

A man and a woman are smiling together in a room. The man is wearing a dark suit and the woman is wearing a dark dress. The background is a warm, reddish-orange color with white molecular graphics scattered throughout. The text "2021 INVESTMENT COMMUNITY MEETING" is overlaid in the center in a bold, white, sans-serif font.

**2021 INVESTMENT
COMMUNITY MEETING**

Lilly

SAFE HARBOR PROVISION



The presentations for Eli Lilly's investment community meeting contain forward-looking statements that are based on management's current expectations, but actual results may differ materially due to various factors. The company's results may be affected by factors including, but not limited to, the risks and uncertainties in pharmaceutical research and development; competitive developments; regulatory actions; the extent and duration of the effects of the COVID-19 pandemic; litigation and investigations; business development transactions; economic conditions; and changes in laws and regulations, including health care reform.

For additional information about the factors that affect the company's business, please see the company's latest Forms 10-K, 10-Q, and any 8-Ks filed with the Securities and Exchange Commission. In addition, certain financial information in this presentation is presented on a non-GAAP basis. Investors should refer to the reconciliations included in these presentations and should consider the company's non-GAAP measures in addition to, not as a substitute for or superior to, measures prepared in accordance with GAAP.

**The company undertakes no duty to update forward-looking statements
except as required by applicable law**



**DAN SKOVRONSKY,
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Chief Scientific and Medical Officer,
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ANDREW ADAMS, PH.D.

Vice President,
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2021 INVESTMENT COMMUNITY MEETING

Lilly

**AFTER 145 YEARS,
OUR PURPOSE
REMAINS AS
CRITICAL AS EVER**



**We unite caring with discovery to create medicines that
make life better for people around the world.**

LILLY'S VIEW: THREE EMERGING TRENDS IN BIOPHARMACEUTICAL INNOVATION

R&D INVESTMENT UNDERLIES LILLY'S CONVICTION ON OPPORTUNITY IN THESE AREAS



1. Obesity is a treatable disease; and by reversing it we can dramatically improve population health outcomes
2. Age-related neurodegeneration will become preventable
3. Medicines comprised of nucleic acids will become a major component of disease treatments

Lilly is investing heavily behind each of these three trends, while also growing a diversified portfolio that expands our leadership in targeted oncology and novel immunology opportunities

OUR TRANSFORMATION JOURNEY



Dec 2018 R&D update focus:

What we've accomplished:

What's next:



Transforming our drug discovery engine

- Created a genetic medicine platform anchored in siRNA and gene therapy
- Refocused molecule making technologies to address hard-to-drug targets with potentially best-in-class therapeutics
- Identified novel targets across therapeutic areas



Improving our development speed and success rates

- Achieved industry-leading speeds across preclinical and clinical development
- Significantly increased clinical success rates while still working in high-risk / high-reward areas



Improving productivity (20 medicines in 10 years)

- 16 new medicines delivered in 8 years, with good visibility to 5 more potential launches
- Many have outsized potential to help patients, for example 7 of these molecules have ~\$3B or more in peak sales potential*

Lilly has created an **industry-leading discovery and development** engine that has yielded a number of high-value medicines

Now we take on the dual challenge of **maximizing our existing game-changing molecules** while also **creating new ones**



Reaching more patients through significant NILEX investment in priority medicines



Sustaining and enhancing R&D productivity, with improvements in speed, success rates, and value creation



Enriching the next generation of innovation through platform investments

*Based on Wall Street peak sales consensus

STRENGTHENING EACH THERAPEUTIC AREA



2018: Where We Were

2021: What We've Done Since

	2018: Where We Were	2021: What We've Done Since
ONCOLOGY	Actively seeking the next wave of IO, including a bet on IL10; believed Verzenio would be differentiated but limited clinical evidence at the time; no small molecule pipeline	<ul style="list-style-type: none">✓ Acquired Loxo Oncology and delivered Retevmo✓ Built out a small molecule portfolio focused on high conviction assets✓ Maximized Verzenio reach
IMMUNO	Recent launches of Taltz and Olumiant; seeking to translate discovery/pre-clinical work into clinical portfolio	<ul style="list-style-type: none">✓ Expanded indications for Taltz and Olumiant✓ Acquired lebrikizumab, mirikizumab positive Phase 3 data✓ Built an early-stage clinical pipeline with promising proof of concept read-outs
NEURO/PAIN	Despite setbacks in Alzheimer's disease, we saw donanemab as a differentiated molecule and designed a thoughtful Phase 2 study heavily leveraging diagnostics with the goal of changing the trajectory of AD	<ul style="list-style-type: none">✓ Generated positive registration data for donanemab✓ Pursued next-gen Alzheimer's medicines✓ Created an early-phase pain pipeline
DIABETES	Aspirations to deliver innovation in incretins and insulins; strong early efficacy data on tirzepatide motivated us to take big bets; competitiveness of Trulicity was questioned	<ul style="list-style-type: none">✓ Reinforced Trulicity with strong efficacy data✓ Progressed innovation across insulins & incretins✓ Generated positive Phase 3 data for tirzepatide✓ Created focus around obesity and potential in CV disease

ON TRACK TO DELIVER 20 NEW MEDICINES IN 10 YEARS



16 New Medicines Delivered in 8 Years

2014	2015	2016	2017	2018	2019	2020	2021

Potential Launches

2022 - 2023

~\$3B+ wall street consensus peak sales
 * sales from EUAs

INVESTED TO MAXIMIZE TRULICITY

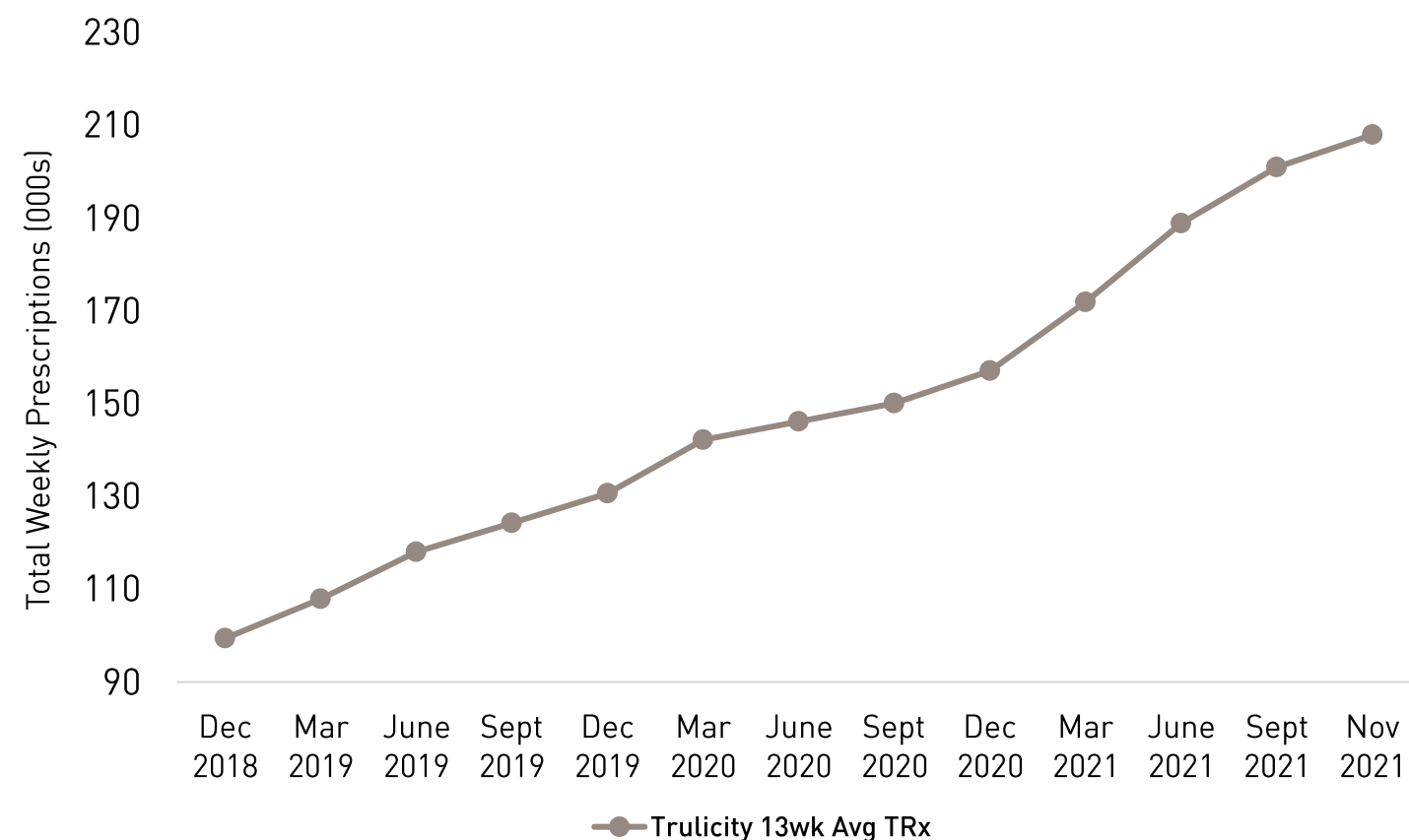


PROGRESS SINCE 2018

- CVOT: Novel REWIND design demonstrated CVOT benefit in broadest patient population in GLP-1 class
- ADA and EASD guidelines updated to include:
 - GLP-1s recommended as 1st injectable medication
 - GLP-1 or SGLT2 with proven CV benefit recommended for patients with CVD
- Higher doses of Trulicity were submitted in <2 years from FRD and now represent over 20% of weekly prescriptions
- Continued market leadership with ~48% TRx SOM of fast-growing injectable GLP-1 class (>25%)

INCREASED GROWTH

Trulicity U.S. TRx have more than doubled since December 2018



CVOT = cardiovascular outcomes trial; ADA = American Diabetes Association; EASD = European Association for the Study of Diabetes; FRD = first registration dose; TRx = total prescriptions; SOM = share of market
Data source: U.S. IQVIA NPA as of week ending 11.19.2021

IQVIA NPA Weekly as of week ending 11.16.2018

INVESTED TO MAXIMIZE JARDIANCE

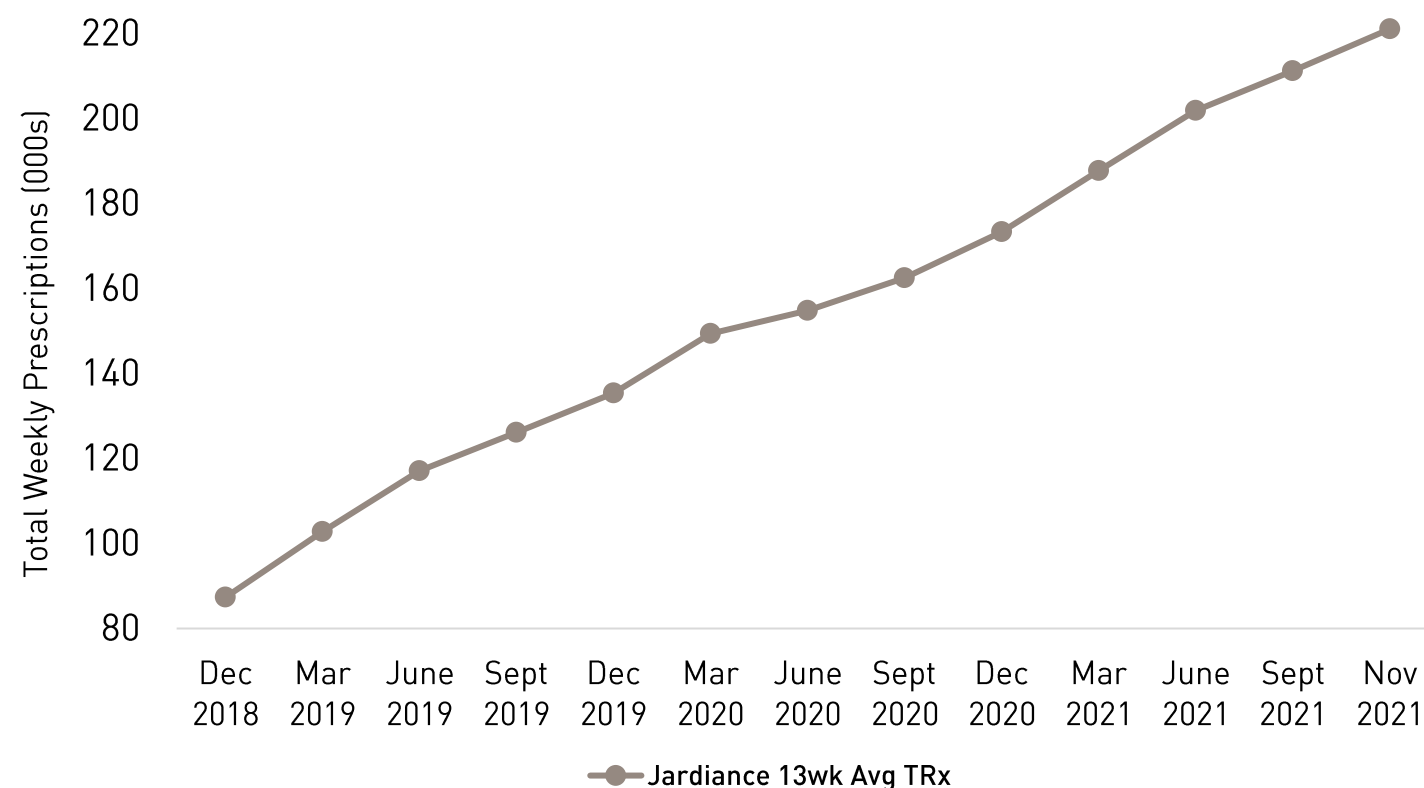


PROGRESS SINCE 2018

- Following EMPA-REG Outcome, the first positive CVOT trial in diabetes, we invested heavily to maximize reach of Jardiance with the intent to fundamentally change how customers think about and treat CV risk in diabetes
- HFrEF: Approved in U.S., Europe, and Japan in 2021
- HFpEF: Jardiance first therapy to show statistically significant improvement in adults with HFpEF, submitted in U.S., Europe and Japan in 2021
- Since Dec. 2018, Jardiance has driven class expansion from ~10% to ~25% in annual TRx growth and Jardiance TRx SOM has increased from ~40% to ~60%

