# 2018 INVESTMENT COMMUNITY MEETING

Lilly

# SAFE HARBOR PROVISION

This presentation contains 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; litigation and investigations; business development transactions; economic conditions; changes in laws and regulations, including health care reform; and uncertainties and risks related to timing and potential value to both Elanco and Lilly of the planned separation of the Elanco animal health business, including business, industry, and market risks, as well as risks involving realizing the anticipated tax-free nature of the separation.

For additional information about the factors that affect the company's business, please see the company's latest Forms 10-K and 10-Q filed with the Securities and Exchange Commission.

**The company undertakes no duty to update forward-looking statements.**

# DANIEL SKOVRONSKY, M.D., Ph.D.

Chief Scientific Officer,
President Lilly Research Labs

Lilly

2018 **INVESTMENT COMMUNITY MEETING**

# Agenda

**R&D Overview & Strategy**

**Oncology**
Verzenio® & Pegilodecakin

**Pain**
Emgality™, Lasmiditan & Tanezumab

**Neurodegeneration**
N3pG, Tau Antibody & D1PAM

**Immunology**
Olumiant® & Mirikizumab

**Diabetes**
Insulins & Connected Care, Trulicity® & Tirzepatide

# A HERITAGE OF DISCOVERY

**1876**

**1923**
INSULIN

**1943**
PENICILLIN-G

**1955**
POLIO

**1961**
VELBAN®

**1982**
HUMULIN®

**1988**
PROZAC®

**1996**
ZYPREXA®
GEMZAR®

**2004**
CYMBALTA®

# KEY FOCUS AREAS

| What we said in 2016 R&D update: | What we've accomplished: |
|---|---|
| **Working to Improve Development Speed** | ▪ Development speed is now a competitive advantage for Lilly |
| **Improving Phase 3 success rate with quality strategy** | ▪ We successfully raised the bar on Phase 3 entries, resulting in higher success rates |
| **Potential for record productivity (could launch 20 medicines in 10 years)** | ▪ 10 new medicines launched in 5 years, 8 with blockbuster sales / potential<br>▪ Two new medicines in regulatory review<br>▪ Good visibility to continued launches |

## What's next:

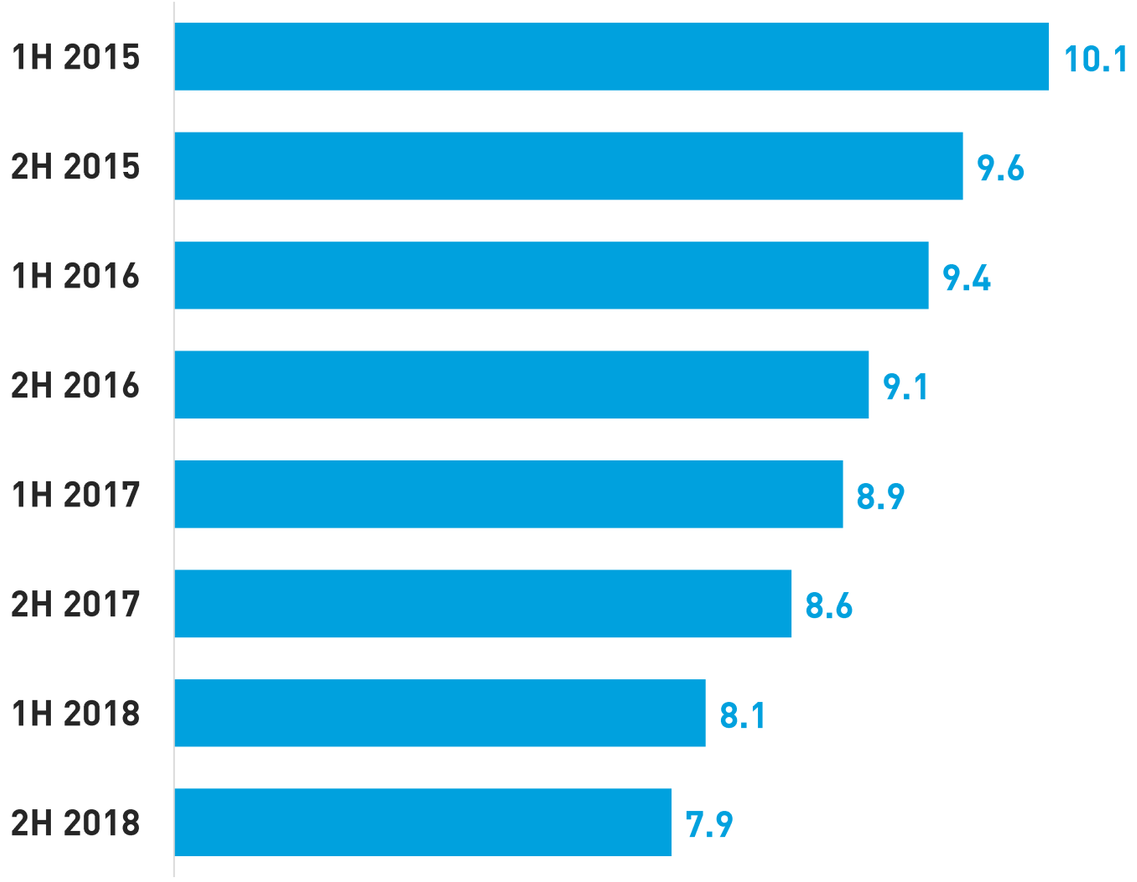
Lilly has delivered an **industry leading late stage development engine**

