



**NEKTAR**<sup>®</sup> NEW PATHWAYS TO  
SMARTER MEDICINE<sup>™</sup>

**41<sup>st</sup> Annual  
J.P. Morgan Healthcare Conference**

Howard Robin  
President & CEO  
January 11, 2023

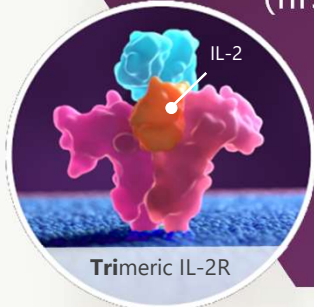
NASDAQ: NKTR

*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, unaudited year-end cash and investments and sufficiency of working capital 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 4, 2022. Nektar undertakes no obligation to update forward-looking statements as a result of new information or otherwise.*

# Nektar: Key Areas of R&D Focus

## Immunology

Focus on development of REZPEG in auto-immune disease with partner Eli Lilly & Co.  
(first in class IL-2 based Treg stimulator)



*Our mission is to discover and develop novel therapies which selectively modulate the immune system to treat cancer and autoimmune disorders*

## Oncology

Focus on development of NKTR-255 (novel IL-15 agonist)

- Cell therapy potentiator in liquid and solid tumors
- ADCC combinations in liquid and solid tumors
- Checkpoint combination in bladder cancer








## Research

Focus on new candidates in immunology and oncology:

- Interferon gamma program
- TNFR2 antibody program
- Autoimmune anti-fibrotic disease program

# Nektar R&D Pipeline

## Immuno-oncology

Program	Indication	Study	Preclinical	Phase 1	Phase 2	Phase 3	Partner
NKTR-255	Bladder Cancer	NKTR-255 + BAVENCIO®	Phase 2				   
	DLBCL	NKTR-255 + Yescarta®/Breyanzi®	Phase 2/3				
	R/R NHL or Multiple Myeloma	NKTR-255 + RITUXAN® or DARZALEX FASPRO®	Phase 1/2				
	Head & Neck and Colorectal	NKTR-255 + ERBITUX®	Phase 1/2				
	[IST] NSCLC	NKTR-255 + IMFINZI®	Phase 1				
	[IST] NHL / DLBCL	NKTR-255 + Breyanzi®	Phase 1				
	[IST] ALL	NKTR-255 + CD19/22 CAR T-cell	Phase 1				
NKTR-288	Solid Tumors	NKTR-288 (interferon gamma)	Preclinical				

## Immunology

Program	Indication	Study	Preclinical	Phase 1	Phase 2	Phase 3	Partner
REZPEG (LY3471851 / NKTR-358)	Systemic Lupus Erythematosus	REZPEG	Phase 2				Lilly Lilly Lilly
	Atopic Dermatitis	REZPEG	Phase 2 Planned				
	(Undisclosed Indication)	REZPEG	Phase 2 Planned				
TNFR2 agonist antibody	Multiple Sclerosis & Other Autoimmune Indications	Preclinical	Preclinical				BioLogicDesign
Cytokine candidate	Liver & Kidney Diseases, Cirrhosis & Other Indications	Preclinical	Preclinical				

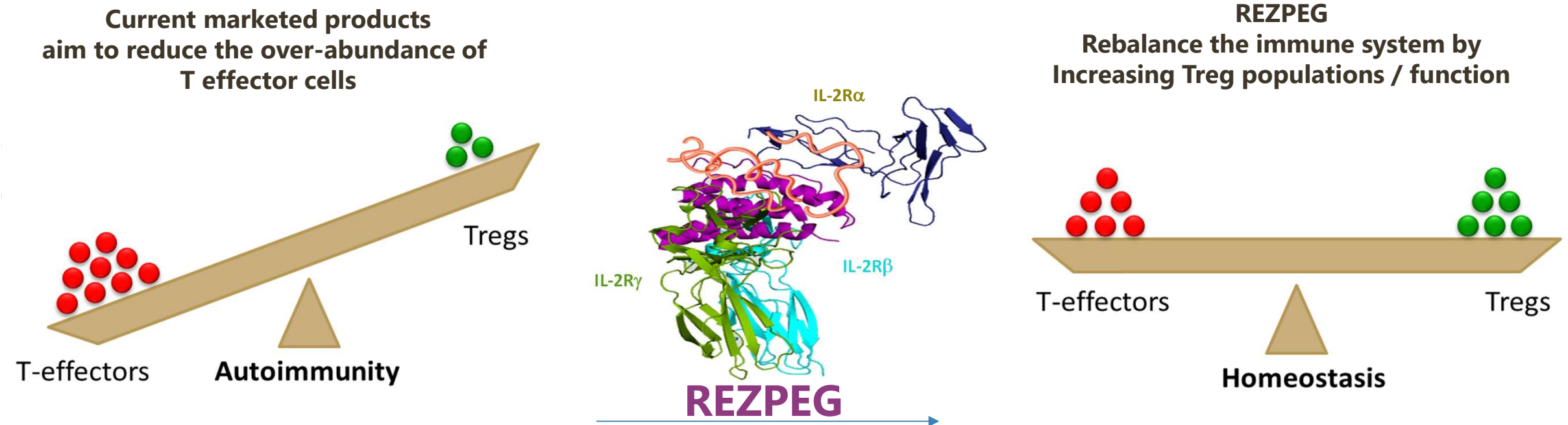
## Anti-viral/anti-bacterial

Program	Indication	Study	Preclinical	Phase 1	Phase 2	Phase 3	Partner
NKTR-288	Anti-viral/anti-bacterial	NKTR-288 (interferon gamma)	Preclinical				

Bavencio is a registered trademark of Merck KGaA; Yescarta is a registered trademark of Gilead Sciences, Inc. , or its related companies; Breyanzi is a registered trademark of Juno Therapeutics, Inc.; Rituxan is a registered trademark of Biogen; Darzalex Faspro is a registered trademark of Janssen Biotech, Inc.; Erbitux is a registered trademark of ImClone LLC., a subsidiary of Eli Lilly & Co.; Imfinzi is a registered trademark of AstraZeneca AB; [IST]: Investigator Sponsored Trial