INCREASED GROWTH

Jardiance U.S. TRx have more than doubled since December 2018



CVOT = cardiovascular outcomes trial; CV = cardiovascular; HFrEF = heart failure with reduced ejection fraction; HFpEF; heart failure with preserved ejection fraction TRx = total prescriptions; SOM = share of market
Data source: U.S. IQVIA NPA as of week ending 11.19.2021

INVESTED TO MAXIMIZE TALTZ

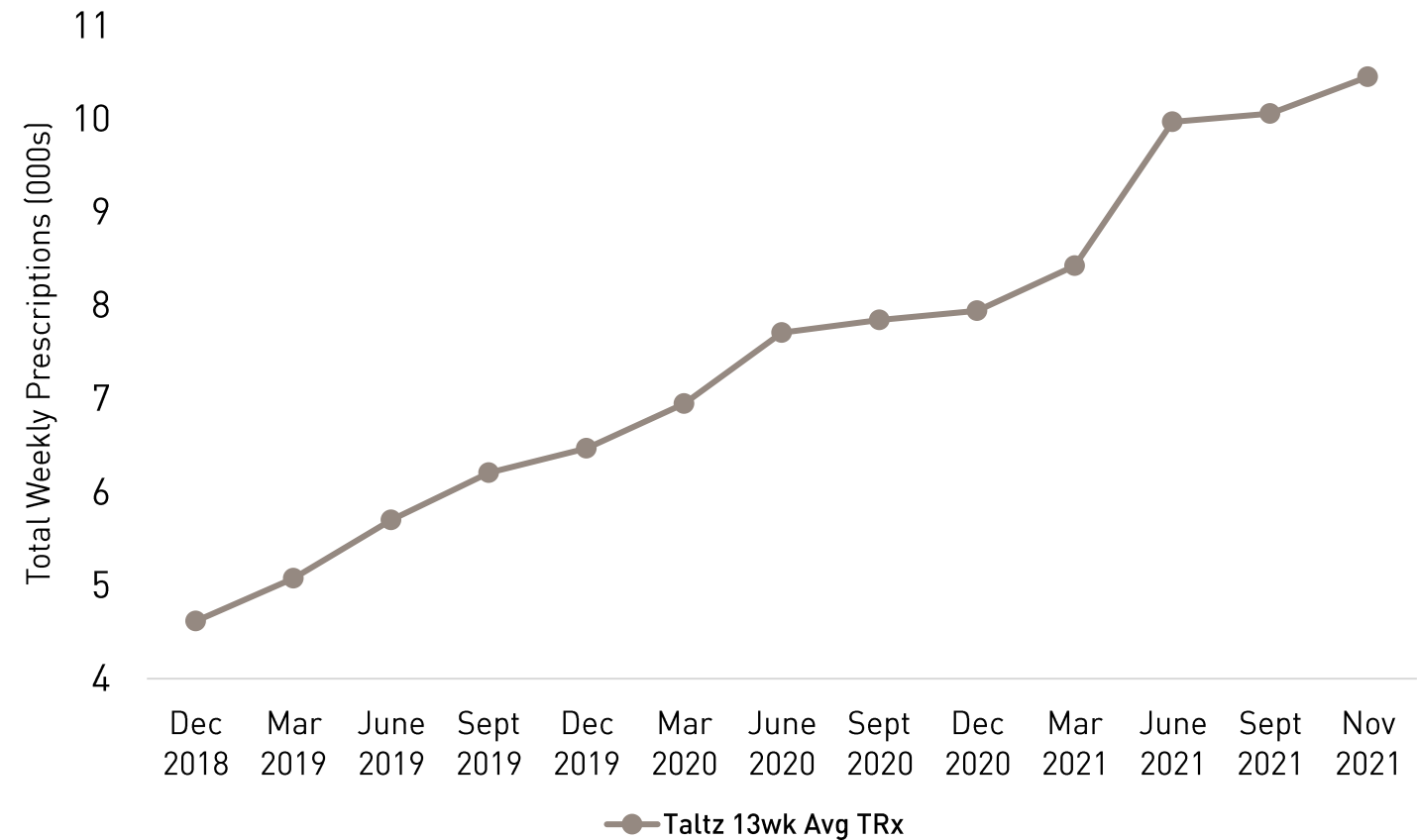


PROGRESS SINCE 2018

- Superiority vs. competitors established in multiple head-to-head studies
- Approvals in radiographic-axSpA and non-radiographic axSpA to expand reach in rheumatology
- With strong efficacy data, we have improved access for patients with TRx more than doubling since Dec 2018
- Continued opportunity for growth, as anti-TNF share remains at ~40% of dermatology and ~70% of rheumatology total prescriptions

INCREASED GROWTH

Taltz U.S. TRx have more than doubled since December 2018



AxSpa = axial spondyloarthritis; TRx = total prescriptions; TNF = tumor necrosis factor
Data source: U.S. IQVIA NPA as of week ending 11.19.2021

CONTINUED INVESTMENT TO MAXIMIZE VERZENIO

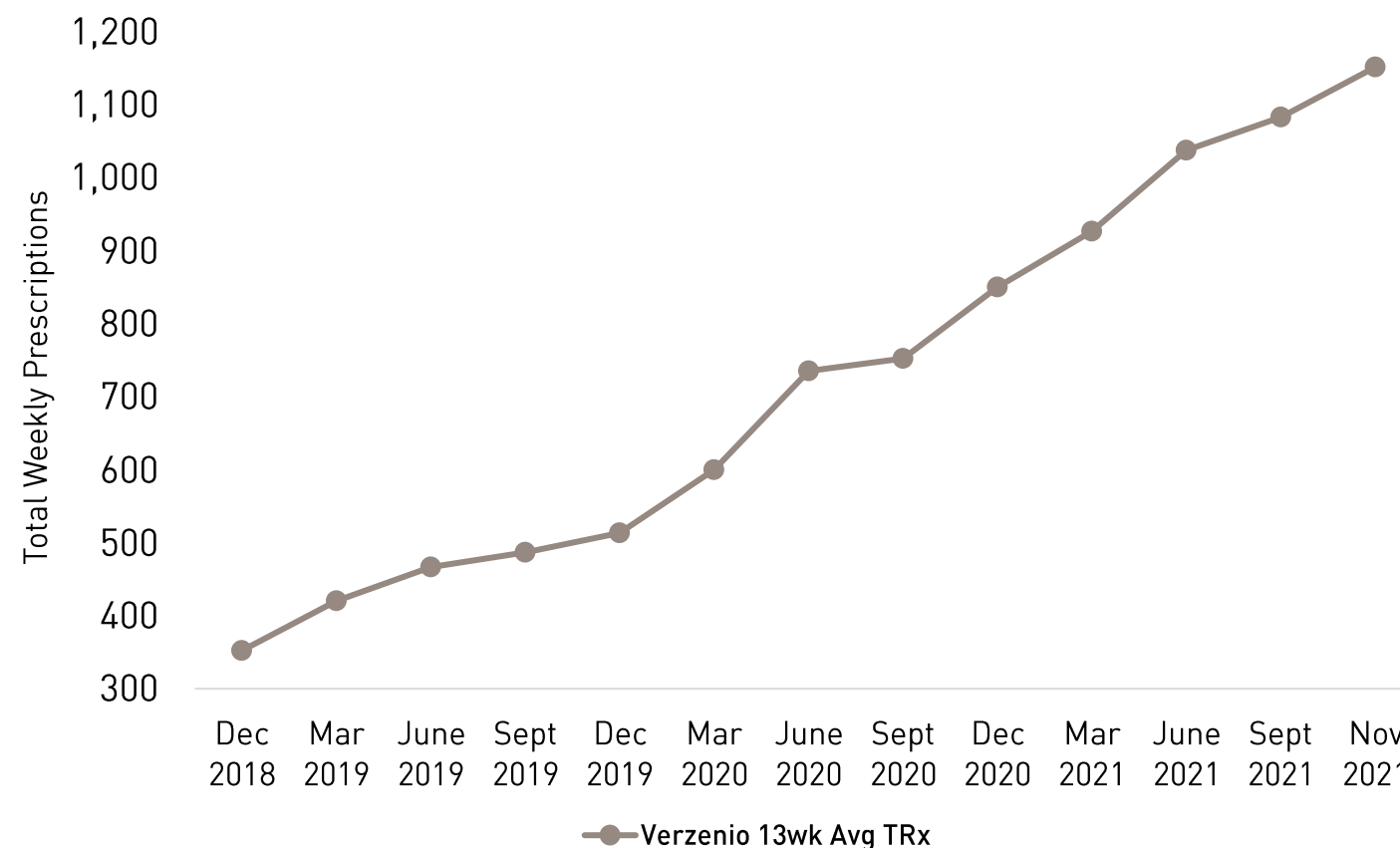


PROGRESS SINCE 2018

- Believed Verzenio was a differentiated CDK 4/6 and we invested in collecting data to prove it
- Monarch2: positive, significant OS data and label update in metastatic breast cancer
- High-risk early breast cancer:
 - Only CDK 4/6 with positive Phase 3 data in early breast cancer to date (monarchE)
 - Approval in the U.S. in high Ki-67 subpopulation
 - Expected approval in Japan before the end of 2021 and in Europe in the first half of 2022
 - Approved label increases U.S. addressable market by 8-10k patients
- Prostate: CYCLONE-2 moved to Phase 3 portion of trial based on Phase 2 interim analysis; CYCLONE-2 U.S. addressable market ~7-14k patients

INCREASED GROWTH

Verzenio U.S. TRx have more than tripled since December 2018



OS = overall survival; TRx = total prescriptions; NBRx = new to brand prescriptions; SOM = share of market
 Data source: IQVIA NPA 13-week average SOM data as of week ending 11.19.21 Note: Q2 2020 IQVIA data was impacted by an addition of data for Verzenio

TIRZEPATIDE TOLERABILITY

TOLERABILITY PROFILE CONSISTENT WITH WELL-ESTABLISHED GLP-1 RECEPTOR AGONIST CLASS



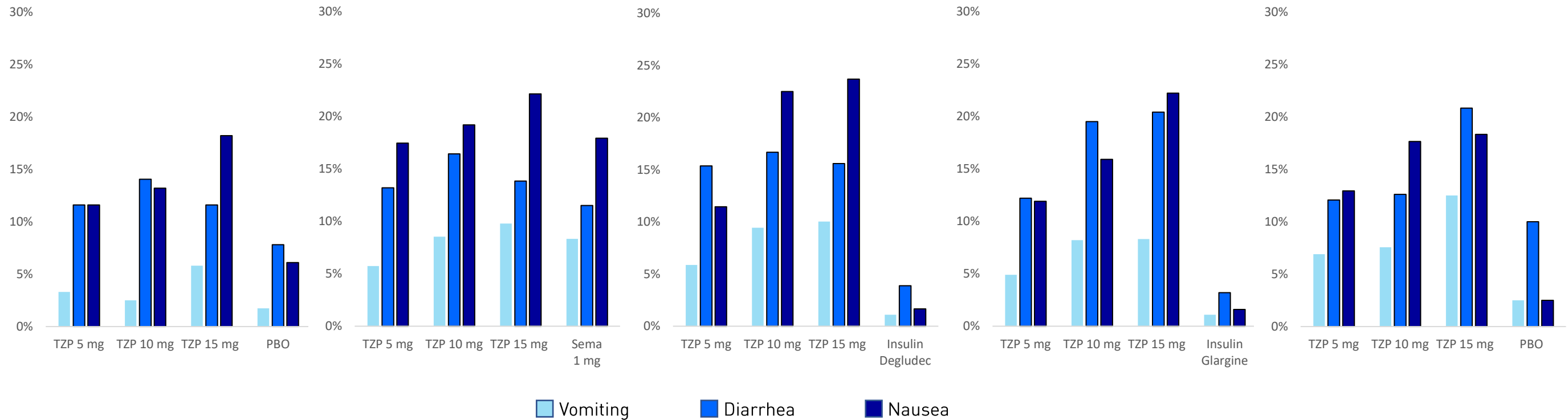
SURPASS-1
vs. placebo
(40 weeks)

SURPASS-2
vs. semaglutide 1mg
(40 weeks)

SURPASS-3
vs. insulin degludec
(52 weeks)

SURPASS-4
vs. insulin glargine
(52 weeks)

