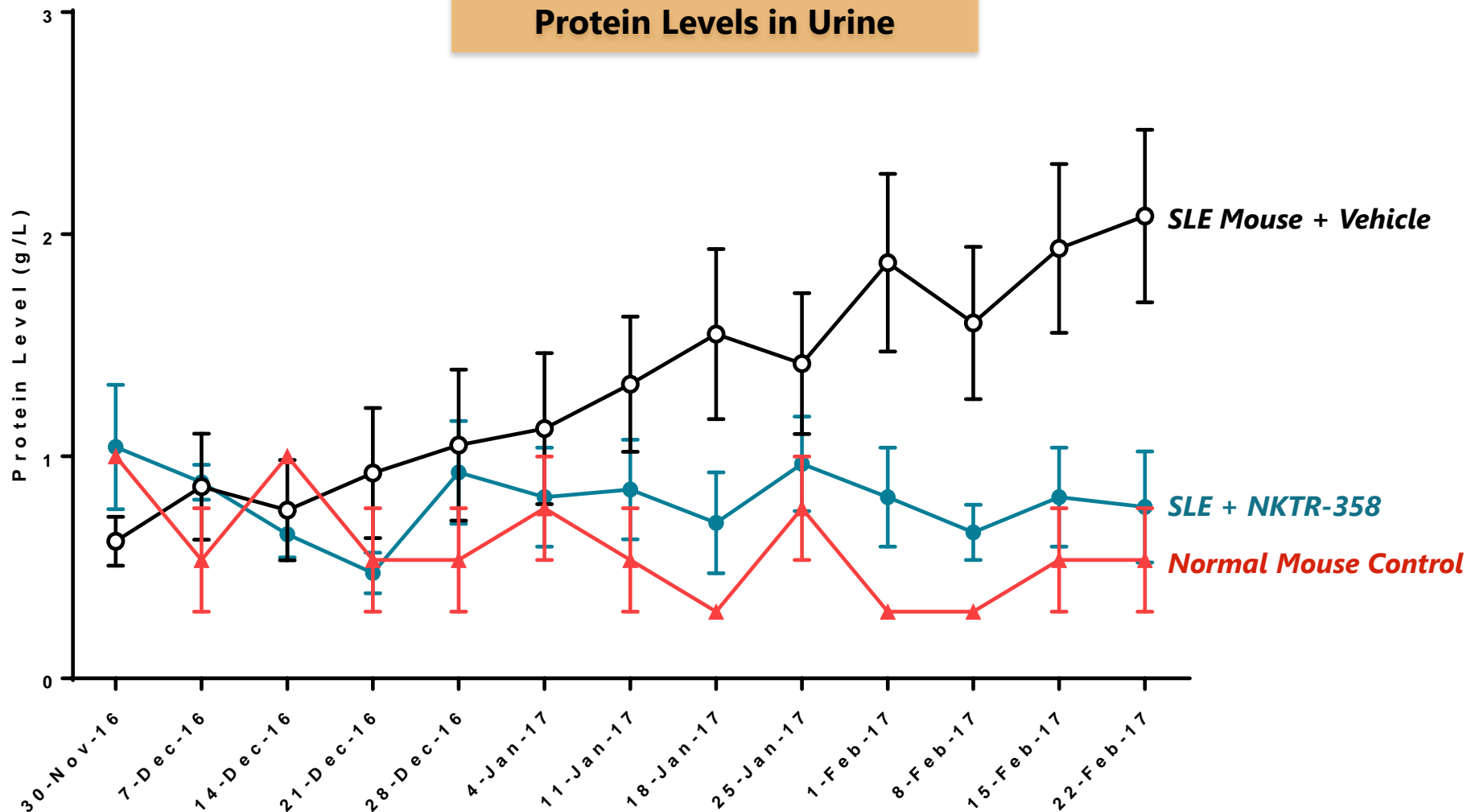
# NKTR-358 Suppresses Disease Progression in a Mouse Model of Systemic Lupus Erythematosus

Protein Levels in Urine



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Protein Levels in Urine



# 2018 Anticipated Milestones

## ► **First Half of 2018**

- Initiate first Phase 1 clinical trial of NKTR-262 with NKTR-214 in cancer patients (solid tumors)
- Initiate Phase 1/2 multiple-ascending dose trial of NKTR-358 in patients with lupus
- Submit New Drug Application (NDA) for NKTR-181 in chronic pain
- Initial data from PIVOT expansion trial (NKTR-214 with Opdivo) in patients with melanoma, non-small cell lung cancer, renal cell carcinoma, bladder cancer and triple-negative breast cancer
- Initial data from sarcoma investigator-sponsored trial of NKTR-214 with Opdivo

## ► **Second Half of 2018**

- Data from PROPEL clinical trial of NKTR-214 with atezolizumab or pembrolizumab in patients with bladder and non-small cell lung cancer
- Data from first-in-human Phase 1 single-ascending dose clinical trial of NKTR-358 presented at major medical meeting
- Initial data from Phase 1 trial of NKTR-262 with NKTR-214
- IND Filing for NKTR-255 (IL-15 Receptor Agonist)

**Ended 2017 with \$353.2 Million in Cash & Investments**