# Rezpegaldesleukin (REZPEG): Novel Treatment Approach for Auto-immune Disorders

**Novel mechanistic approach:** Resolution/restoration of immune system



**REZPEG preferentially stimulates expansion of T regulatory cells with minimal effects on T-effectors**

# REZPEG: Phase 2 Development Program

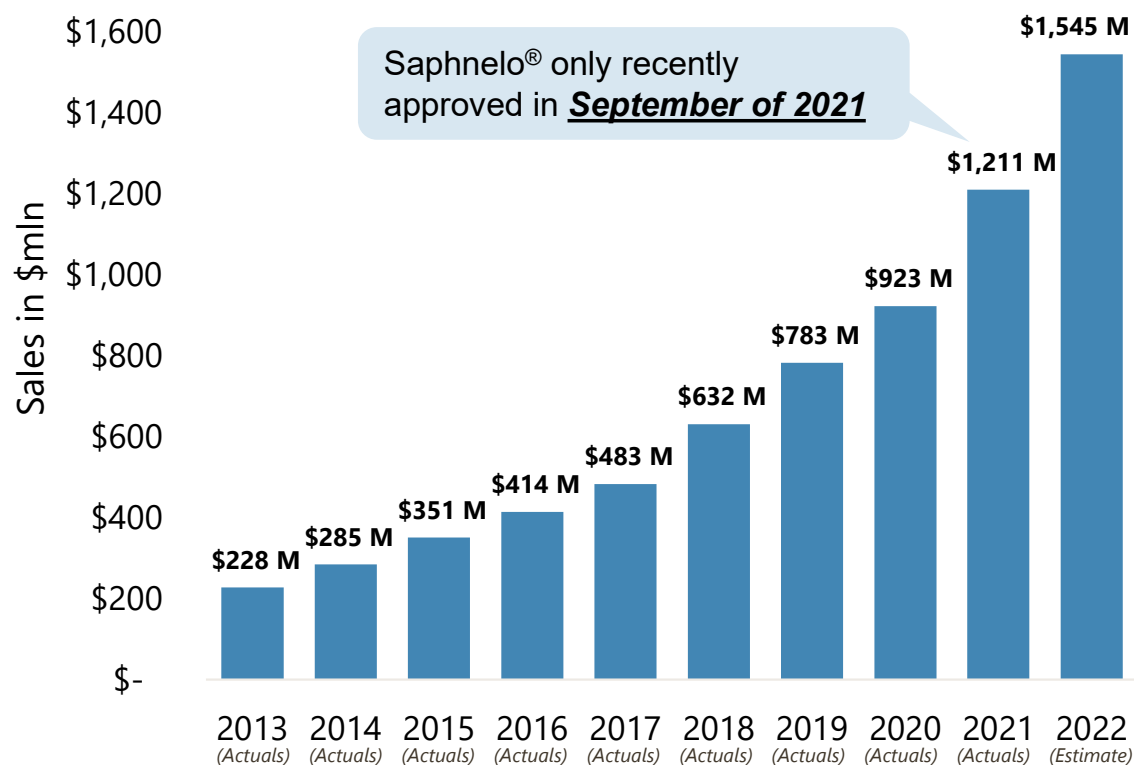
	Partner	Indication	Program	Preclinical	Phase 1	Phase 2	2022 WW Sales <sup>1</sup>
Immunology		<b>Systemic Lupus Erythematosus</b> <i>NCT04433585</i>	<b>REZPEG</b>	<b>ISLAND-SLE</b> Primary endpoint: Reduction in SLEDAI at 6 months (Data H1' 2023) <i>N = 280</i>			<b>~\$1-2B</b> <i>Lupus</i>
		<b>Atopic Dermatitis</b> <i>Bio-Naïve &amp; Bio-Experienced Patients</i>	<b>REZPEG</b>	<b>Planned Phase 2b study/ H1' 2023 start</b> <i>N = 340</i>			<b>~\$6-7B</b> <i>Atopic Dermatitis</i>
		<b>New Undisclosed Indication</b> <i>TBD</i>	<b>REZPEG</b>	<b>Planned Phase 2 study</b> <i>N = NA</i>			Estimated sales of treatments in these announced indications <b>~\$7B to \$9B</b>

- ▶ New phase 2b study in atopic dermatitis will enroll a total of 340 Dupixent-naïve and Dupixent-experienced patients



# High Unmet Need for New Mechanism and Treatment Option for Patients with Systemic Lupus Erythematosus (SLE)

## Combined Benlysta® & Saphnelo® sales<sup>1</sup>



- **Benlysta®** was standard of care for a decade and only **12% of patients have placebo-adjusted SRI-4 response with Benlysta® (primary endpoint)<sup>2</sup>**
- **A range of 16 to 18% of patients have placebo-adjusted BICLA response with Saphnelo® (primary endpoint)<sup>3</sup>**
  - Range of 4 to 18% placebo-adjusted SRI-4 response (secondary endpoint)
- **REZPEG: Opportunity for new mechanism in field with a first-in-class T regulatory cell stimulator (IL-2)**
- **Goal is to offer differentiated efficacy and safety profile**

***In the US, over 322,000 patients are estimated to have SLE<sup>4</sup>***

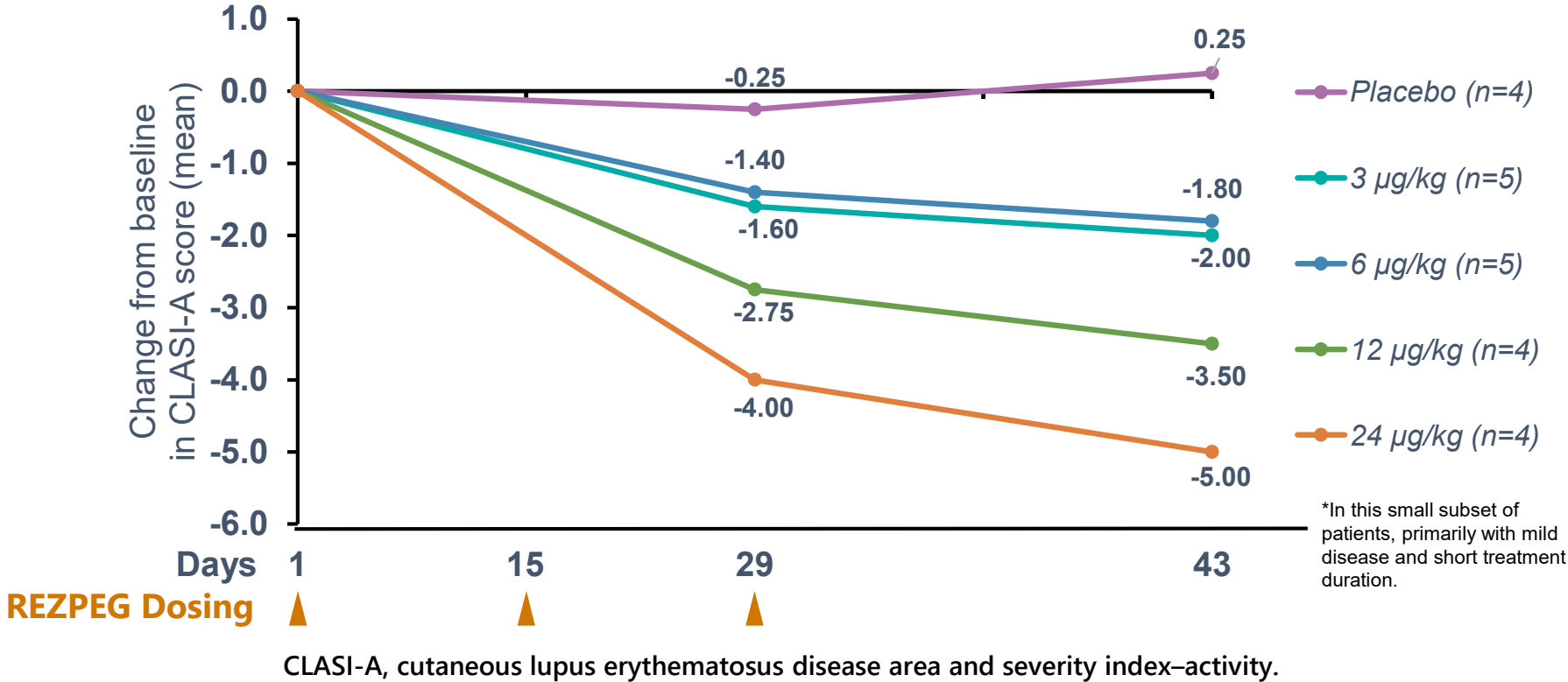
BENLYSTA is a registered trademark of GlaxoSmithKline (GSK) group of companies.; SAPHNELO is a registered trademark and AstraZeneca Access 360 is a trademark of the AstraZeneca group of companies.