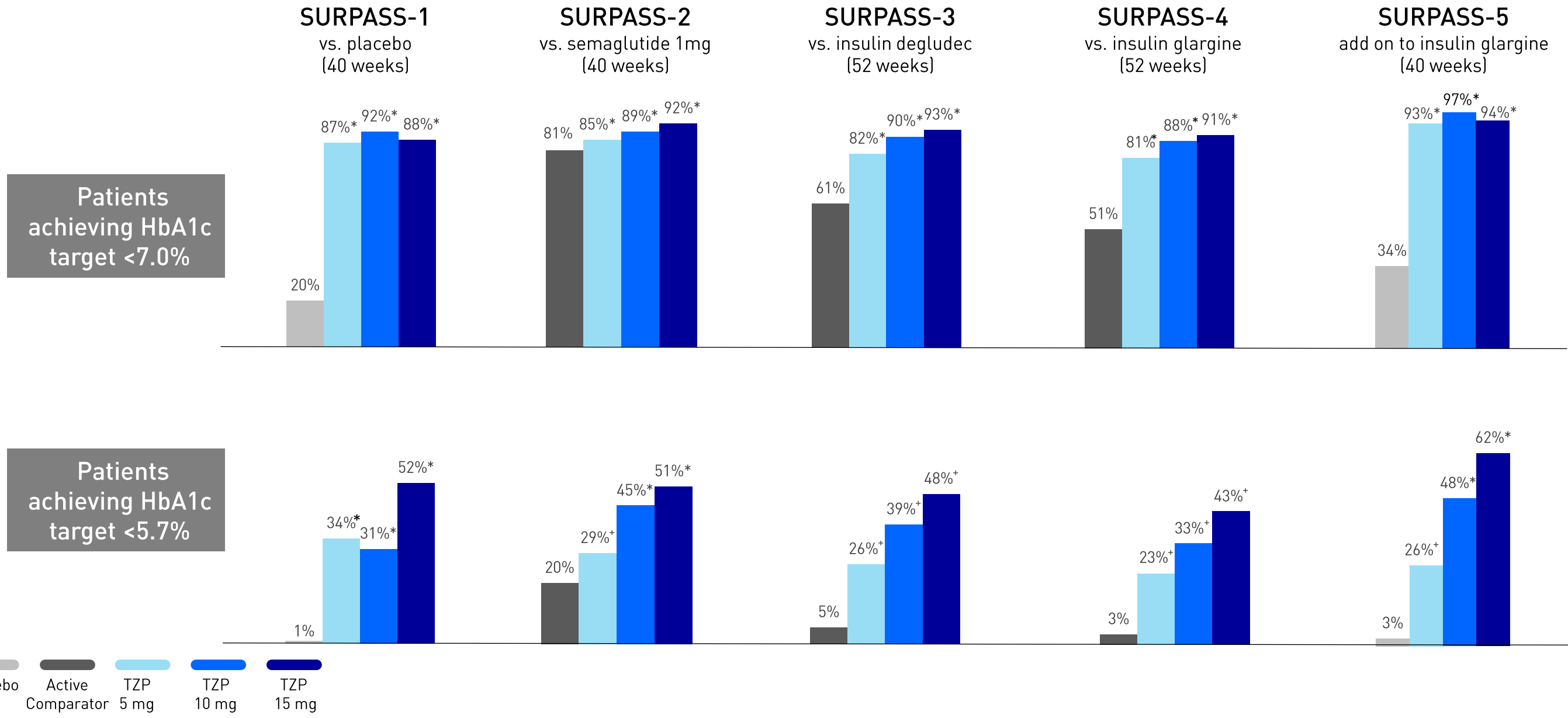
SURPASS-5
add on to insulin glargine
(40 weeks)



Most cases of nausea, vomiting and diarrhea were mild-to-moderate and most frequently occurred during the dose-escalation period across all doses of tirzepatide

TIRZEPATIDE T2D SURPASSED EXPECTATIONS

HELPED UP TO 97% AND 62% OF PATIENTS REACH HBA1C BELOW 7.0% AND 5.7%, RESPECTIVELY

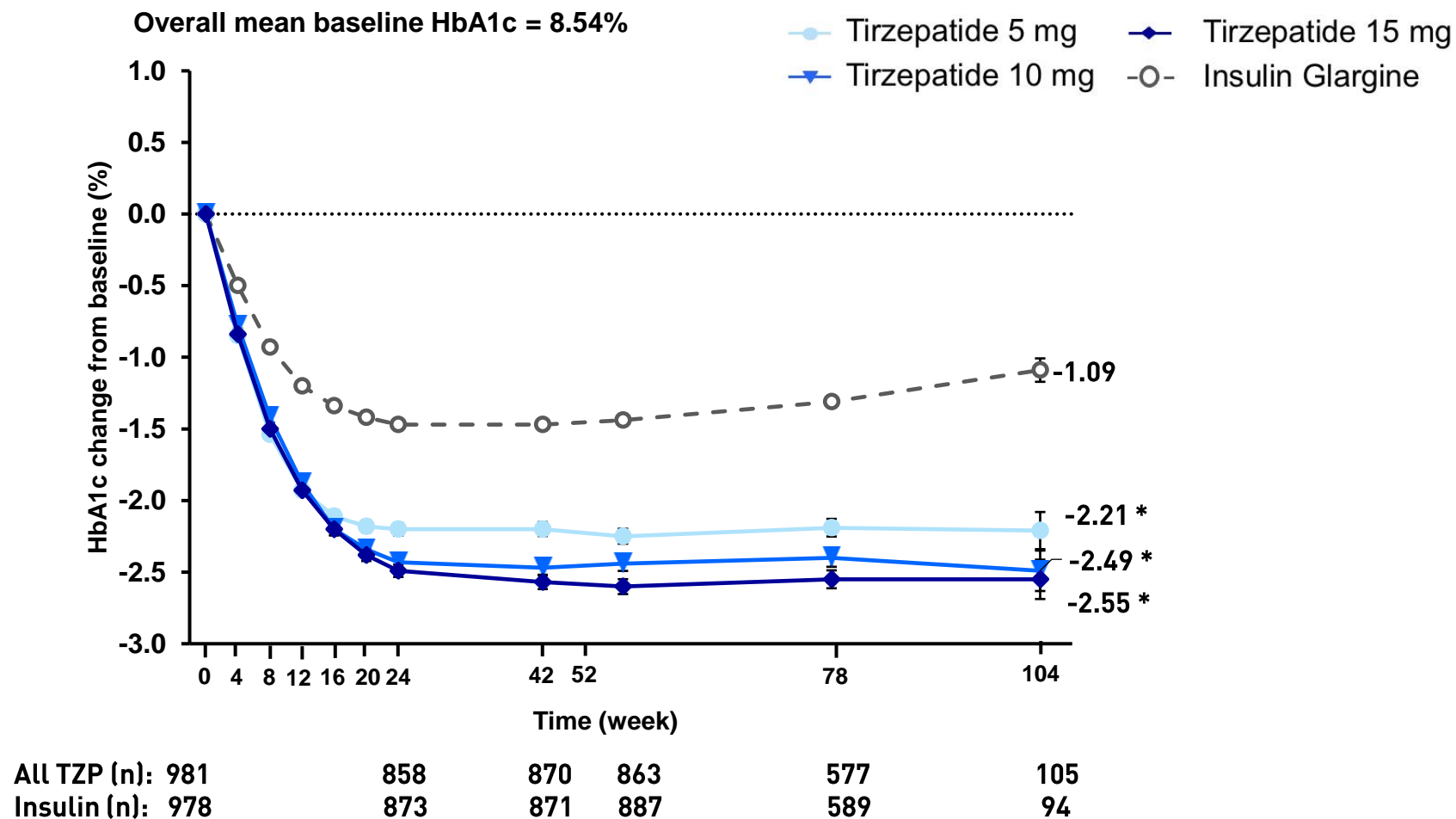


*denotes statistical significance to comparator; + denotes not controlled for type 1 error

TZP = tirzepatide; Results presented using the efficacy estimand, which represents efficacy prior to discontinuation of study drug or initiating rescue therapy for persistent severe hyperglycemia

TIRZEPATIDE DURABILITY

SURPASS-4 CHANGE FROM BASELINE IN HBA1C TO END OF STUDY

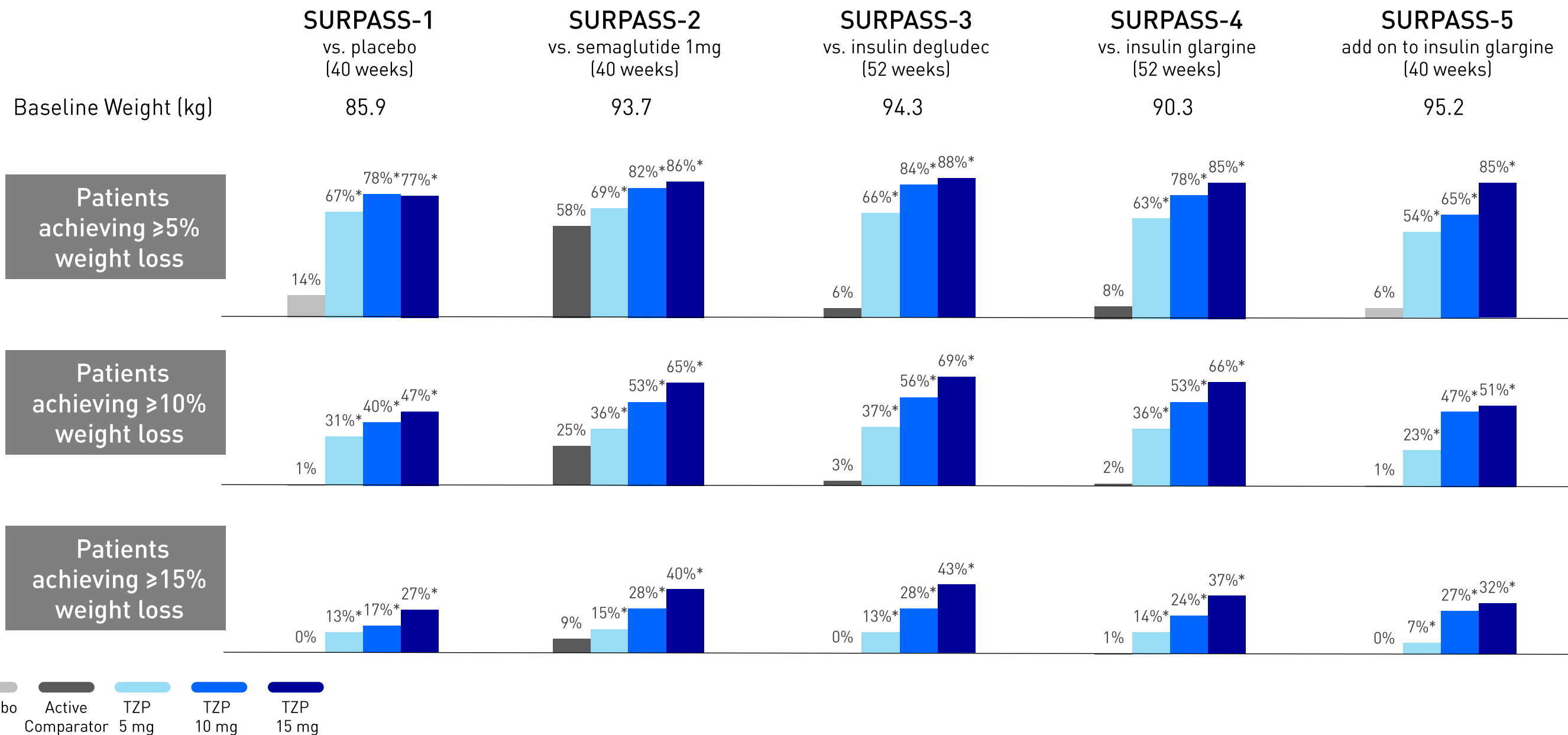


HbA1c reduction plateaued by ~24 weeks and was maintained up to 104 weeks for all three tirzepatide doses

MMRM analysis; Modified intent-to-treat population (efficacy analysis set); Data presented are LS means ± standard errors; tirzepatide vs. insulin glargine at 104 weeks: *p<0.001.

TIRZEPATIDE WEIGHT LOSS

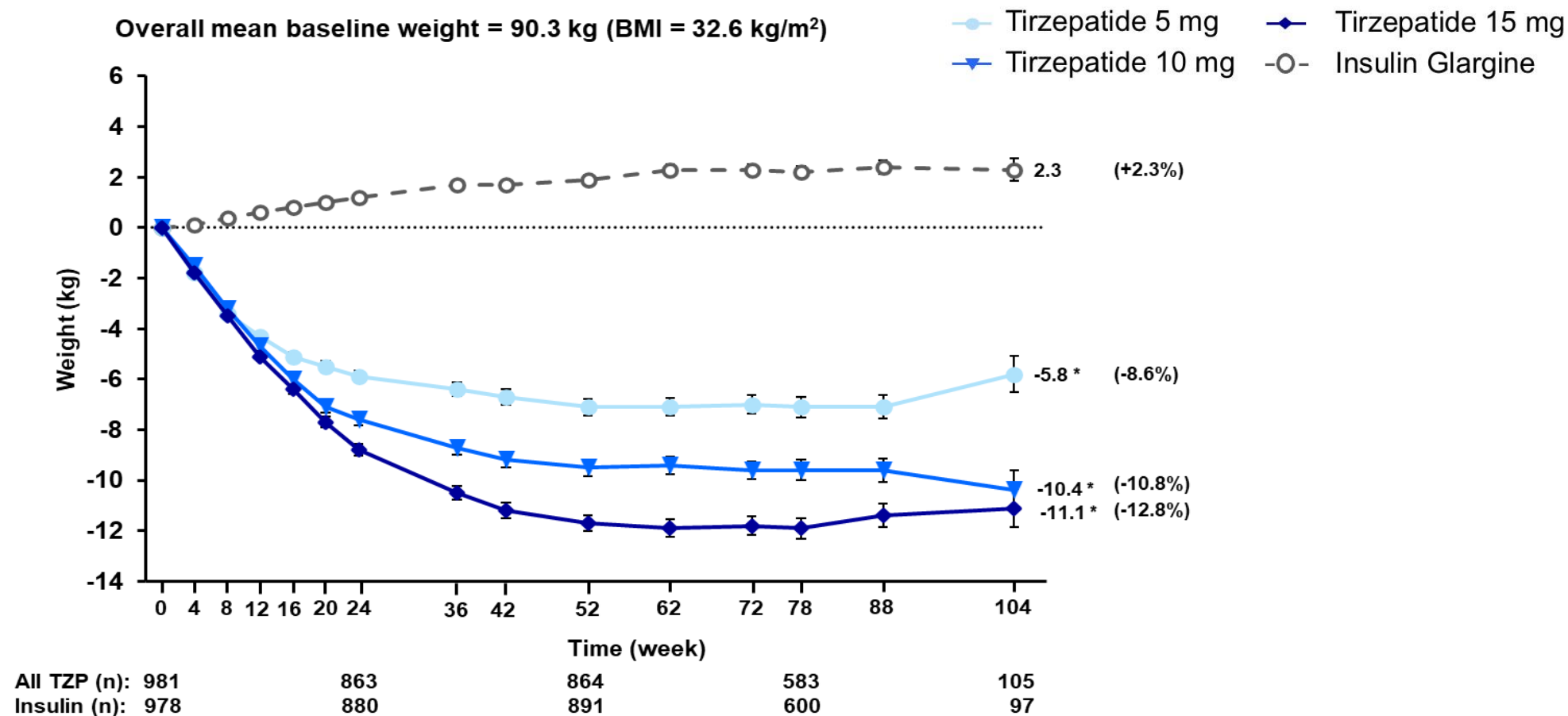
PROVIDED STATISTICALLY SIGNIFICANT WEIGHT REDUCTION VERSUS ALL COMPARATORS STUDIED