Now we are focused on **transformation of our drug discovery engine**

- Speed from target identification to human proof-of-concept studies
- Novel target identification
- Access to novel modalities

# FASTER DEVELOPMENT TIMELINES

## First Human Dose to Launch (Years)




**Tirzepatide** — First human dose to Phase 3 start in 31 months

**Emgality** — Narrowed launch gap vs. leading competitor from 15 to 4 months

**Ultra Rapid Lispro** — First human dose to submission projected at < 4 years

# IMPROVED PHASE 3 SUCCESS RATES

| | 2007 – 2013 | 2014-present (78%) |
|---|---|---|
| Approvals and Submissions | Effient® | Olumiant, Taltz®, Portrazza®, Basaglar®, Cyramza®, Jardiance®, Trulicity, Flortaucipir, Ultra Rapid Lispro*, Nasal Glucagon, Lasmiditan, Emgality, Verzenio®, Lartruvo™ |
| Terminations | Pomaglumetad, Tasisulam, Teplizumab, Semagacestat, Dirucotide, Arzoxifene, Edivoxetine, Enzastaurin | Lanabecestat, Evacetrapib, Insulin Peg-Lispro, Tabalumab |

*Pending Submissions

**Dramatic improvement in Phase 3 success rates due to emphasis on:**

- Target Validation
- Patient Population
- Molecule Optimization
- Robust Phase 2 Data
- Phase 3 Design