Source: <sup>1</sup>Evaluate Ltd (accessed: 1/5/2023); <sup>2</sup>Benlysta [package insert]. Rockville, MD: GSK group of companies. 06/2018.; <sup>3</sup>Saphnelo [package insert]. Wilmington, DE: AstraZeneca. 07/2021.;

<sup>4</sup>Centers for Disease Control and Prevention (CDC)

# REZPEG Demonstrated Dose-dependent Reduction in CLASI-A Skin Scores in Mild Lupus Patients in Phase 1b Study

Phase 1b placebo-controlled study: Mean change in CLASI-A score patients [N=22] with a CLASI-A score of  $\geq 4$  at baseline\*



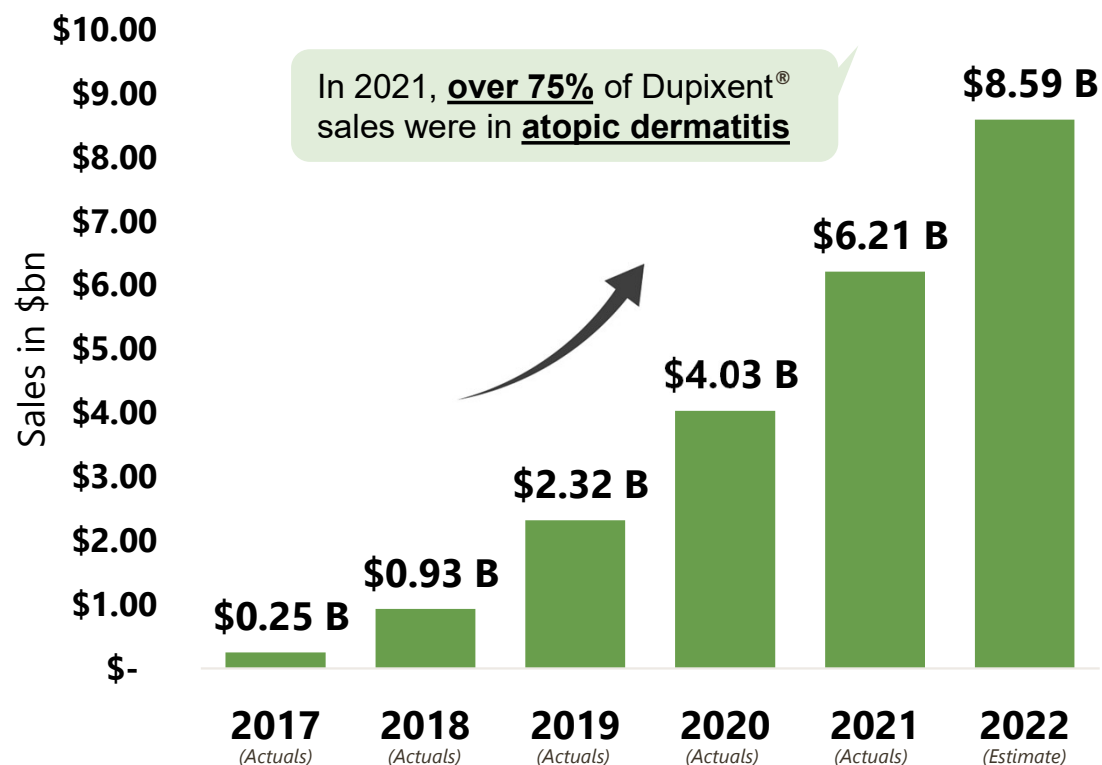
- ▶ 7 of 18 patients had a  $\geq 4$ -point reduction in CLASI-A score from baseline by Day 43
- ▶ One patient (24 µg/kg) experienced a reduction in CLASI-A score from 22 at baseline to 5 by Day 43 (2 weeks after last dose)
- ▶ No observed changes in SLEDAI or joint scores were noted due to the short treatment duration in this study

**Data led to ongoing 280-patient phase 2 study of REZPEG in moderate-to-severe lupus patients;  
In May of 2022, Phase 2 passed interim analysis at 60% of patients completing 24 weeks of treatment and study continuing to completion without modification**



# Rapid Adoption of Biologic Treatments for Atopic Dermatitis

## Dupixent® Sales<sup>1</sup>



- >60% of patients taking Dupixent® fail to have an IGA response<sup>2</sup>
- >50% of patients taking Dupixent® fail to have an EASI-75 response<sup>2</sup>
- Dupixent dosed every 2 weeks with observed loss of response if dosed less frequently (every 4 weeks and 8 weeks)<sup>3</sup>
- High unmet need for a new mechanism

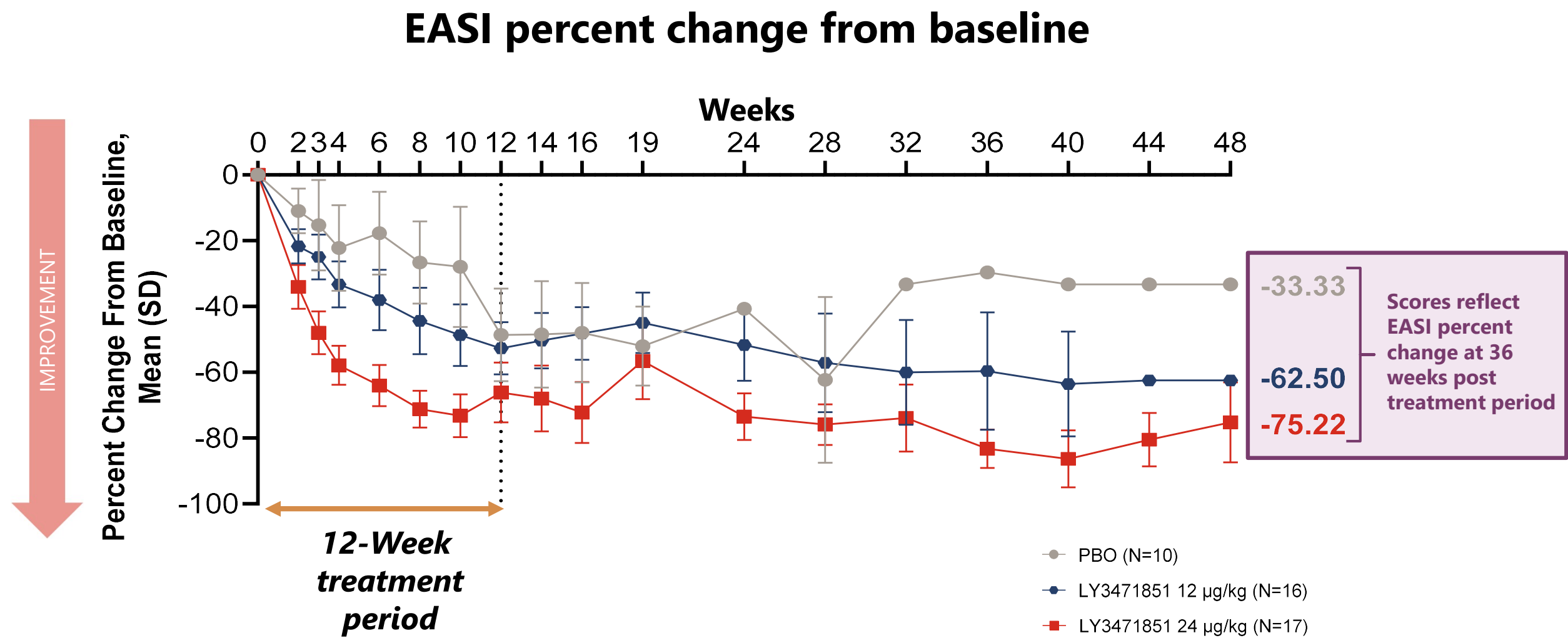
**>4.9 million biologic eligible atopic dermatitis patients worldwide<sup>4</sup>**

DUPIXENT® and DUPIXENT MyWay® are registered trademarks of Sanofi Biotechnology.