*denotes statistical significance to comparator; All TZP arms were not controlled for type 1 error
TZP = tirzepatide; Results presented using the efficacy estimand, which represents efficacy prior to discontinuation of study drug or initiating rescue therapy for persistent severe hyperglycemia

TIRZEPATIDE DURABILITY

SURPASS-4 CHANGE FROM BASELINE IN BODY WEIGHT TO END OF STUDY



Weight loss plateaued at ~52 weeks and was maintained up to 104 weeks; ~15% weight difference at 104 weeks between tirzepatide 15mg and insulin glargine

MMRM analysis; Modified intent-to-treat population (efficacy analysis set); Data presented are LS means ± standard errors; tirzepatide vs. insulin glargine at 104 weeks: *p<0.001. BMI = body mass index

CONTINUED INVESTMENT TO MAXIMIZE TIRZEPATIDE

SIGNIFICANT INVESTMENT BEYOND T2D TO EXPAND REACH



Investigating the potential for earlier and sustained glycemic control and weight reduction in T2D and clinically relevant weight loss



Generating data in the SURMOUNT program with the goal of making tirzepatide the standard of care for obesity and providing evidence that lower body weight improves outcomes



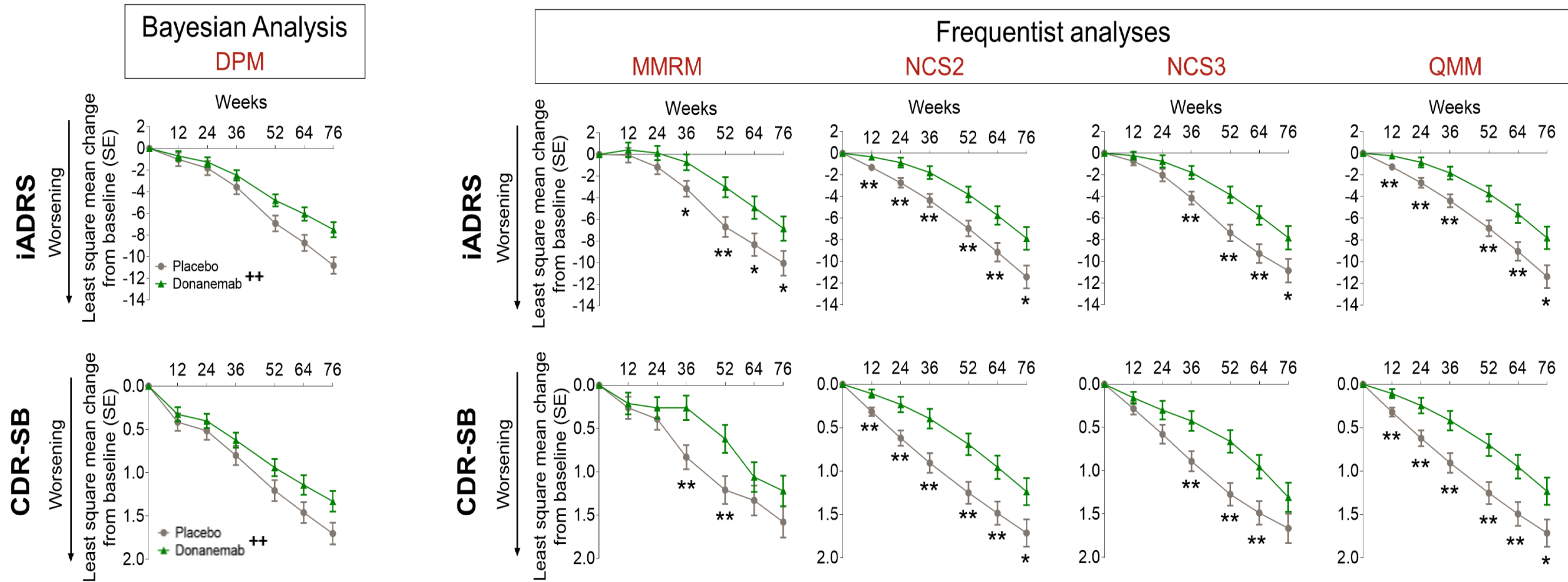
Conducting clinical trials in NASH, HFpEF, obstructive sleep apnea, and renal impairment

DONANEMAB BREAKTHROUGH EFFICACY DATA

CONSISTENCY OF CLINICAL BENEFIT ACROSS STATISTICAL METHODS



Consistency of TRAILBLAZER-ALZ Results Across Statistical Methods



DPM = Disease Progression Model; MMRM = Mixed Model for Repeated Measure; NCS2 = Natural Cubic Spline with 2 degrees of freedom; NCS3 = Natural Cubic Spline with 3 degrees of freedom; QMM = Quadratic Mixed Model; For frequentist analyses *p<0.05; **p<0.01 vs. placebo; for DPM ++ indicates posterior probability of at least 0% slowing >99%; iADRS = Integrated Alzheimer's Disease Rating Scale; CDR-SB = Clinical Dementia Rating-Sum of Boxes

DONANEMAB BIOMARKER DATA

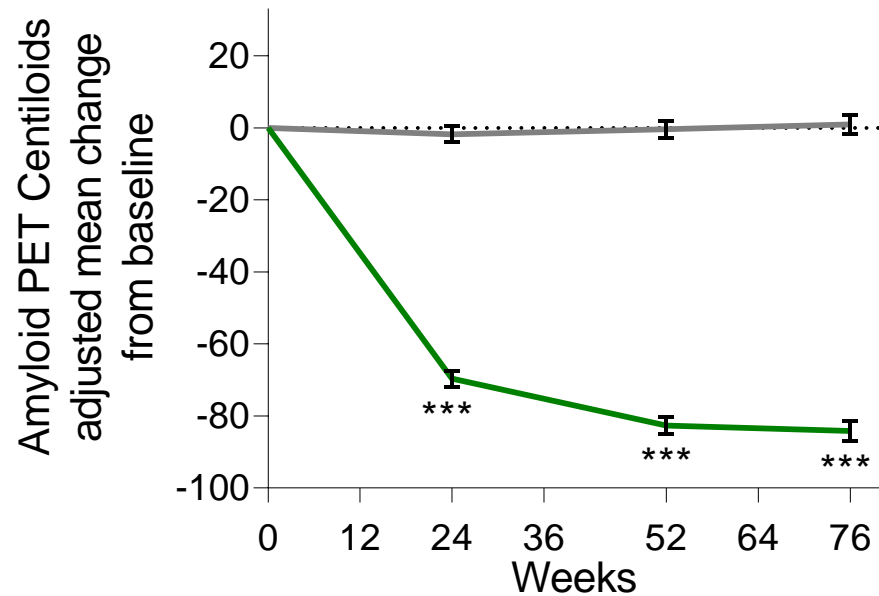
IMPACT ON BOTH AMYLOID AND TAU PATHOLOGY IN TRAILBLAZER-ALZ



DONANEMAB LOWERED AMYLOID PLAQUE

DONANEMAB SLOWED REGIONAL TAU SPREAD

Amyloid plaque significantly lowered with donanemab treatment (MMRM)

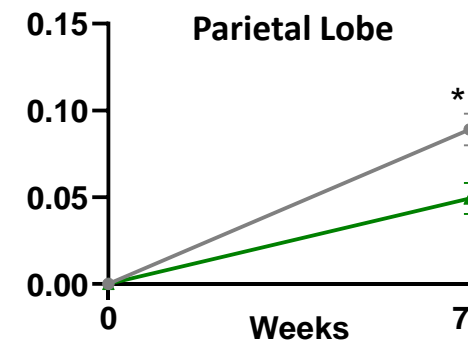
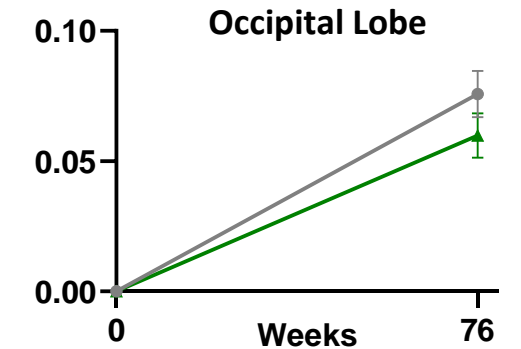
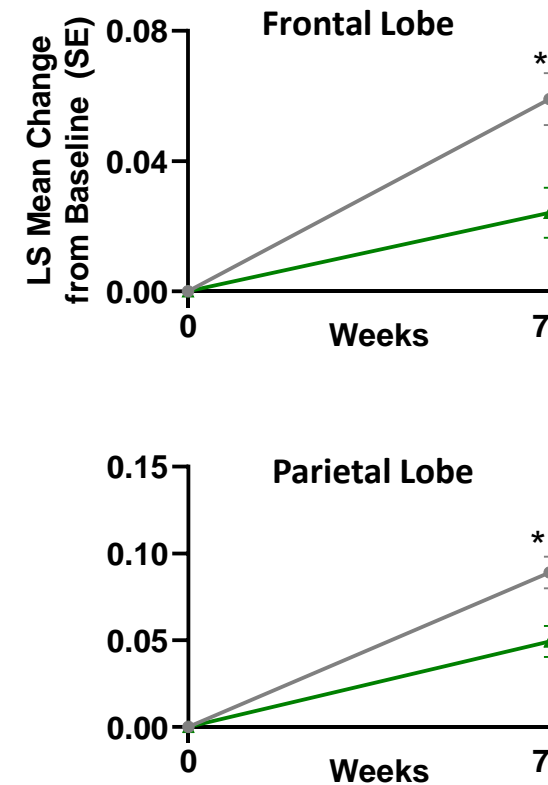


Placebo n =	112	111	91	91
Donanemab n =	121	115	92	90

Data points show mean +/- standard error
 LS = Least Square; MMRM = Mixed Model Repeated Measures; PET = Positron Emission Tomography; p = p-value

** p<0.01; *** p<0.001; **** p<0.0001 vs placebo
 All p-values are nominal

Donenamab slowed regional tau growth on flortaucipir PET



Region	Slowing	p-value
Frontal Lobe	59.1%	0.0020
Occipital Lobe	21.0%	0.2036
Parietal Lobe	44.6%	0.0024
Mesial Temp. Lobe	NA	0.0459
Lateral Temp. Lobe	31.8%	0.0328

CONTINUED INVESTMENT TO MAXIMIZE DONANEMAB

SIGNIFICANT INVESTMENT IN GENERATING ADDITIONAL DATA FOR THE FIELD



Expanding globally from 500 to over 1,500 patients for potentially confirmatory study of donanemab in patients with early Alzheimer's disease



Testing donanemab for prevention of Alzheimer's disease in pre-symptomatic population using novel decentralized trial design and p-Tau 217 diagnostic for inclusion



Initiating head-to-head study vs aducanumab to assess superiority on the level of brain amyloid plaque clearance in early symptomatic Alzheimer's disease at specific timepoints



Investing in next-generation N3pG antibody amyloid-lowering agent with potential for subcutaneous dosing