# ON PACE TO LAUNCH 20 NEW MEDICINES IN 10 YEARS

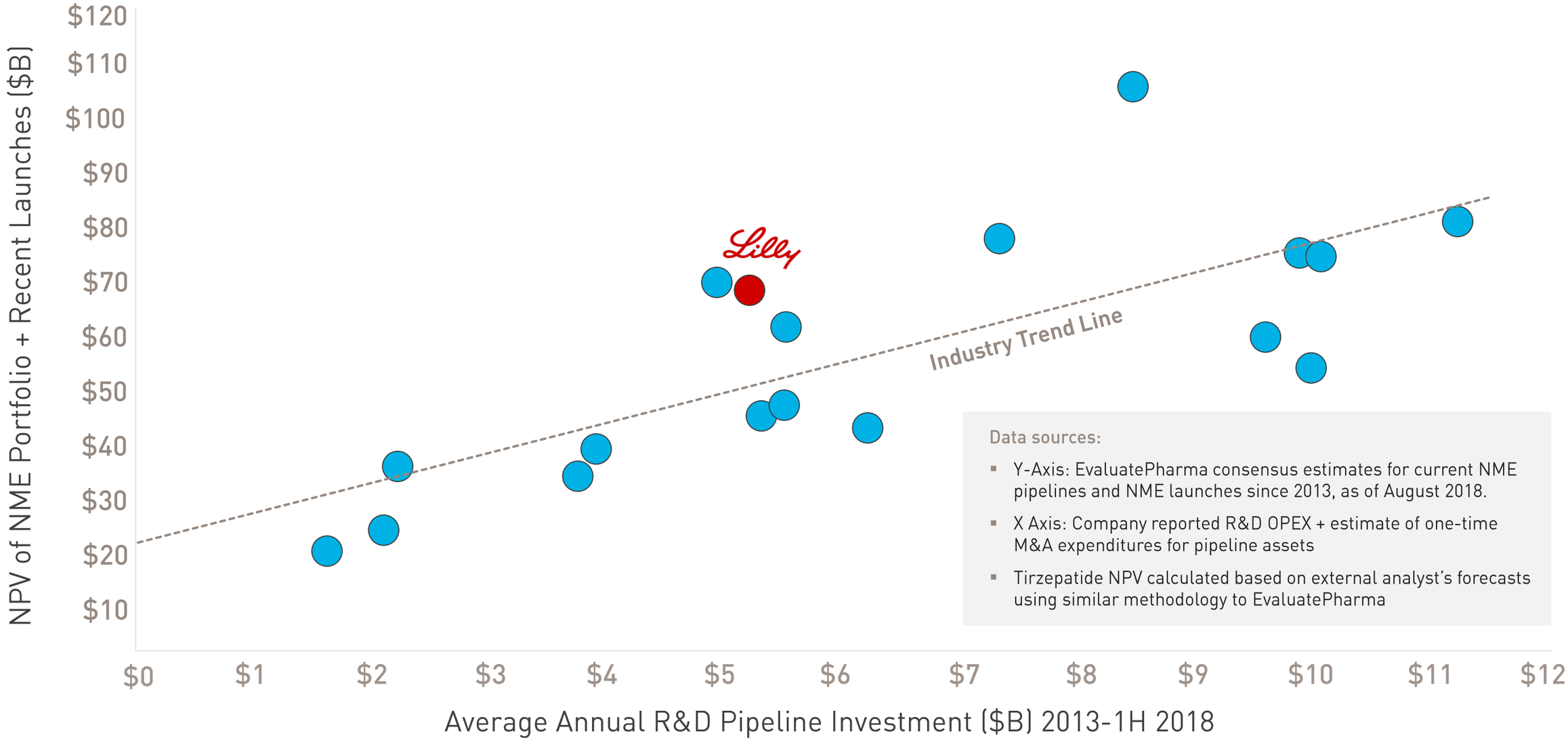
## 10 Global Launches in 5 Years

| 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|
| trulicity | basaglar | taltz | Verzenio | Emgality |
| Jardiance | Portrazza | Lartruvo | olumiant | |
| CYRAMZA | | | | |