Source: <sup>1</sup>Evaluate Ltd (accessed: 1/5/2023); <sup>2</sup>N Engl J Med 2016; 375:2335-2348 DOI: 10.1056/NEJMoa1610020; <sup>3</sup>JAMA Dermatol. 2020;156(2):131-143. doi:10.1001/jamadermatol.2019.3617;






<sup>4</sup>Sanofi Corporate Presentation (3/29/2022)

# Dose-dependent Improvement in EASI Scores was Observed with REZPEG up to Week 48 in Phase 1b Study




Nektar R&D Pipeline

Immuno-oncology

Program	Indication	Study	Preclinical	Phase 1	Phase 2	Phase 3	Partner
NKTR-255	Bladder Cancer	NKTR-255 + BAVENCIO®	Phase 2				   
	DLBCL	NKTR-255 + Yescarta®/Breyanzi®	Phase 2/3				
	R/R NHL or Multiple Myeloma	NKTR-255 + RITUXAN® or DARZALEX FASPRO®	Phase 1/2				
	Head & Neck and Colorectal	NKTR-255 + ERBITUX®	Phase 1/2				
	[IST] NSCLC	NKTR-255 + IMFINZI®	Phase 1				
	[IST] NHL / DLBCL	NKTR-255 + Breyanzi®	Phase 1				
	[IST] ALL	NKTR-255 + CD19/22 CAR T-cell	Phase 1				
NKTR-288	Solid Tumors	NKTR-288 (interferon gamma)	Preclinical				

Immunology

Program	Indication	Study	Preclinical	Phase 1	Phase 2	Phase 3	Partner
REZPEG (LY3471851 / NKTR-358)	Systemic Lupus Erythematosus	REZPEG	Phase 2				Lilly Lilly Lilly
	Atopic Dermatitis	REZPEG	Phase 2 Planned				
	(Undisclosed Indication)	REZPEG	Phase 2 Planned				
TNFR2 agonist antibody	Multiple Sclerosis & Other Autoimmune Indications	Preclinical	Preclinical				
Cytokine candidate	Liver & Kidney Diseases, Cirrhosis & Other Indications	Preclinical	Preclinical				

Anti-viral/anti-bacterial

Program	Indication	Study	Preclinical	Phase 1	Phase 2	Phase 3	Partner
NKTR-288	Anti-viral/anti-bacterial	NKTR-288 (interferon gamma)	Preclinical				

Bavencio is a registered trademark of Merck KGaA; Yescarta is a registered trademark of Gilead Sciences, Inc. , or its related companies; Breyanzi is a registered trademark of Juno Therapeutics, Inc.; Rituxan is a registered trademark of Biogen; Darzalex Faspro is a registered trademark of Janssen Biotech, Inc.; Erbitux is a registered trademark of ImClone LLC., a subsidiary of Eli Lilly & Co.; Imfinzi is a registered trademark of AstraZeneca AB; [IST]: Investigator Sponsored Trial

# 3 Pillars of NKTR-255 Development Strategy

**Augment ADCC therapies in highly refractory patient populations**

- Enhance response to ADCC-mediated therapy through NK-Cell restoration

**Potentiate cellular therapies**

- Improve CAR T-cell persistency in cell therapy regimens

**Synergize with checkpoint inhibitors**

- Augment response to PD-1/PD-L1 checkpoint inhibitor therapies

# 3 Pillars of NKTR-255 Development Strategy

**Augment ADCC  
therapies in highly  
refractory patient  
populations**

- Enhance response to ADCC-mediated therapy through NK-Cell restoration

**Potentiate  
cellular therapies**

- Improve CAR T-cell persistency in cell therapy regimens

**Synergize with  
checkpoint inhibitors**

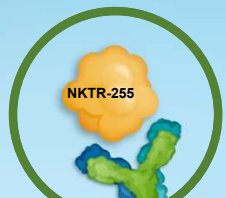
- Augment response to PD-1/PD-L1 checkpoint inhibitor therapies

# NKTR-255 Designed to Restore NK-Cell Numbers and Function After ADCC NK-Cell Depletion

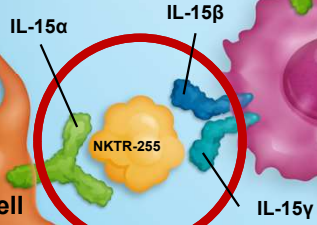
## NKTR-255 retains the full spectrum of IL-15 biology unlike other IL-15 agents in development

- Full length IL-15 molecule results in fully functional IL-15 downstream signaling
- Both cis and trans presentation signaling

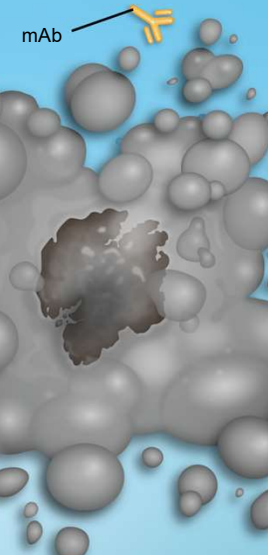
Cis-presentation



Trans-presentation



Enhances response to ADCC-mediated therapy



NK cell proliferation and activation

Tumor cell death

CD8+ cells Survival and expansion

## Key ongoing clinical studies for NKTR-255

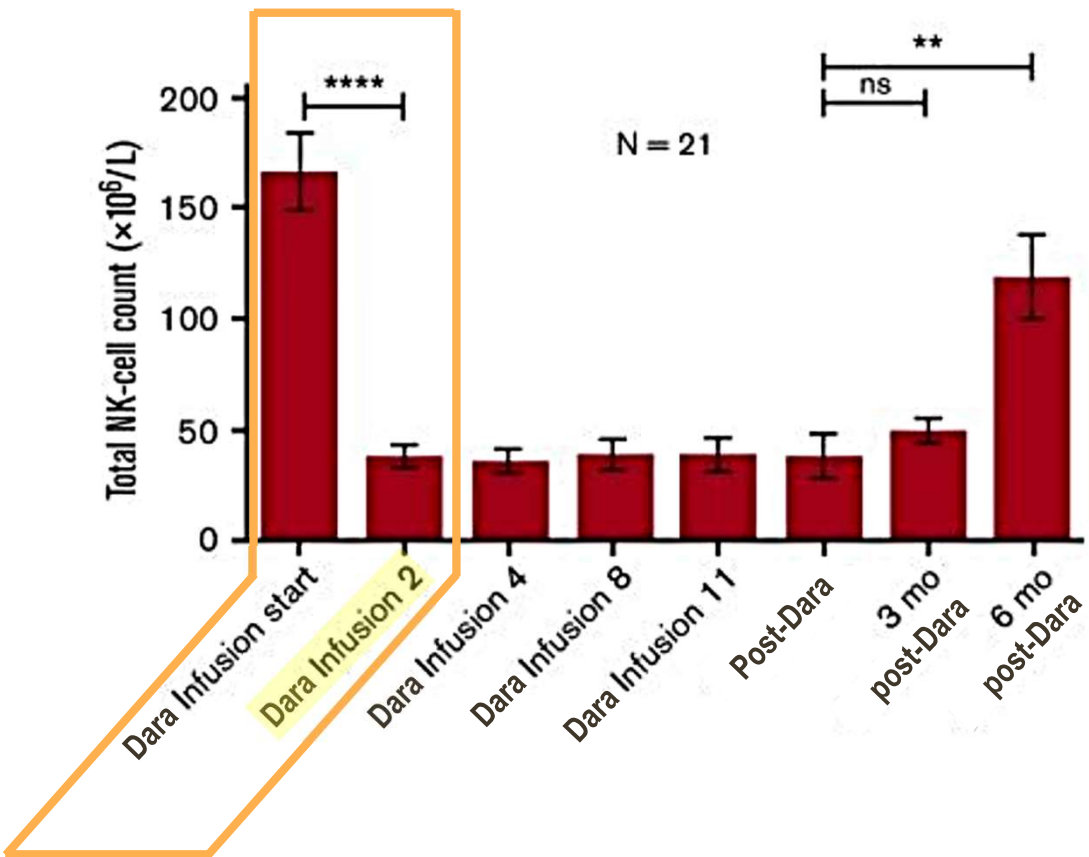
+ Daratumumab (Darzalex Faspro) in relapsed/refractory multiple myeloma patients