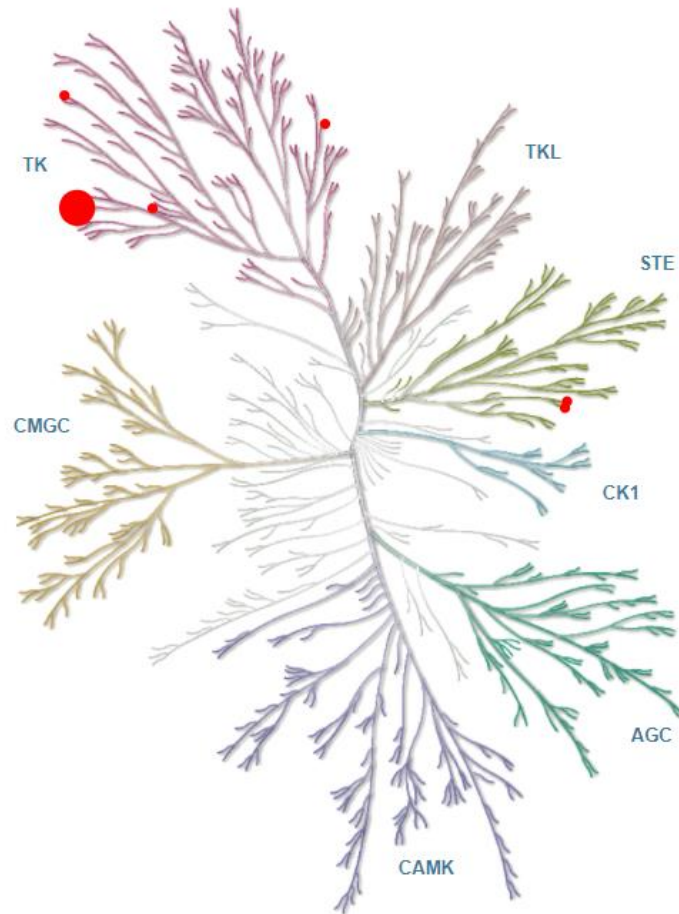
PIRTOBRUTINIB

PRECLINICAL DATA PROMPTED INITIAL THESIS IN C481-MUTANT POPULATION



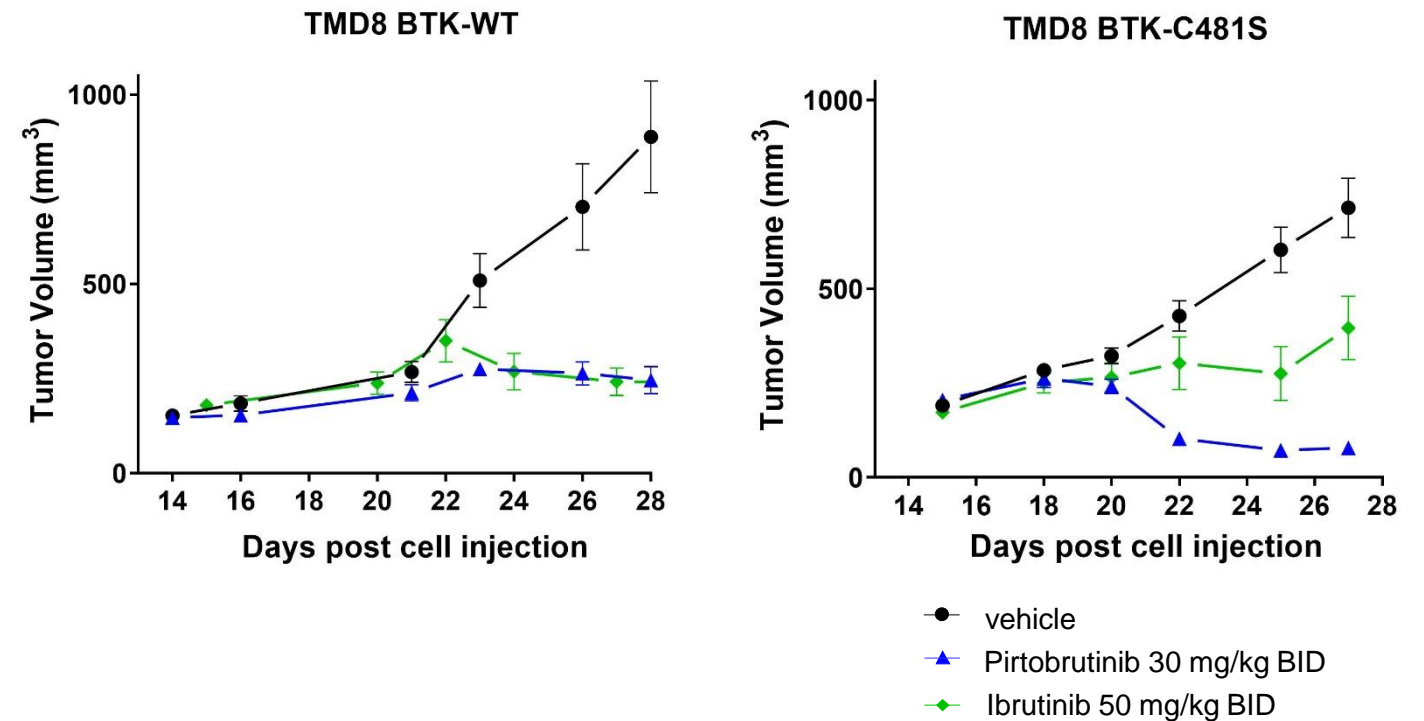
KINOME SELECTIVITY

Highly selective for BTK¹



XENOGRAFT MODELS

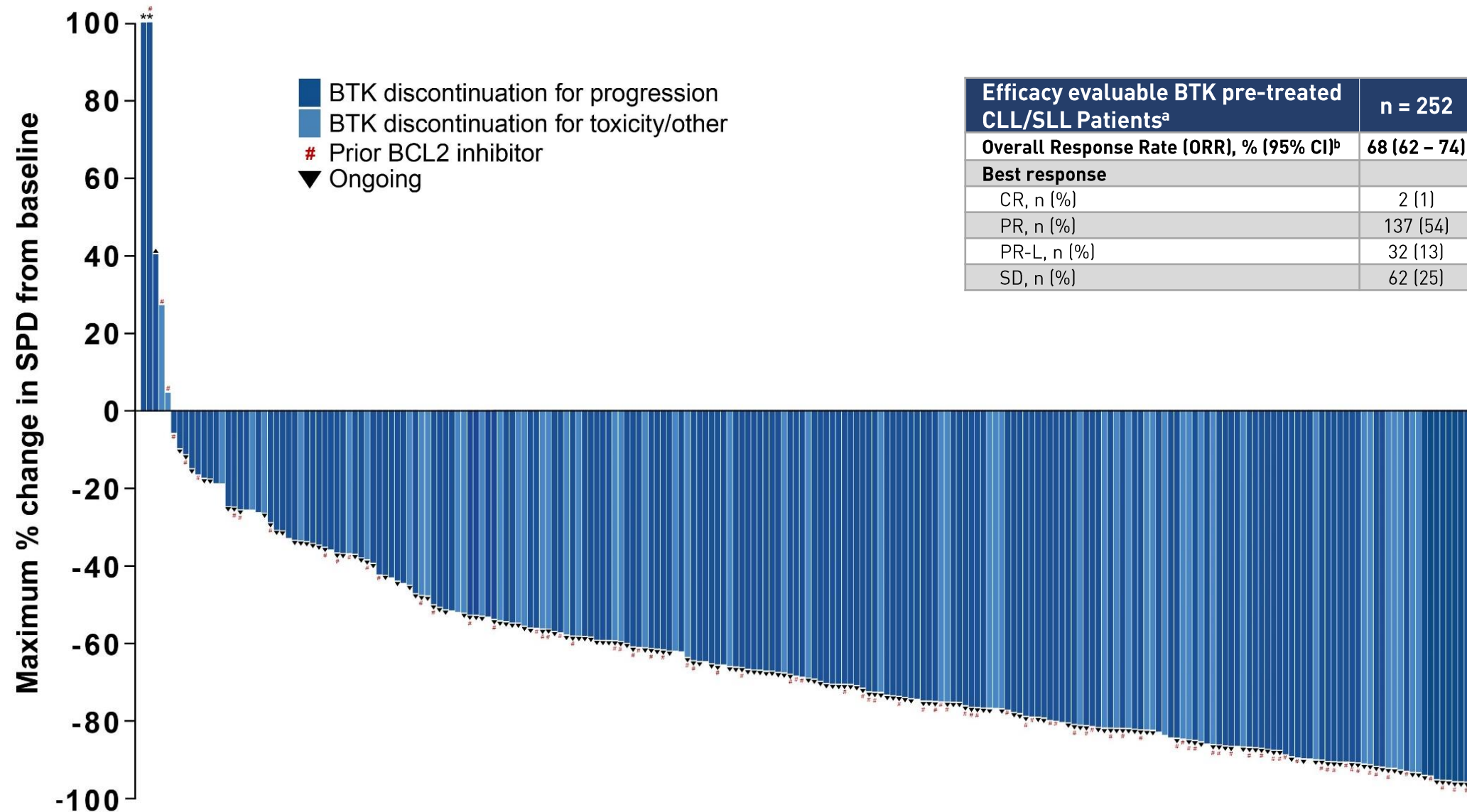
In vivo activity similarly effective as ibrutinib in WT; superior in C481S



- Nanomolar potency against WT & C481-mutant BTK in cell and enzyme assays²
- >300-fold selectivity for BTK vs 370 other kinases²
- Due to reversible binding mode, BTK inhibition not impacted by intrinsic rate of BTK turnover²
- Favorable pharmacologic properties allow sustained BTK inhibition throughout dosing interval²

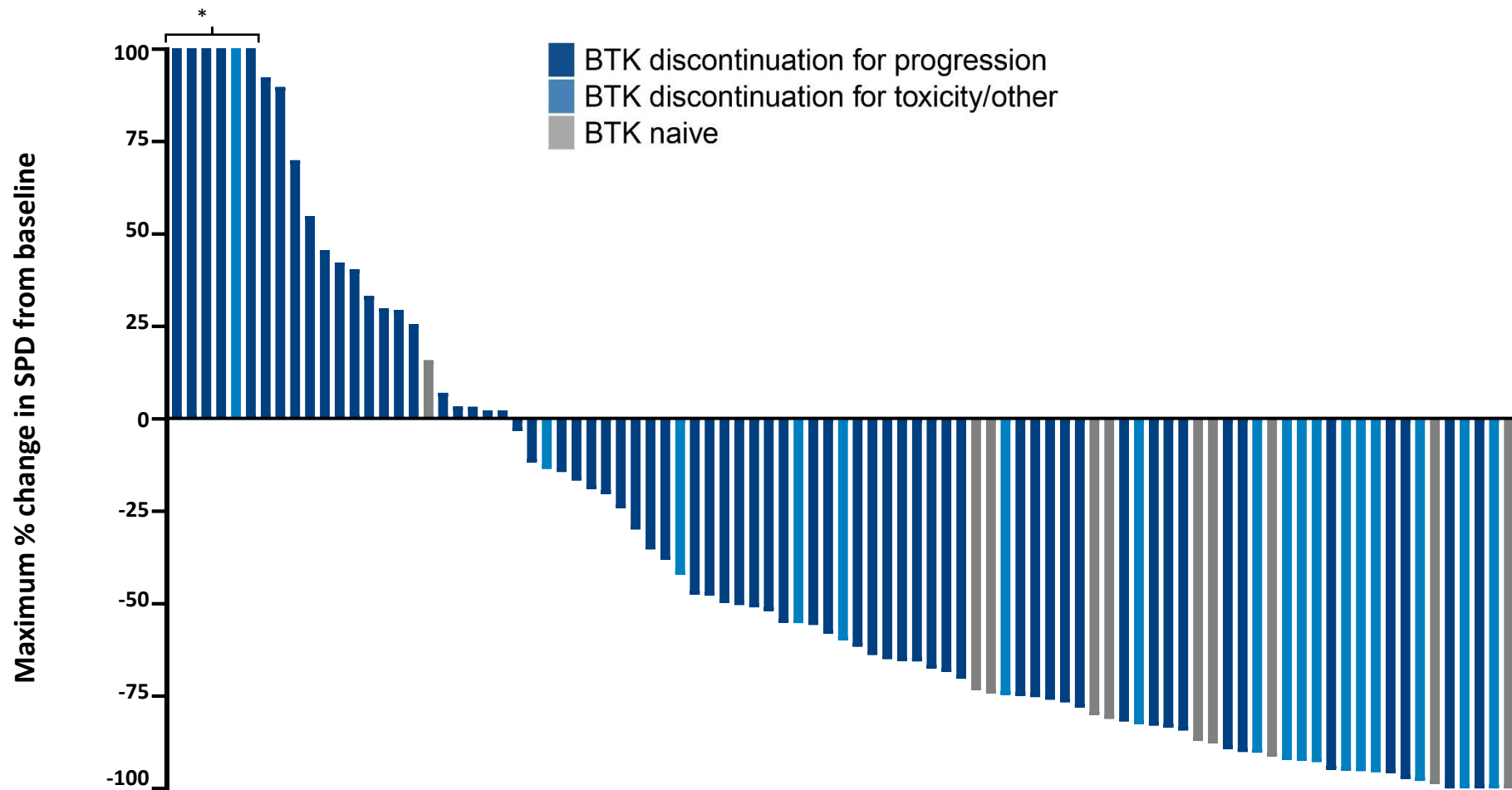
BID, twice-daily; BTK, Bruton tyrosine kinase. ¹Mato et al, *Lancet*, 2021:397:892-901. ²Brandhuber BJ, et al. *Clin. Lymphoma Myeloma Leuk*. 2018.18:S216. Illustration reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com)

PIRTOBRUTINIB DATA IN CLL/SLL



Data cutoff date of 16 July 2021. *Patients with >100% increase in SPD. Data for 30 patients are not shown in the waterfall plot due to no measurable target lesions identified by CT at baseline, discontinuation prior to first response assessment, or lack of adequate imaging in follow-up. ^aEfficacy evaluable patients are those who had at least one post-baseline response assessment or had discontinued treatment prior to first post-baseline response assessment. ^bORR includes patients with a best response of CR, PR, and PR-L. Response status per iwCLL 2018 according to investigator assessment. Total % may be different than the sum of the individual components due to rounding. CLL = Chronic lymphocytic leukemia; SLL = small lymphocytic lymphoma; CR = complete response; PR = partial response; SD = stable disease

PIRTOBRUTINIB DATA IN MCL



BTK Pre-Treated MCL Patients ^a		n=100
Overall Response Rate (ORR)^b, % (95% CI)		51% (41-61)
Best Response		
CR, n (%)		25 (25)
PR, n (%)		26 (26)
SD, n (%)		16 (16)
BTK Naive MCL Patients ^a		n=11
Overall Response Rate^b, % (95% CI)		82% (48-98)
Best Response		
CR, n (%)		2 (18)
PR, n (%)		7 (64)
SD, n (%)		1 (9)

Data cutoff date of 16 July 2021. Data for 20 MCL patients are not shown in the waterfall plot due to no measurable target lesions identified by CT at baseline, discontinuation prior to first response assessment, or lack of adequate imaging in follow-up. *Indicates patients with >100% increase in SPD. ^aEfficacy evaluable patients are those who had at least one post-baseline response assessment or had discontinued treatment prior to first post-baseline response assessment. ^bORR includes patients with a best response of CR and PR. Response status per Lugano 2014 criteria based on investigator assessment. Total % may be different than the sum of the individual components due to rounding; CR = complete response; PR = partial response; SD = stable disease

CONTINUED INVESTMENT TO MAXIMIZE PIRTOBRUTINIB

SIGNIFICANT INVESTMENT TO MAXIMIZE REACH



Initiating a significant Phase 3 program, with five trials in more than 2,000 patients studying pirtobrutinib alone and in combination in first-line and refractory patients in CLL, SLL, and MCL



Program focused on establishing pirtobrutinib as the potential preferred agent for people with relapsed disease following a covalent BTK inhibitor, as well as exploring potential to move to earlier lines of treatment, including a head-to-head superiority trial compared to ibrutinib



In-licensed a preclinical BCL-2 inhibitor now in Phase 1 with the potential for combination with pirtobrutinib in hematological malignancies

CLL = chronic lymphocytic leukemia; SLL = small lymphocytic lymphoma;
MCL = mantle cell lymphoma

MIRIKIZUMAB & LEBRIKIZUMAB

POSITIVE PHASE 3 RESULTS FOR TWO NEW MOLECULES IN IBD AND DERM



MIRIKIZUMAB

- Positive Phase 3 induction and maintenance results for ulcerative colitis
- Global submission in H1 2022 could lead to first-in-class anti-IL-23p19 monoclonal antibody treatment for ulcerative colitis
- Crohn's disease Phase 3 readout in early 2024
- Addressable markets with unmet need:
 - Ulcerative colitis ~1.1M patients in U.S. and ~1.2M patients in Europe
 - Crohn's disease ~900K patients in U.S. and ~1M patients in Europe