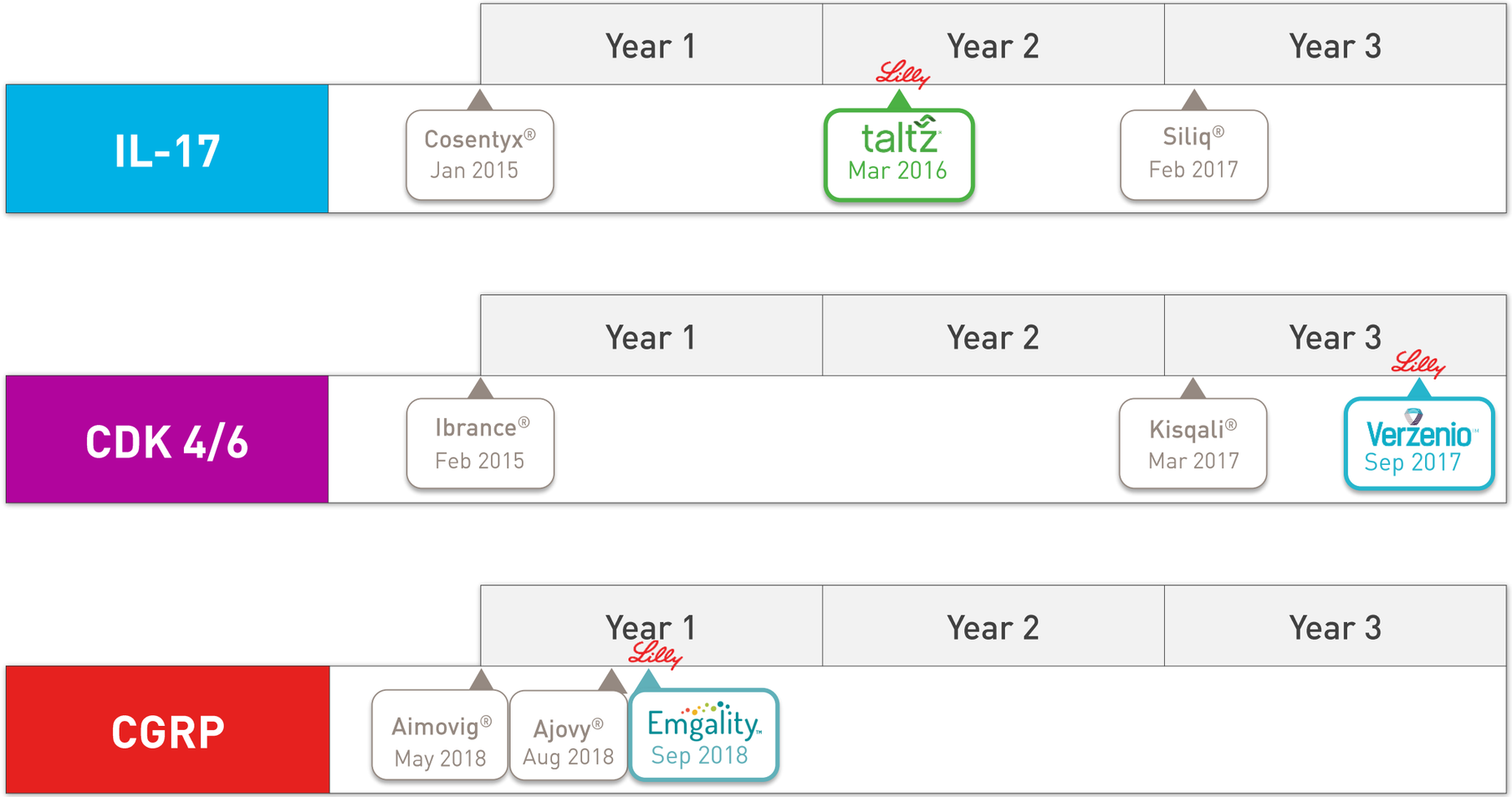
## Potential Launches

| 2019 | 2020 | 2021 | 2022-2023 |
|---|---|---|---|
| **Nasal Glucagon** (submitted) | **Tanezumab** (NGF1 mAb) | **Mirikizumab** (IL-23 mAb) | **Tirzepatide** (GIP/GLP1 Dual Agonist) |
| **Lasmiditan** (submitted) | **Ultra Rapid Lispro** | **Pegilodecakin** (Pegylated IL-10) | ▪ D1-PAM<br>▪ IL-33 mAb<br>▪ TIM-3 Abs and Combinations<br>▪ AurA Kinase Inhibitor |
| **Connected Pen** | | **Automated Insulin Delivery System** | |