+ Cetuximab in Cetuximab refractory head and neck cancer patients

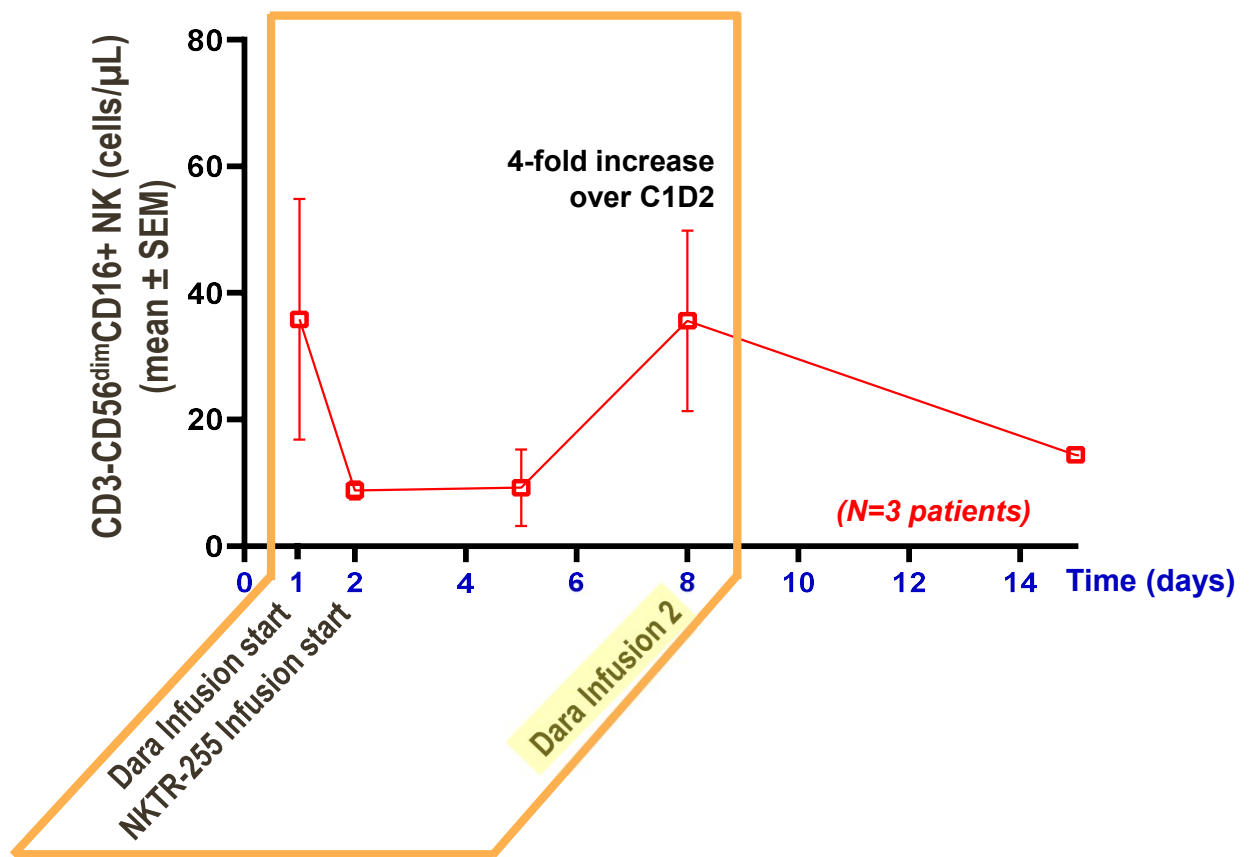


# NKTR-255 Rescues Daratumumab-Induced NK-Cell Depletion

Daratumumab monotherapy depletes NK cells<sup>1</sup>



NKTR-255 given after start of daratumumab restores NK-cell levels



Daratumumab administered weekly (Weeks 1-8), q2w (Weeks 9-24); q4w (Week 25+); NKTR-255 in Cycles 1-3 is administered on Day 2 of the cycle and on Day 1 Cycle 4+  
Source: <sup>1</sup>[Blood Adv.](#) 2017 Oct 24; 1(23): 2105–2114. Published online 2017 Oct 24. doi: [10.1182/bloodadvances.2017006866](#); <sup>2</sup>2022. “Safety, Tolerability, PK/PD, and Preliminary Efficacy of NKTR-255, a Novel IL-15 Receptor Agonist, in Patients with Relapsed/Refractory Hematologic Malignancies”, [Poster]. ASH, 12 January 2022, New Orleans, Louisiana.

# 3 Pillars of NKTR-255 Development Strategy

Augment ADCC  
therapies in highly  
refractory patient  
populations

- Enhance response to ADCC-mediated therapy through NK Cell restoration

Potentiate  
cellular therapies

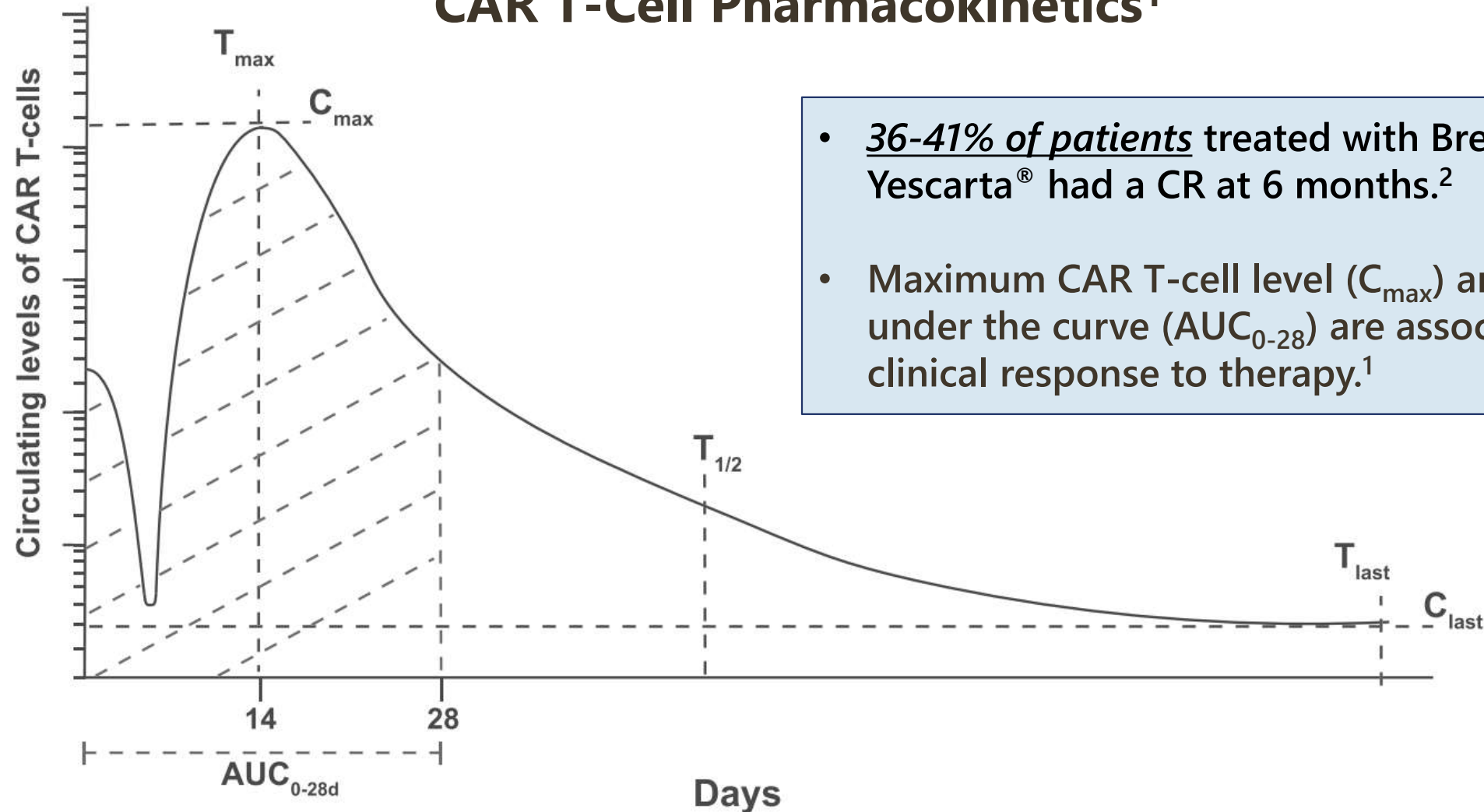
- Improve CAR T-cell persistency in cell therapy regimens