LEBRIKIZUMAB

- Positive Phase 3 monotherapy induction results in 2021 for atopic dermatitis establishes competitive profile vs. Dupixent
- Phase 3 results expected in late 2021/early 2022 for atopic dermatitis in combination with topical corticosteroids
- Monotherapy maintenance data expected in H1 2022, with global submissions expected by year-end 2022
- Addressable market with unmet need:
 - ~18M patients in U.S. and ~2.5M receive diagnosis
 - ~400K patients diagnosed as moderate-to-severe

COVID-19 THERAPEUTICS



DISCOVERY and DEVELOPMENT

- In partnership with AbCellera, went from discovery to EUA for bamlanivimab in only eight months
- EUA for bamlanivimab + etesevimab granted in Q1 2021
- Authorized for both ambulatory and post-exposure prophylaxis use in U.S.
- Baricitinib evaluated to treat critically ill COVID-19 patients



SUPPLY

- Supplied U.S. and international markets beginning in November 2020
- BARDA estimates that bamlanivimab alone and bamlanivimab + etesevimab saved over 10,000 lives in the U.S. alone
- ~2 million doses of COVID-19 neutralizing antibodies supplied globally in past 13 months




PATIENT ACCESS and EASE OF USE

- Worked with governments to ensure neutralizing antibodies at no cost to patients wherever possible
- Donated 400k baricitinib tablets to India and royalty-free licensing to combat COVID-19 pandemic
- Developed partnerships to provide access to COVID-19 neutralizing antibodies for patients in low-income countries

RESULTS FROM OUR TRANSFORMATION JOURNEY




Improved
development speed


Target identification to
clinical testing in < 3 years


Industry leading speed


Improved Phase 3
success rates


Novel target
identification


Improved clinical success rates


Record productivity:
On track for 20
launches in 10 years

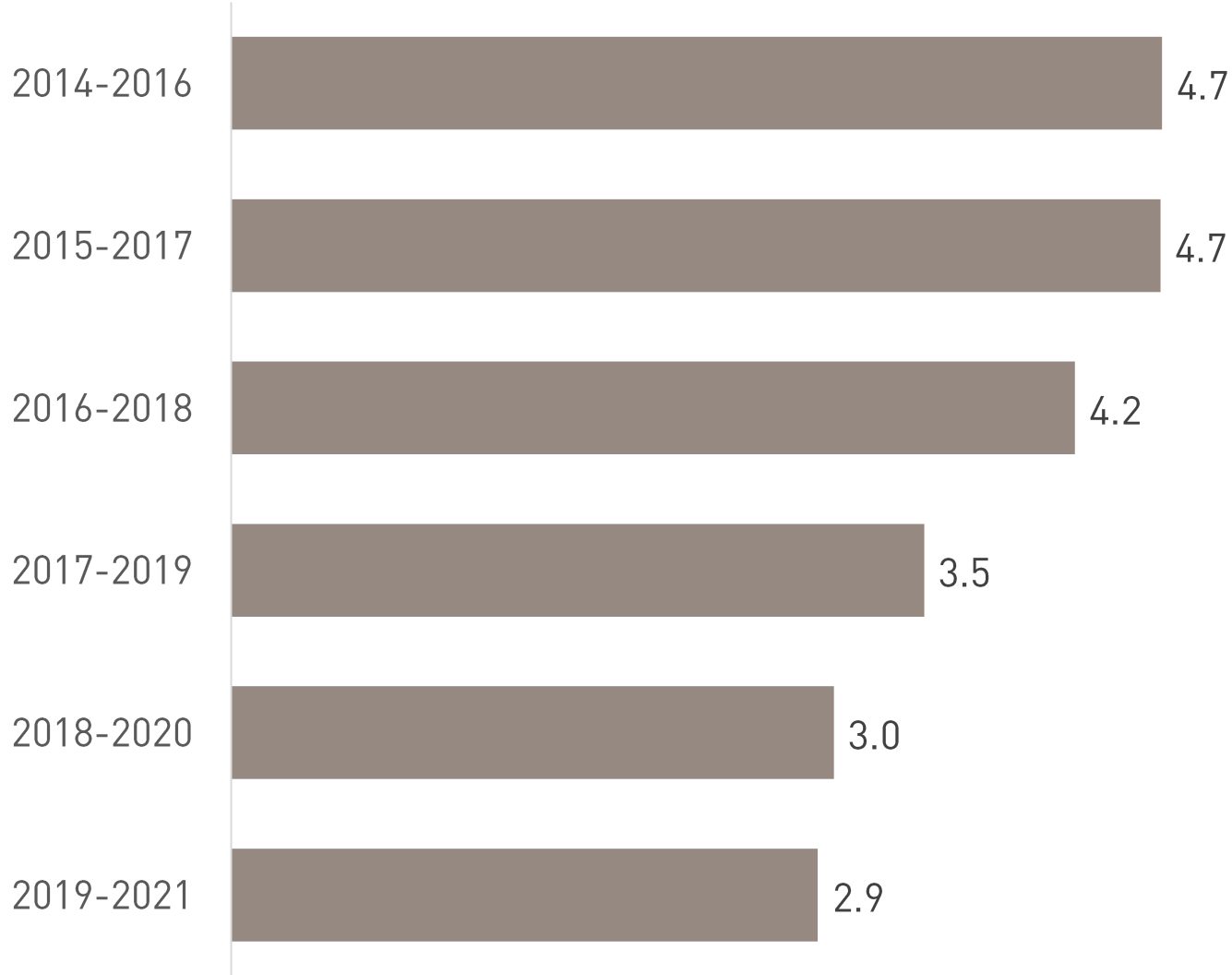

Access to novel
modalities


Significant value creation

FASTER PRE-CLINICAL DEVELOPMENT TIMELINES



Target Identification to Clinic Entry (Years)



GGG Tri-agonist Target to clinic in ~2.5 years

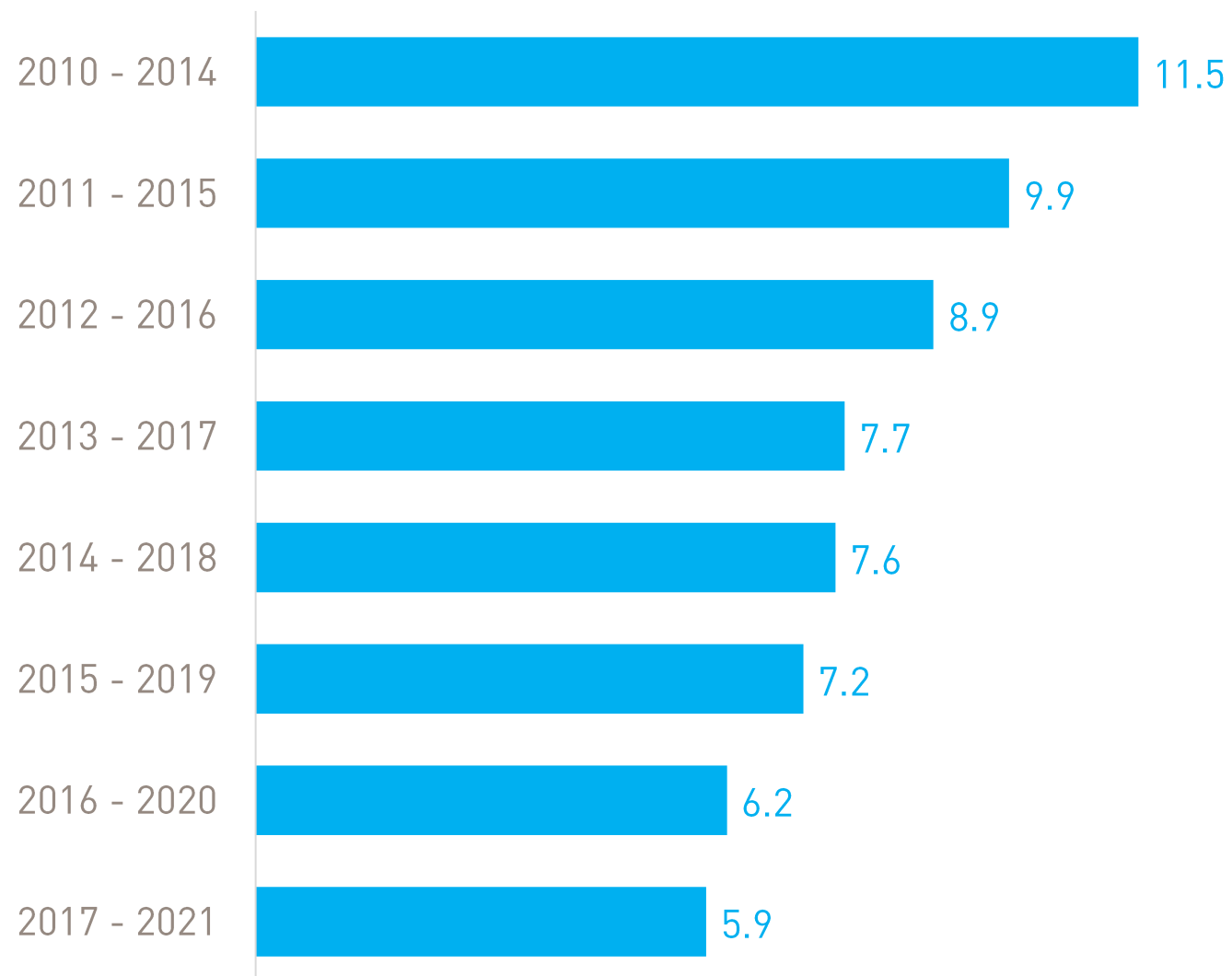
ANGPTL3 siRNA & Lp(a) siRNA Target to clinic in ~2 years

Imlunestrant Target to clinic in ~3.4 years

FASTER CLINICAL DEVELOPMENT TIMELINES



First Human Dose to Launch (Years)