# LILLY R&D PRODUCTIVITY IS FAVORABLE VS. PEERS



# ENABLING MORE FIRST-IN-CLASS MEDICINES




Previously **slow to translate** discoveries from labs to patients

**We will move faster** to **proof-of-concept** studies with future **novel mechanisms**

# INCREASING SPEED AND NOVELTY

## SPEED

**3 year goal** from target identification to clinical testing

**Technology investments** including automation and IT

**Biotech-like operating model** with reduced emphasis on committees

## NOVELTY

**External innovation focus** on early-stage molecules and technologies

**Efficient proof-of-concept studies** testing for large effect size

Conviction to **blaze new trails**

# EXTERNAL INNOVATION

## ENABLING NOVEL MEDICINES

Lilly will continue to invest in its established R&D platforms, including insulins and incretins, to deliver best-in-class innovation

To enable first-in-class medicines with large effect sizes, we are increasing our access to novel targets, modalities, and discovery tools

External Innovation is a key element of our first-in-class strategy

**Novel Targets**

UC San Diego
NextCure
GLADSTONE INSTITUTES
SBP SANFORD BURNHAM PREBYS
DANA-FARBER CANCER INSTITUTE
PURDUE UNIVERSITY

**Novel Modalities**

Dicerna pharmaceuticals
CUREVAC
sigilon therapeutics

**Tools**

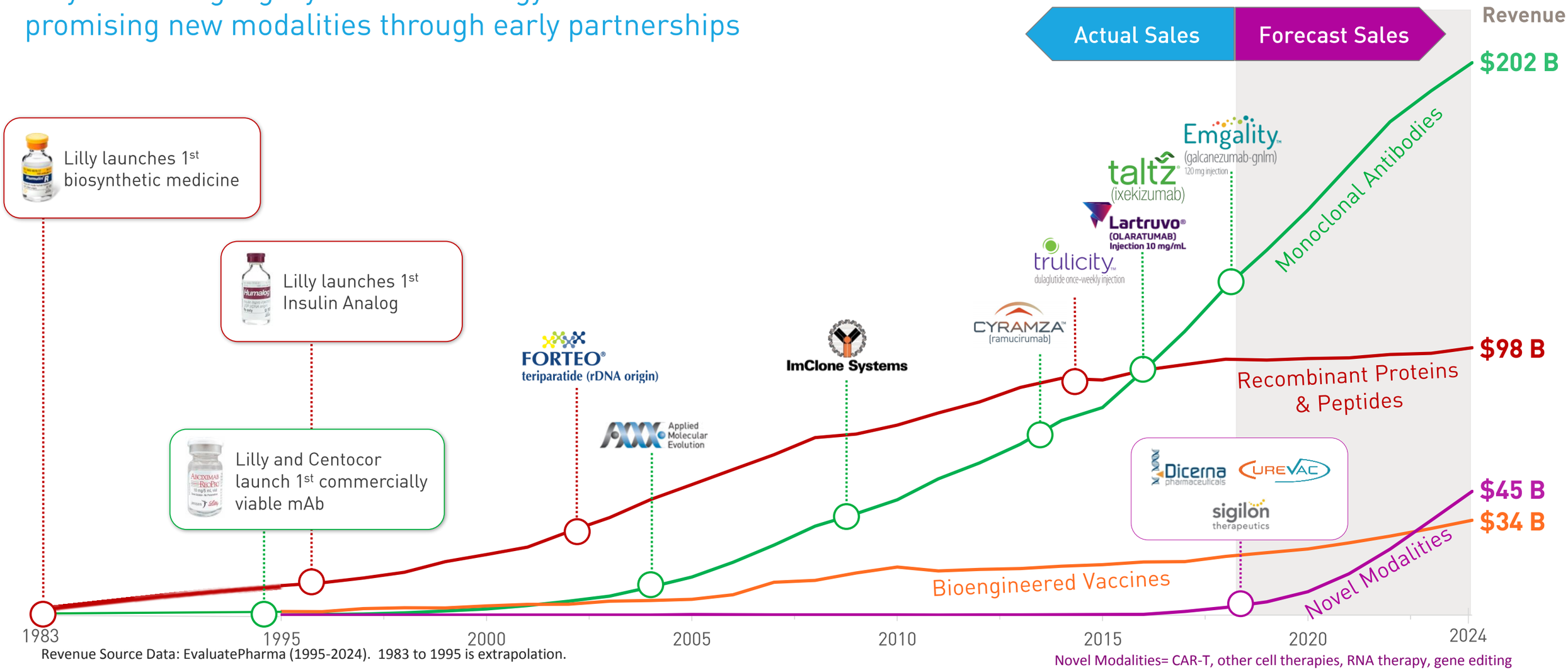
transcriptic
CytoSite Biopharma
Adimab
ABLEXIS
zymeworks