Synergize with  
checkpoint inhibitors

- Augment response to PD-1/PD-L1 checkpoint inhibitor therapies

# Opportunity to Increase CAR T-Cell C<sub>max</sub> and Extend Persistence in B-Cell Lymphomas for Better Patient Outcomes

## CAR T-Cell Pharmacokinetics<sup>1</sup>

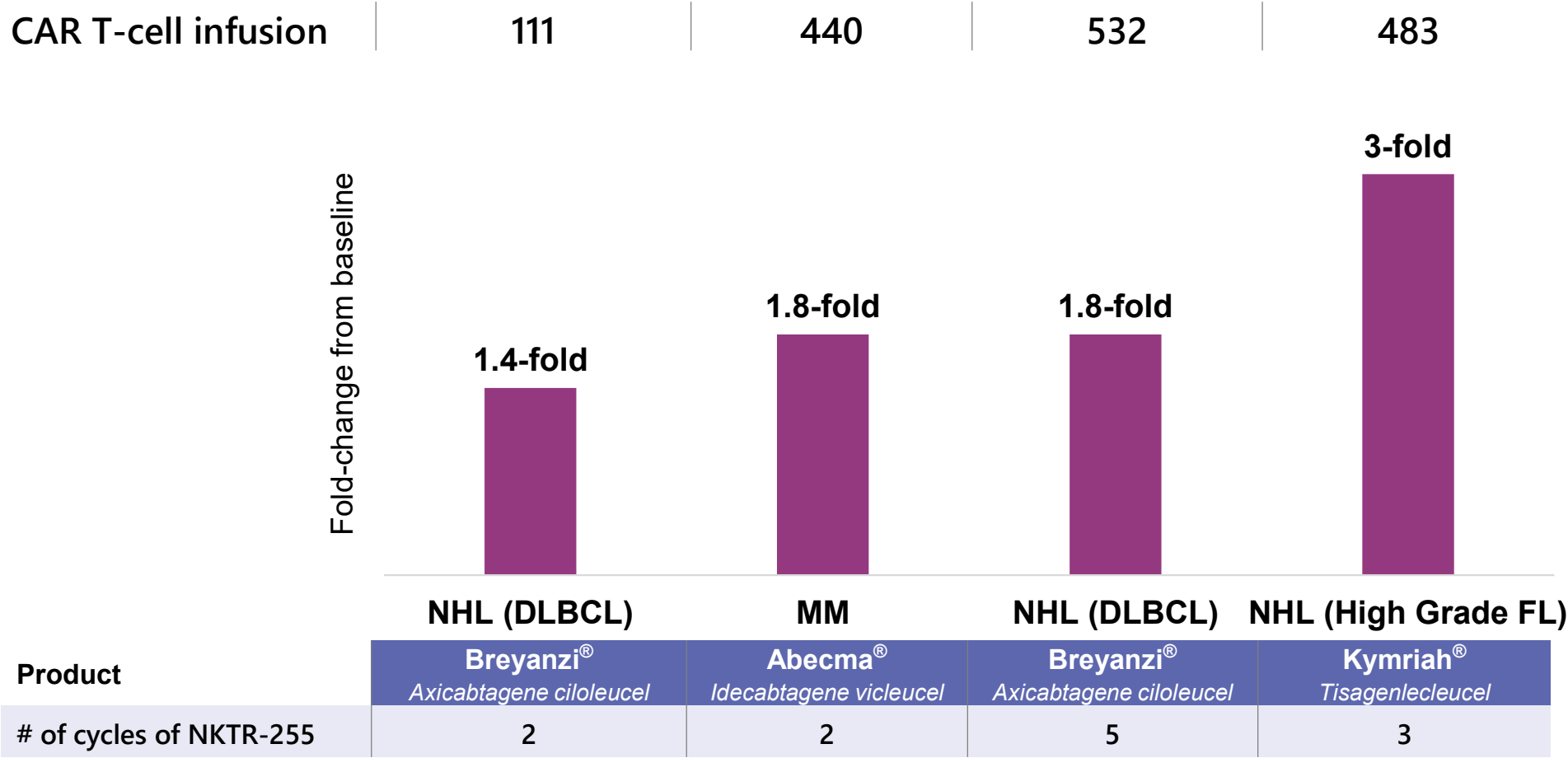


- 36-41% of patients treated with Breyanzi<sup>®</sup> and Yescarta<sup>®</sup> had a CR at 6 months.<sup>2</sup>
- Maximum CAR T-cell level ( $C_{max}$ ) and area under the curve ( $AUC_{0-28}$ ) are associated with clinical response to therapy.<sup>1</sup>

Breyanzi is a registered trademark of Juno Therapeutics, Inc.; Yescarta is a registered trademark of Gilead Sciences, Inc., or its related companies

Source: <sup>1</sup>Dasyam N, George P, Weinkove R. Chimeric antigen receptor T-cell therapies: Optimising the dose. Br J Clin Pharmacol. 2020 Sep;86(9):1678-1689. doi: 10.1111/bcp.14281. Epub 2020 Mar 24. PMID: 32175617; PMCID: PMC7444796.; <sup>2</sup>Chavez JC, Bachmeier C, Kharfan-Dabaja MA. CAR T-cell therapy for B-cell lymphomas: clinical trial results of available products. Ther Adv Hematol. 2019 Apr 15;10:2040620719841581. doi: 10.1177/2040620719841581. PMID: 31019670; PMCID: PMC6466472.