Tirzepatide

First human dose to submission in 5.3 years

Pirtobrutinib

First human dose in March 2019

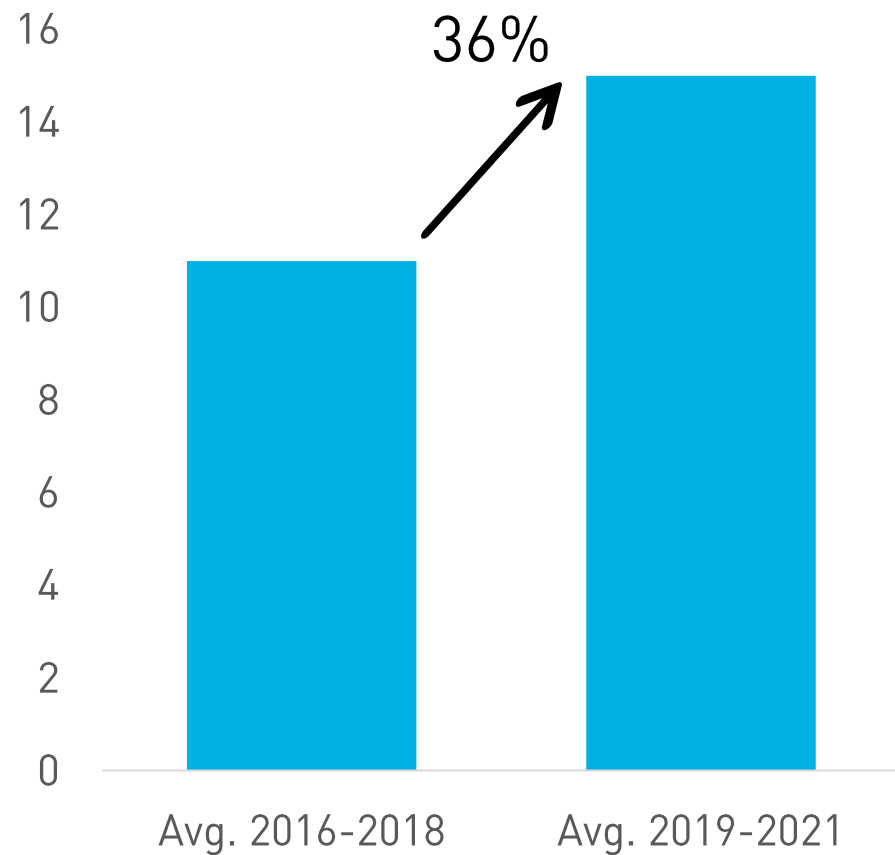
Bamlanivimab & Etesevimab

First human dose to EUA in <8 months

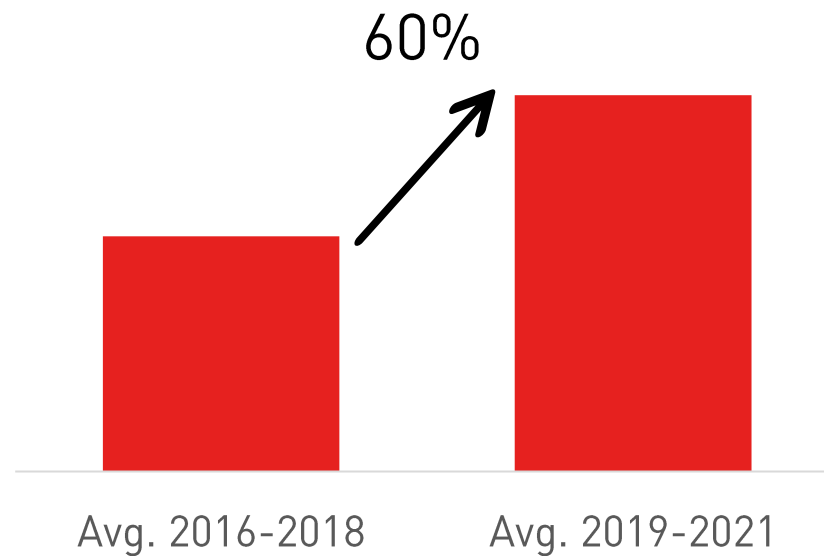
WE CONTINUE TO GROW OUR PORTFOLIO



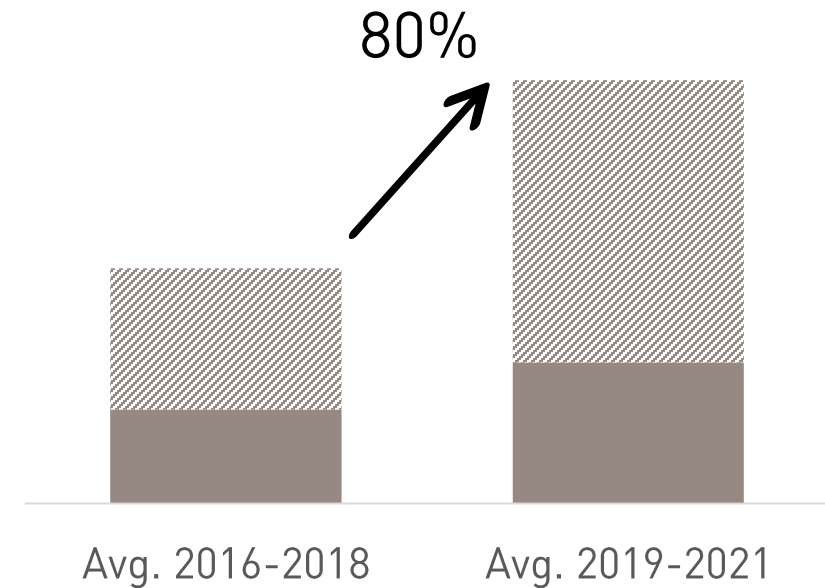
PHASE 1 ENTRIES



PHASE 2 ENTRIES



PHASE 3 ENTRIES

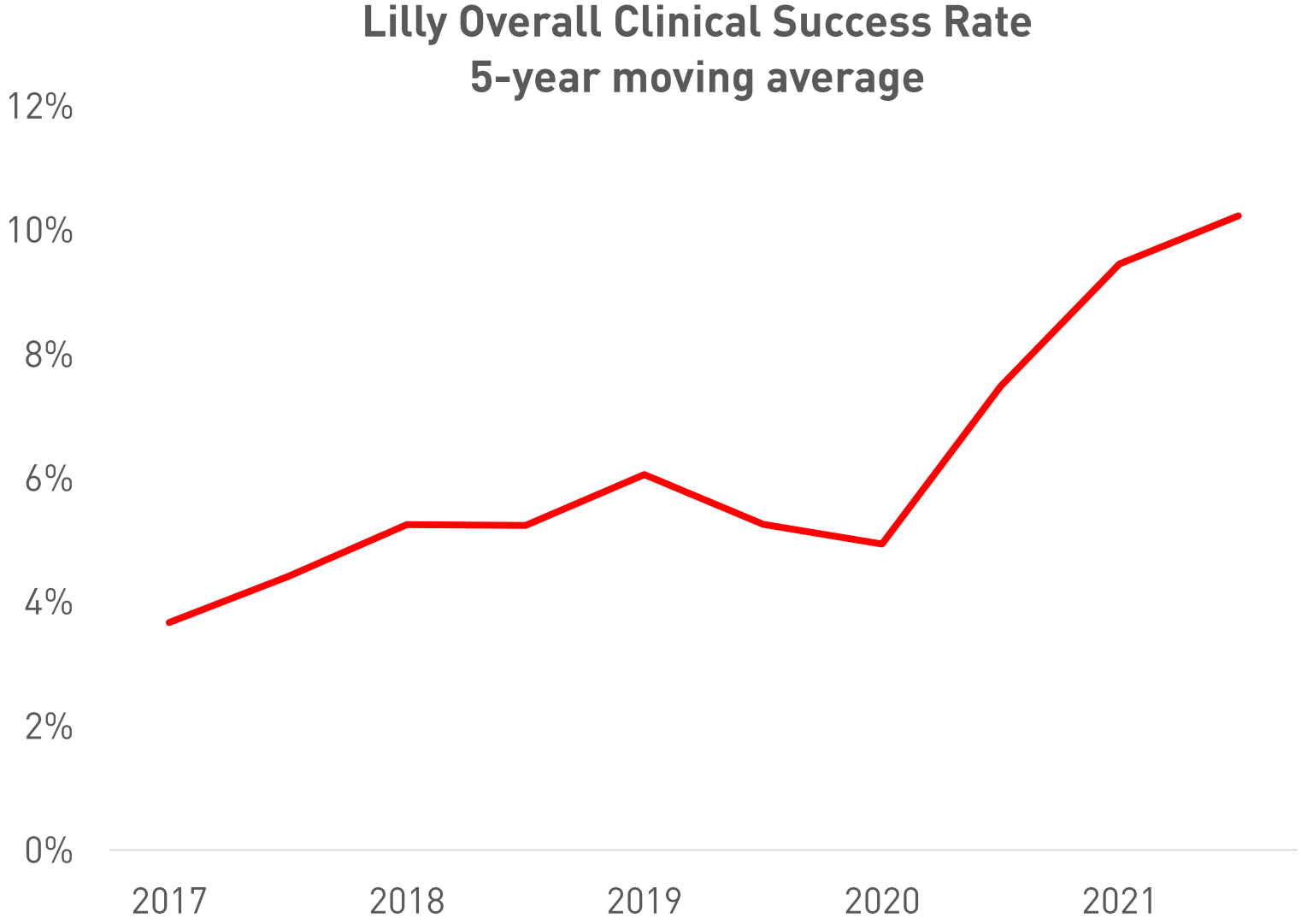


■ NILEX
■ NME

INCREASED CLINICAL SUCCESS RATES

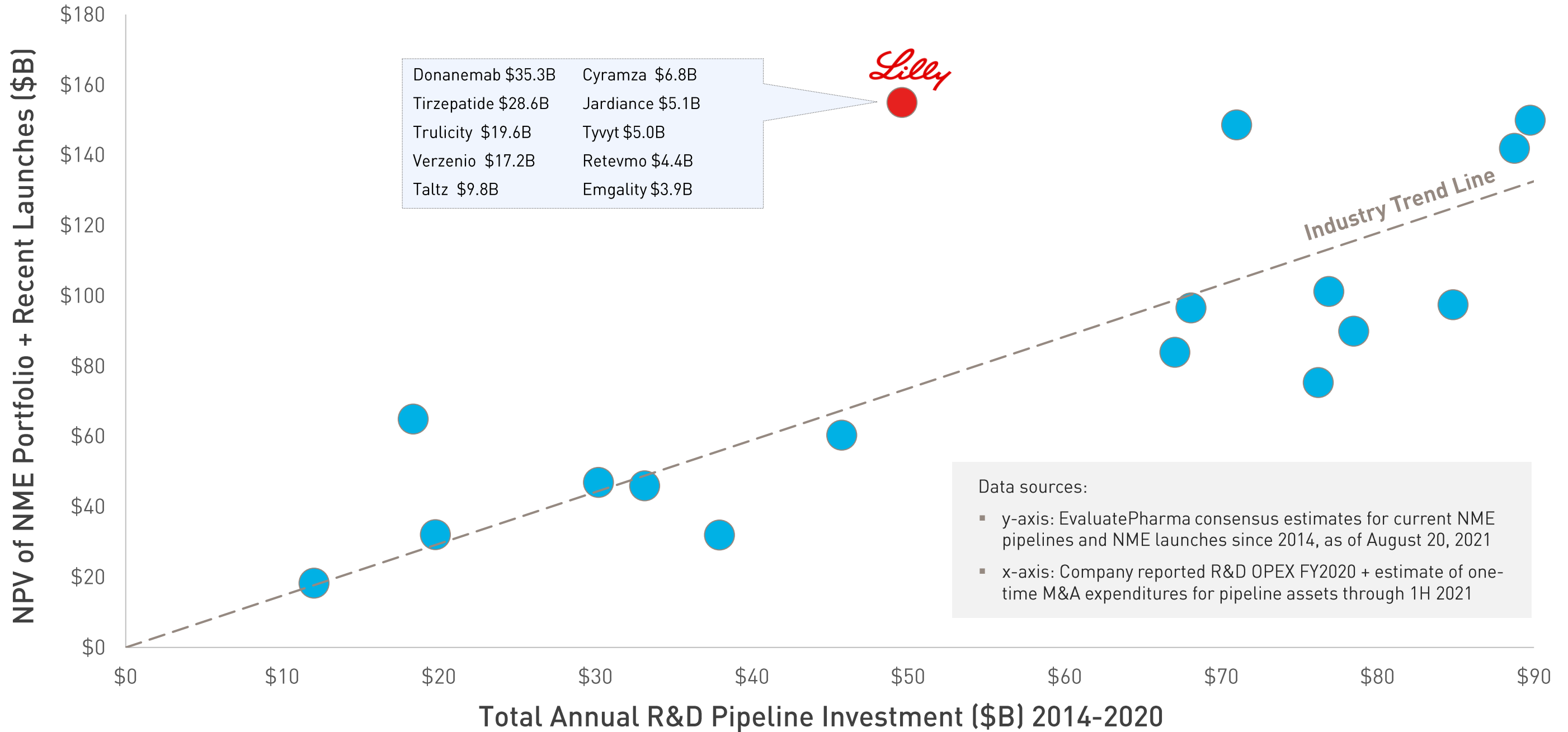


	Industry* Average 2016-2020	<i>Lilly</i> 2017-2021
Phase 1	42%	45%
Phase 2	34%	31%
Phase 3	73%	81%
Registration	99%	91%
Clinical Overall	10%	10%



* Industry peers are based on the Pharmaceutical Benchmarking Forum’s participant companies: AbbVie, Inc.; Allergan PLC (which was acquired by AbbVie, Inc. in May 2020); Bayer AG; Bristol-Myers Squibb Company; Eli Lilly and Company; Gilead Sciences, Inc.; Johnson & Johnson Corporation; Merck & Co, Inc.; Novartis AG; Pfizer; Roche, Inc. and Sanofi S.A

LILLY R&D PRODUCTIVITY VS. PEERS



Data sources:

- y-axis: EvaluatePharma consensus estimates for current NME pipelines and NME launches since 2014, as of August 20, 2021
- x-axis: Company reported R&D OPEX FY2020 + estimate of one-time M&A expenditures for pipeline assets through 1H 2021

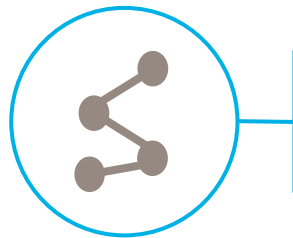
WE ARE WELL POSITIONED TO DELIVER



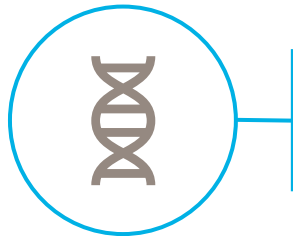
STRONG SCIENTIFIC FOUNDATION



Deep Expertise in neurodegenerative pathology, insulins and incretins, targeted small molecules for oncology, and immunology check points

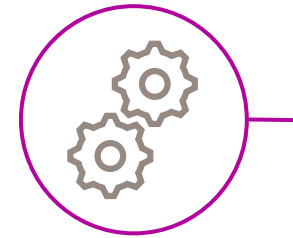


Best-in-class **Molecule Making** against difficult targets

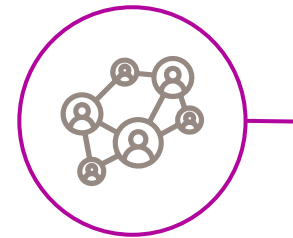


Building a portfolio of **Novel Modality Platforms** with siRNAs and gene therapies that access the CNS + strategic focus on additional tissues & enabling technologies

DIFFERENTIATED CLINICAL EXECUTION



Translating our **Operational Excellence** to new ways of working; became the first company to obtain EUA for COVID-19 therapies



Making research more diverse and accessible for every patient using **Decentralized Capabilities** to run the first-ever decentralized Alzheimer's trial



External Innovation that expands our capabilities with free-standing units like Loxo Oncology, and access to novel targets and platforms