**Medicines**

ARMO BIOSCIENCES — Pegilodecakin
NEKTAR — IL-2 Conjugate
AurKa Pharma Inc. — Aurora A Kinase Inhibitor
CHUGAI — GLP-1 Non Peptide Agonist

# ACCESSING NOVEL MODALITIES

Lilly has a long legacy in biotechnology and will access promising new modalities through early partnerships




Revenue Source Data: EvaluatePharma (1995-2024). 1983 to 1995 is extrapolation.

Novel Modalities= CAR-T, other cell therapies, RNA therapy, gene editing

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# ONCOLOGY

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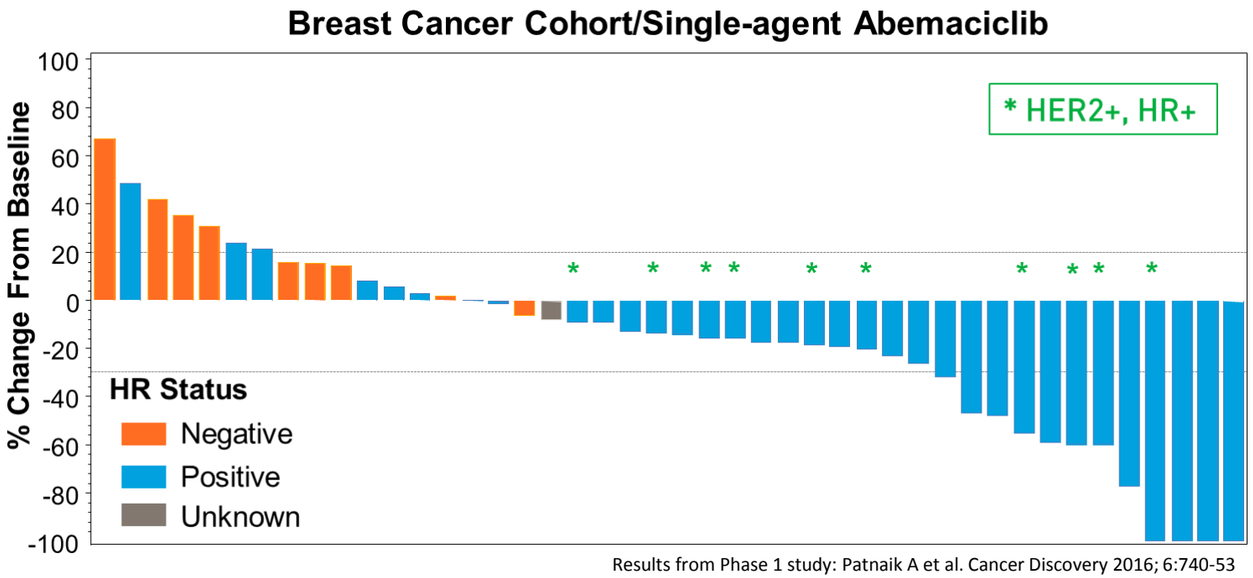
# VERZENIO
## FUTURE GROWTH CATALYSTS