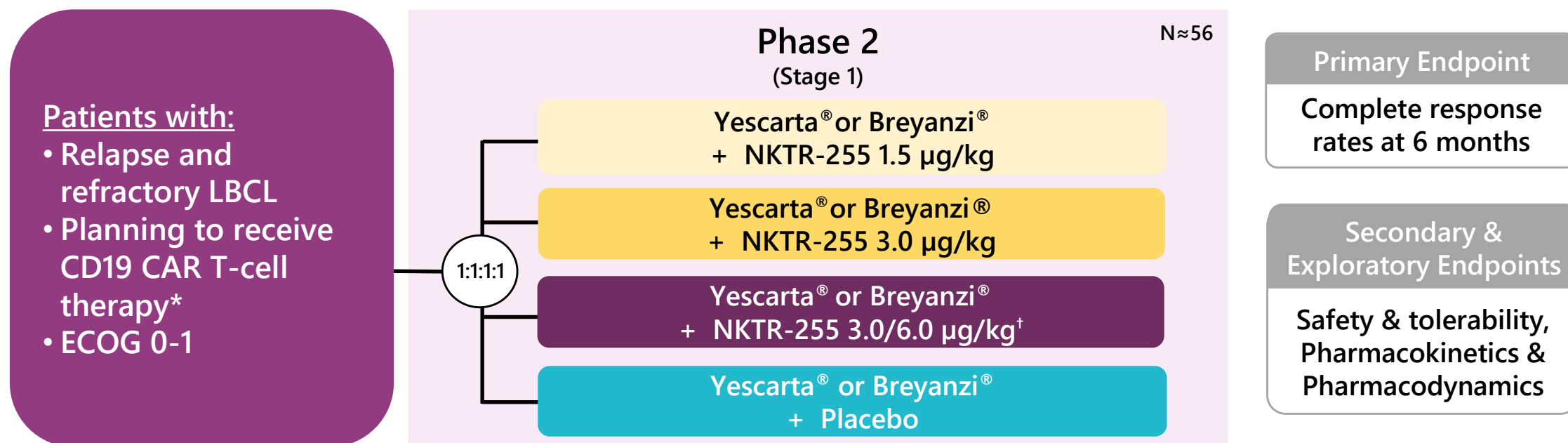
# NKTR-255 Monotherapy Increased CAR T-cell Levels in Patients Greater Than One Year Past CAR T-Cell Infusion



All patients had achieved a partial or complete response to prior CAR-T therapy. Pharmacodynamic data were analyzed for patients with measurable CAR T-cells at baseline; fold change was calculated as treatment with NKTR-255 over baseline (baseline=1); DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; MM, multiple myeloma; NHL, non-Hodgkin lymphoma.

Breyanzi is a registered trademark of Juno Therapeutics, Inc.; ABECMA is a registered trademark of Celgene Corporation, a Bristol-Myers Squibb Company.; Yescarta is a registered trademark of Gilead Sciences, Inc. , or its related companies. Source: Turtle, et al., Blood, Vol 138, Supplement 1, 2021, Page 2815.

# Phase 2/3 Study Initiated for NKTR-255 following Yescarta® or Breyanzi® in Large B-cell Lymphoma (LBCL)



Based upon results of the Phase 2 portion of the study, final design of the Phase 3 portion of the study will be determined, including NKTR-255 dose, sample size and endpoints

*Initial data expected in 2H 2024*

Clinicaltrials.gov Identifier: NCT05664217

\* Step-up dose regimen initiating with 3.0 µg/kg NKTR-255 in Cycle 1 and continuing in Cycle 2 and beyond with 6.0 µg/kg NKTR-255; Randomization will be stratified according to the cellular product that the patient receives (ie, axi-cel or liso-cel [or tisa-cel in Stage 2]) and baseline LDH, and should take place no more than 1 day prior to the first study drug administration.

**NEKTAR**

# 3 Pillars of NKTR-255 Development Strategy

Augment ADCC  
therapies in highly  
refractory patient  
populations

- Enhance response to ADCC-mediated therapy through NK Cell restoration

Potentiate  
cellular therapies

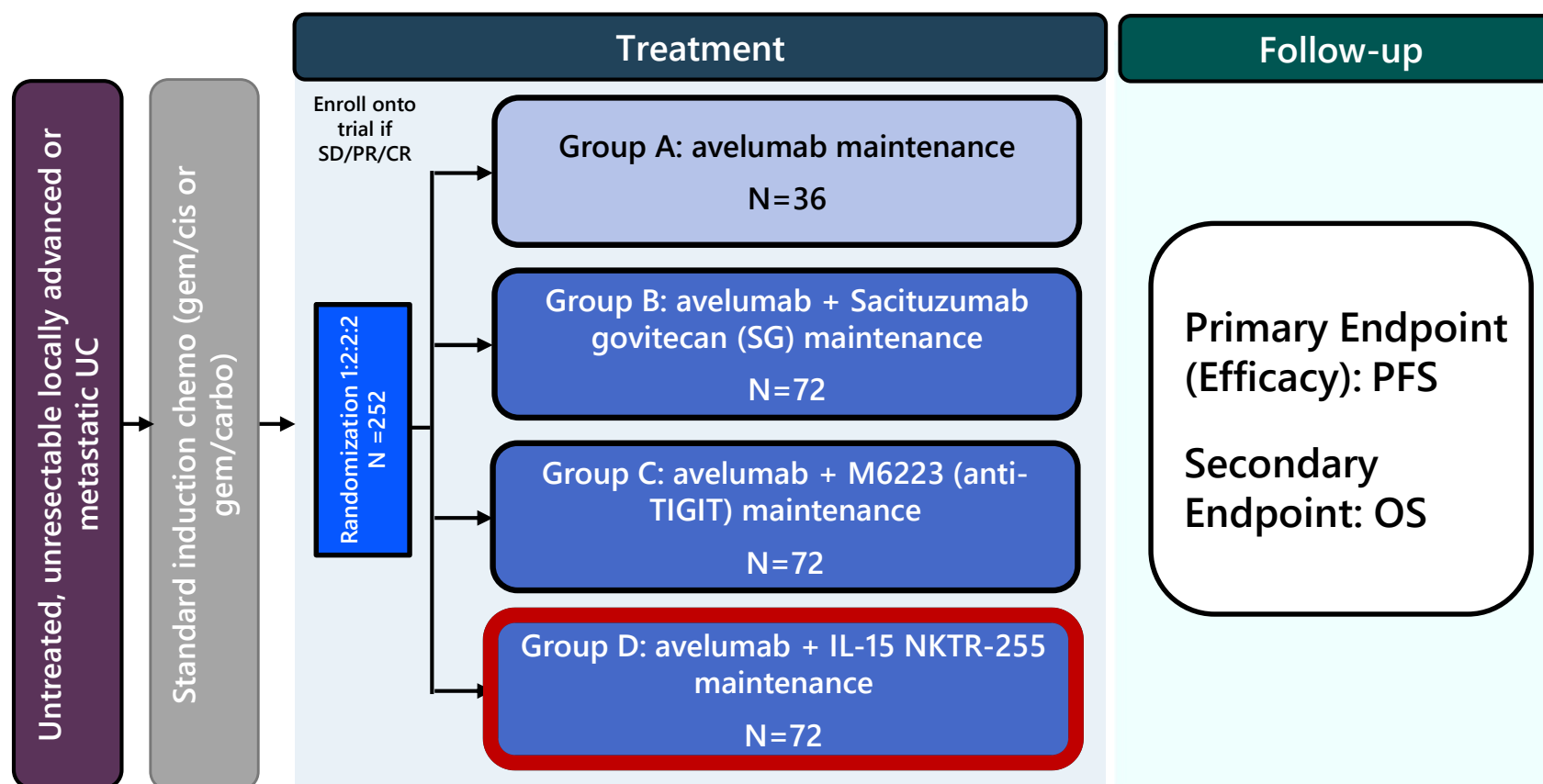
- Improve CAR T-cell persistency in cell therapy regimens