EXTERNAL INNOVATION THAT EXPANDS OUR CAPABILITIES



Free Standing Units



Molecules



Retevmo
Pirtobrutinib



Lebrikizumab



SSTR4
Agonist



RIPK1
Inhibitor



P2X7 Receptor
Antagonist



GLP-1 Non-
Peptide Agonist



PI3K α
inhibitor



Bamlanivimab
Etesivimab

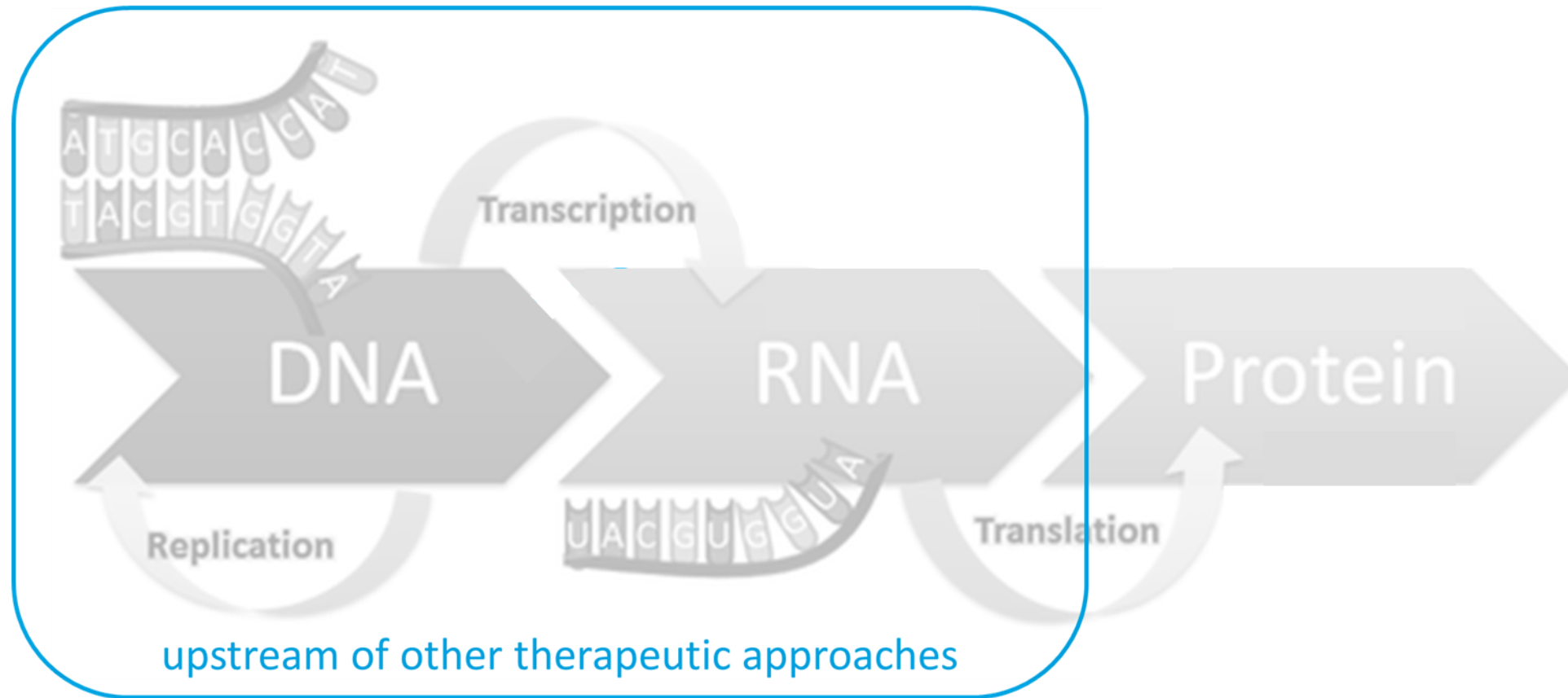
Novel Targets



Modality Platforms



NOVEL MODALITIES WILL DRIVE THE NEXT WAVE OF INNOVATION



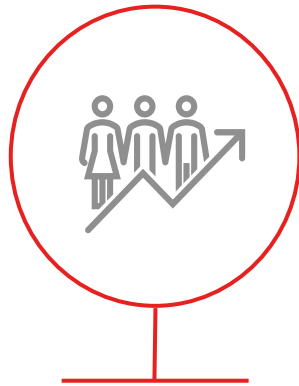
~20,000 human proteins

In 2017, approved drugs only targeted 667 human proteins

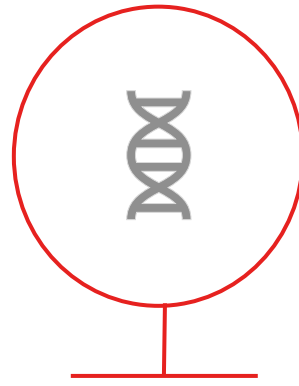
Significant opportunity to reach historically undruggable targets with novel therapeutics

N. Dammes, *et al.* Trends in Pharmacol Sci.2020

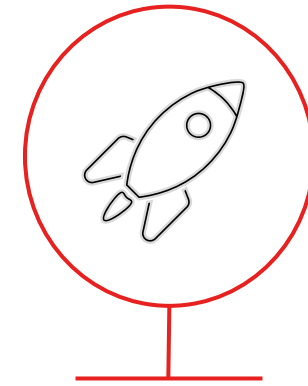
NOVEL MODALITIES AT LILLY



Develop expertise in novel modalities & genetic medicine



Access novel chemistry platforms via external innovation



Pursue delivery approaches to unlock new tissues & targets

EMBRACING THE POWER OF PLATFORMS



Building capabilities internally

- Established a team of dedicated subject matter experts in Indianapolis & Cambridge
- Quickly integrated personnel and technologies
- Intensively built development capabilities to support clinical study of oligonucleotides
- Progressed initial candidates into clinical testing with accelerated timelines

External innovation has allowed us to access foundational science

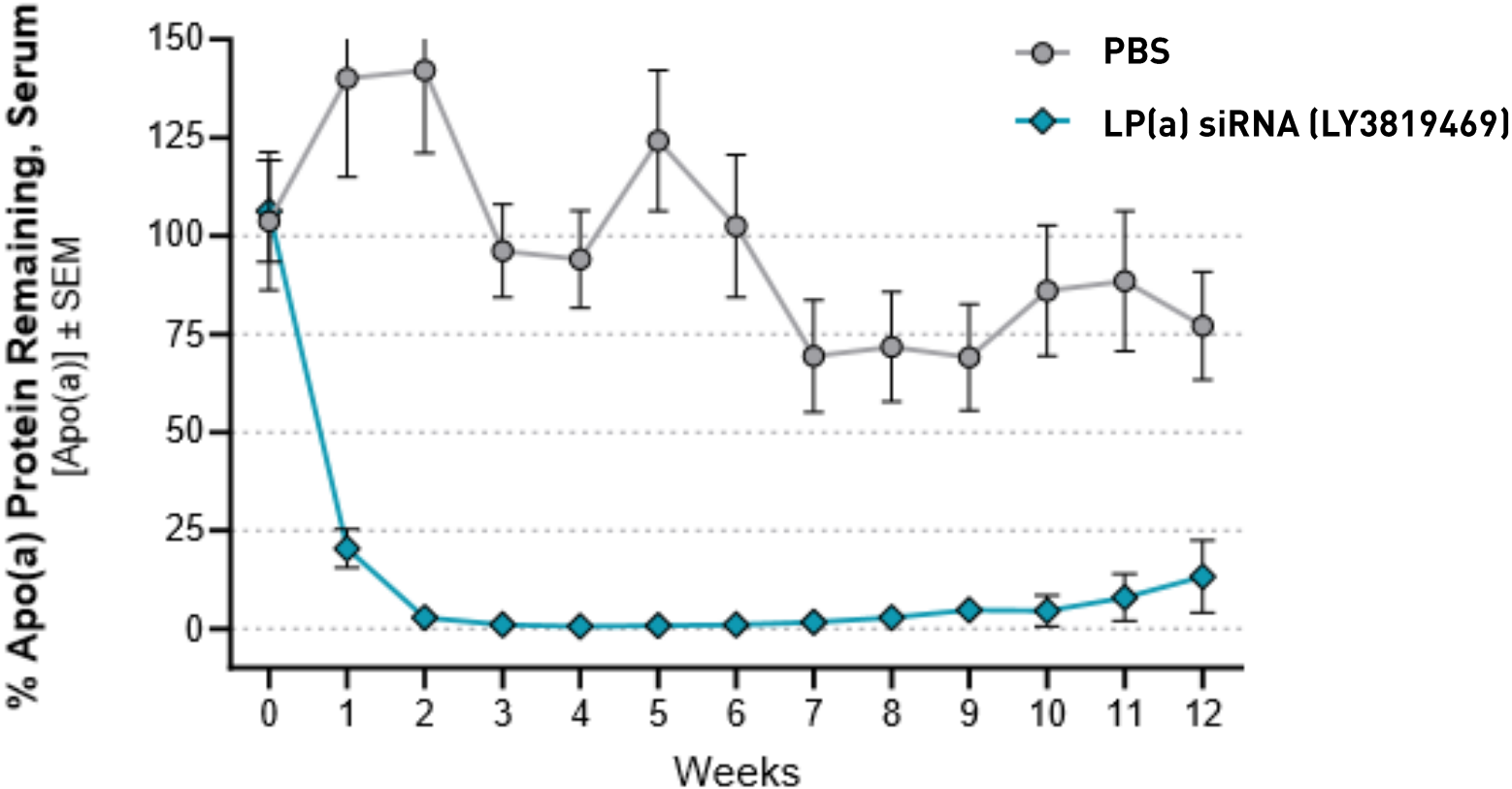
	siRNA	saRNA	mRNA Editing	Gene Editing	Gene Therapy
Effect	Downregulating Genes	Upregulating Genes	Editing at the RNA Level	Editing at the DNA Level	Gene Replacement
Partner/ Collaborator					
Duration of action	Months	Months	TBD	Years	Years
Signed	2018	2021	2021	2020	2020

Genetic medicines now represent >20% of Lilly's diabetes, immunology, and neuroscience research portfolio

OUR COLLABORATIONS HAVE DELIVERED EXCITING MOLECULES



Circulating Apo(a) is reduced >99% by LP(a) siRNA in cynomolgus monkey between weeks 3-7 following a single dose



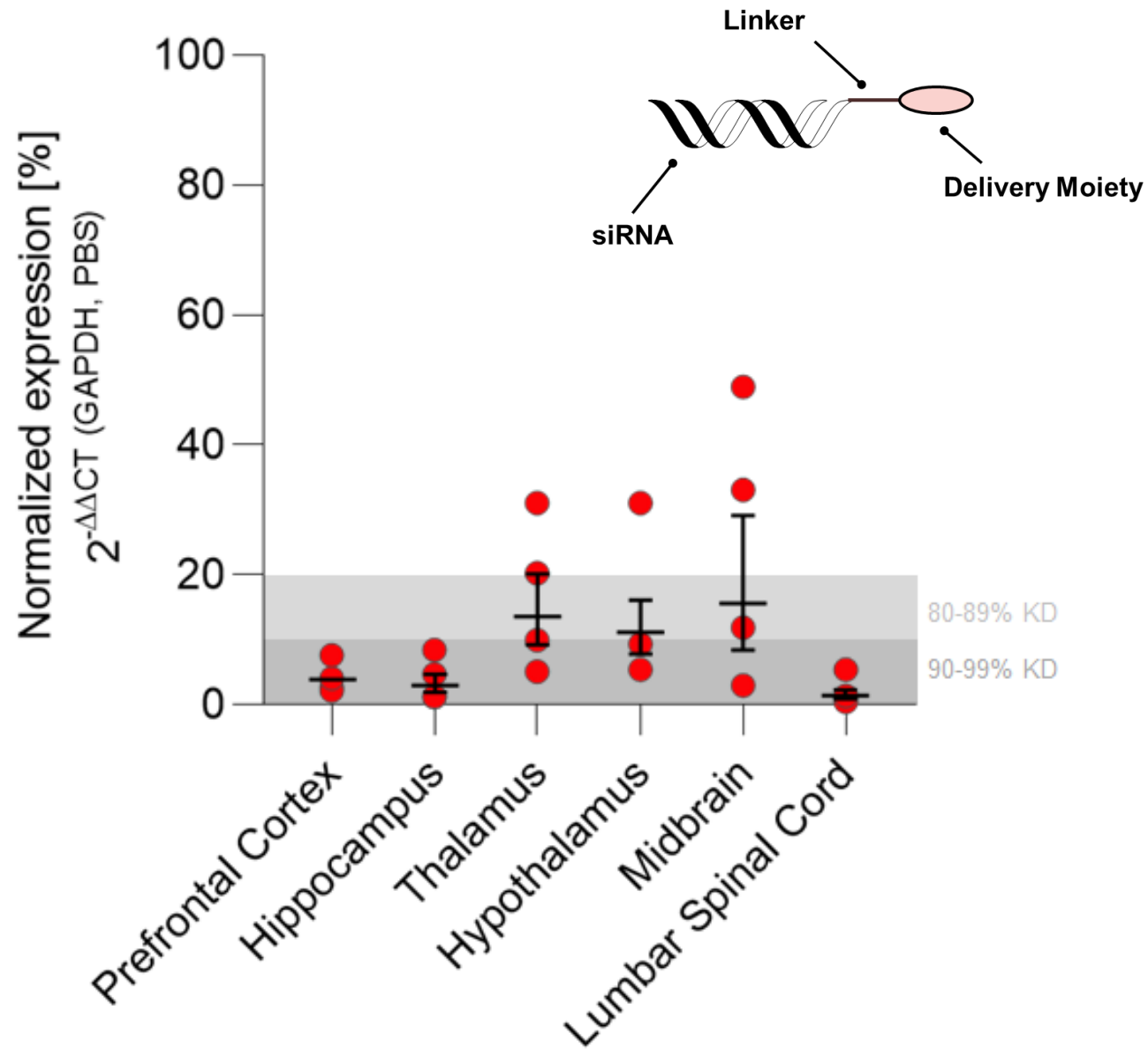
- Sustained suppression of Apo(a) protein in monkeys
- Potential for best-in-class Lp(a) efficacy and durability – targeting 3-6 month dosing

Key goals

- Meaningful outcomes**
Genetic evidence is promising
- Compelling preclinical data**
>99% sustained LP(a) reduction in NHP
- Infrequent dosing**
Targeting Q3 to Q6 monthly dosing
- Competitive cost to manufacture**
On track

Apo(a) = apolipoprotein A; Lp(a) = lipoprotein (a); PBS = phosphate buffered saline; NHP = non-human primate

INTERNAL PROGRESS IN DELIVERY OF RNA THERAPEUTICS TO THE CNS



NHP
 IT Delivery Single Dose
 28 days

Proprietary Lilly siRNA Design
 Novel delivery moiety with favorable biodistribution, including to disease-relevant deep brain structures (e.g., Cortex)

Compelling preclinical data
 >90% sustained reduction in target RNA in gold standard NHP model

Early durability is encouraging
 Sustained reduction in mRNA out to 28 days following a single dose

CNS = central nervous system; GAPDH = glyceraldehyde-3-phosphate dehydrogenase; PBS = phosphate buffered saline; NHP = nonhuman primate; IT = intrathecal; KD = equilibrium dissociation constant

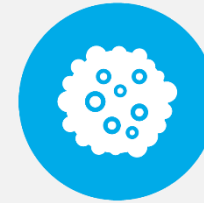
WHAT'S NEXT



Strong scientific foundation



Differentiated clinical execution



GGG Tri-Agonist

GLP-1 Receptor NPA

Oxyntomodulin

Weekly Basal Insulin Fc

ANGPTL3 siRNA

IL-2 Conjugate

CD200R Agonist Ab

CXCR1/2L

RIPK1 Inhibitor

Imlunestrant

KRAS G12C

PD-1 Agonist Ab

IDH1/2 Inhibitor

PI3Ka mutant selective

BTLA Agonist Ab

Tau siRNA

N3pG IV

FGFR3 Inhibitor



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and President of Lilly Research Laboratories



ANDREW ADAMS, PH.D.

Vice President,
Lilly Genetic Medicine