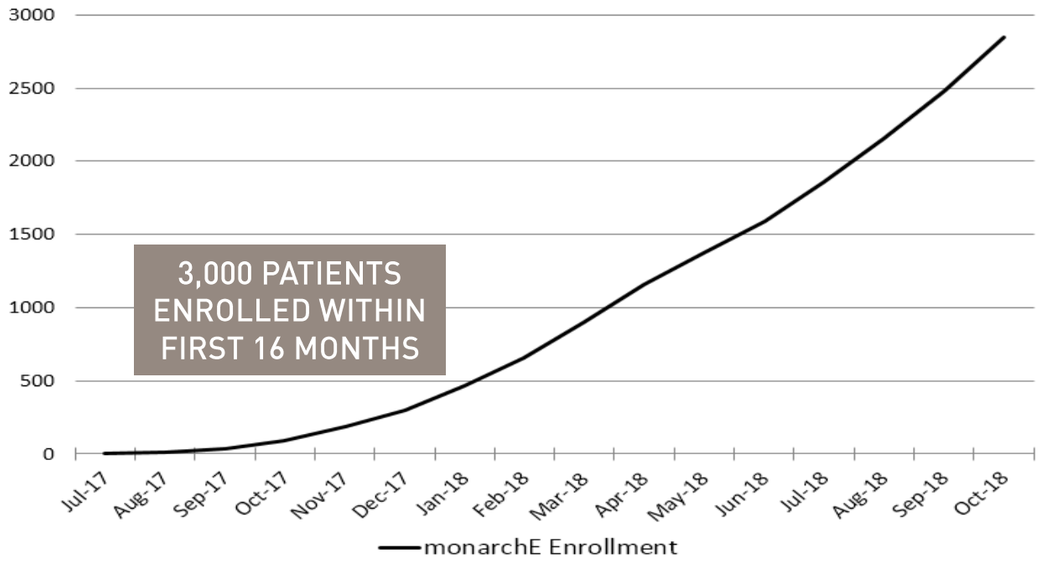
## HER2+




Results from Phase 1 study: Patnaik A et al. Cancer Discovery 2016; 6:740-53

- May expand potential metastatic breast cancer patient population for Verzenio (~15%-20% of MBC market)
- Phase 2 trial readout in early 2019

## ADJUVANT




- MonarchE could significantly expand Verzenio's eligible patient population in a much longer treatment setting
- Phase 3 trial readout in 2021

**MONARCH-2 Overall Survival (OS) Readout Expected in 2020**

# PEGILODECAKIN
## MOLECULE OVERVIEW

### PEGILODECAKIN

**BIOLOGIC RATIONALE**

Increases (neo)antigen-activated, intra-tumoral CD8+ T cells

Achieves tumor-specific T cell expansion by a distinct mechanism form immune checkpoint blockade