Synergize with  
checkpoint inhibitors

- Augment response to PD-1/PD-L1 checkpoint inhibitor therapies



# NKTR-255: JAVELIN Bladder Medley Study Being Conducted by Merck KGaA in Combination with Avelumab






- Avelumab has both checkpoint inhibitor and ADCC components to its mechanism
- NK cells shown to contribute to avelumab outcomes in Javelin Bladder 100 Study
- Tolerability of combo expected to be good and allow for long duration of treatment (> 10 months)
- Expansion in the future into earlier stages of UC possible

*Topline data expected in 2H 2024*

Nektar R&D Pipeline

Immuno-oncology

Program	Indication	Study	Preclinical	Phase 1	Phase 2	Phase 3	Partner
NKTR-255	Bladder Cancer	NKTR-255 + BAVENCIO®	Phase 2				
	DLBCL	NKTR-255 + Yescarta®/Breyanzi®	Phase 2/3				
	R/R NHL or Multiple Myeloma	NKTR-255 + RITUXAN® or DARZALEX FasPRO®	Phase 1/2				
	Head & Neck and Colorectal	NKTR-255 + ERBITUX®	Phase 1/2				
	[IST] NSCLC	NKTR-255 + IMFINZI®	Phase 1				
	[IST] NHL / DLBCL	NKTR-255 + Breyanzi®	Phase 1				
	[IST] ALL	NKTR-255 + CD19/22 CAR T-cell	Phase 1				
NKTR-288	Solid Tumors	NKTR-288 (interferon gamma)	Preclinical				

Immunology

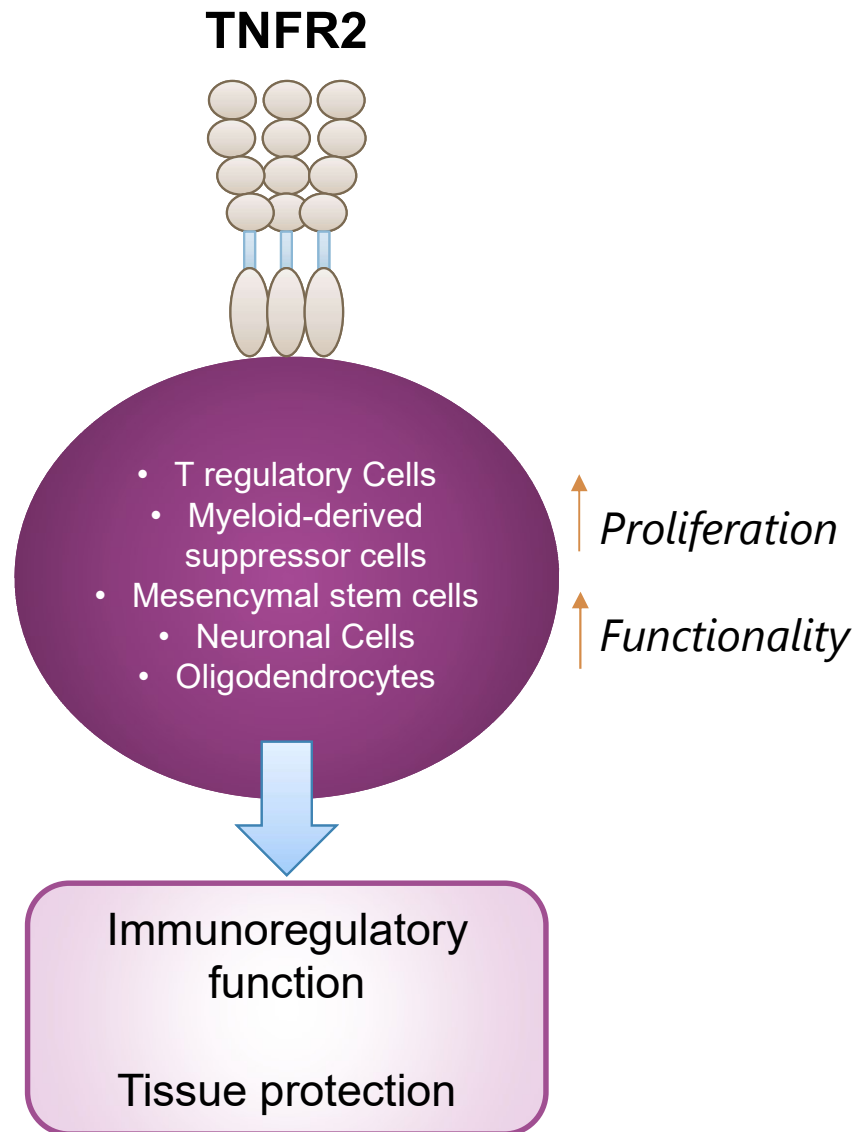
Program	Indication	Study	Preclinical	Phase 1	Phase 2	Phase 3	Partner
REZPEG (LY3471851 / NKTR-358)	Systemic Lupus Erythematosus	REZPEG	Phase 2				Lilly Lilly Lilly
	Atopic Dermatitis	REZPEG	Phase 2 Planned				
	(Undisclosed Indication)	REZPEG	Phase 2 Planned				
TNFR2 agonist antibody	Multiple Sclerosis & Other Autoimmune Indications	Preclinical	Preclinical				BioLogicDesign
Cytokine candidate	Liver & Kidney Diseases, Cirrhosis & Other Indications	Preclinical	Preclinical				

Anti-viral/anti-bacterial

Program	Indication	Study	Preclinical	Phase 1	Phase 2	Phase 3	Partner
NKTR-288	Anti-viral/anti-bacterial	NKTR-288 (interferon gamma)	Preclinical				

Bavencio is a registered trademark of Merck KGaA; Yescarta is a registered trademark of Gilead Sciences, Inc. , or its related companies; Breyanzi is a registered trademark of Juno Therapeutics, Inc.; Rituxan is a registered trademark of Biogen; Darzalex Faspro is a registered trademark of Janssen Biotech, Inc.; Erbitux is a registered trademark of ImClone LLC., a subsidiary of Eli Lilly & Co.; Imfinzi IMFINZI is a registered trademark of AstraZeneca AB; [IST]: Investigator Sponsored Trial

# TNFR2 Agonist Antibody Program: Targeting TNF Receptor 2 (TNFR2) For The Treatment of Auto-immune Diseases



- TNFR2 signaling drives immunoregulatory function and could provide direct protective effect for tissue cells
- Unique Nektar antibody candidates show selective T regulatory cell binding and signaling profiles enabling it to be developed for the treatment of auto-immune diseases
- Program targets multiple MOAs including suppression of inflammation, regrowth of myelin after demyelination (MS) and promotion of immune resolution
- Targeting IND readiness for lead candidate in 2023

# Upcoming 18-month Milestones: Ended 2022 With \$500 Million in Cash & Investments

## REZPEG

- 1H 2023: Topline results from Phase 2 study in patients with systemic lupus erythematosus (n=280)
- 1H 2023: Initiation of Phase 2 study in patients with Atopic Dermatitis (n=340)
- 1H 2023: Unveiling of the new undisclosed indication for REZPEG

## NKTR-255

- 1H 2023: Results from first patients in Stanford IST of NKTR-255 + CD-19/CD-22 directed CAR T-cell therapy in patients with r/r B-ALL
- 2H 2023: Results from first patients in Fred Hutch IST of NKTR-255 + Breyanzi® in r/r LBCL
- 2H 2023: Results from expansion stage at RP2D of Phase 1/2 study + Darzalex Faspro® in prior anti-CD38 treated multiple myeloma patients
- 2H 2023: Results from expansion stage at RP2D of Phase 1/2 study + cetuximab in cetuximab-refractory head and neck cancer patients

## TNFR2 Program

- 1H 2024: Submit IND filing for first clinical study