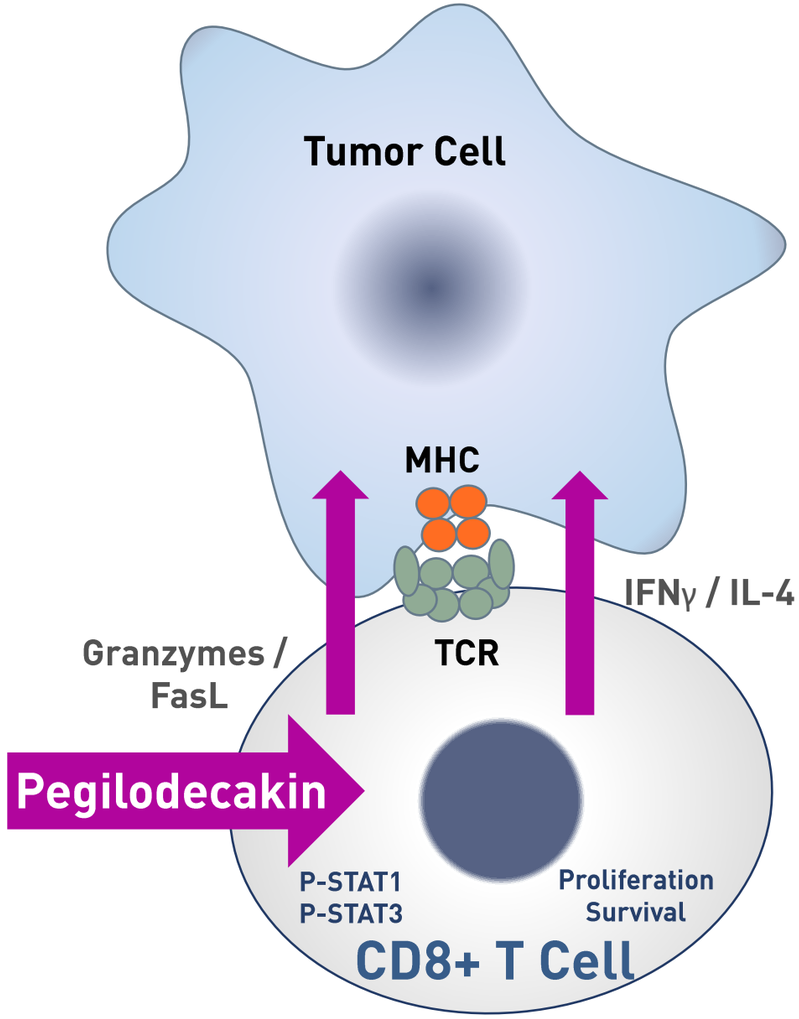
Reduces inflammatory cytokine responses

**OPPORTUNITY**

Strong biological rationale for "foundational" potential

First-in-class positioning

Potential for impact across multiple cancer types



# PEGILODECAKIN
## DEVELOPMENT PROGRAM

## ONGOING CLINICAL PROGRAM

### CYPRESS 1: 1L NSCLC Phase 2
- Combo with pembrolizumab, ›50% PDL1
- Topline results late 2019

### CYPRESS 2: 2L NSCLC Phase 2
- Combo with nivolumab, IO Naive, ‹50% PDL1
- Topline results late 2019

### SEQUOIA: 2L Pancreatic Cancer Phase 3
- Combo with FOLFOX
- Topline results mid-2020

## FUTURE OPPORTUNITIES

### Non-Small Cell Lung Cancer (NSCLC)
- Positive data would trigger additional lung cancer trials
- 1L in multiple PD-L1 selection settings
- 2L IO refractory

### Renal Cell Carcinoma (RCC)
- Monotherapy activity in Phase 1
- Plan to start Phase 2 in 2019

### Pancreatic Cancer
- Positive 2L data would trigger move into 1L

### Additional tumor types
- Biomarker-guided exploratory studies in other tumor types under consideration

# ONCOLOGY PORTFOLIO
## UPCOMING EARLY-STAGE READOUTS

### TIM-3 ANTIBODY

**BIOLOGIC RATIONALE**

Immune checkpoint receptor often expressed in exhausted T-cell populations

May enhance the antitumor activity of exhausted CD8+ T-cells

**OPPORTUNITY**

Monotherapy and in combo with PD-L1

A novel bispecific antibody now in Phase 1

**DEVELOPMENT**

Phase 1 readouts expected in 2019

Identifying biomarkers is a key focus

### AURORA A KINASE INHIBITOR

**BIOLOGIC RATIONALE**

Key roles in cell division by controlling chromosomal segregation

Tumors with Rb1 loss, MYC amplification and/or AurA overexpression may have heightened sensitivity

**OPPORTUNITY**

Selectivity which could be leveraged to reduce toxicity

First-in-class potential

**DEVELOPMENT**

Phase 1 readout expected in 2019

### PREXASERTIB

**BIOLOGIC RATIONALE**

CHK1 inhibition has shown efficacy in tumors with DNA repair defects or replicative stress

Active in BRCA wild-type high-grade ovarian cancer

**OPPORTUNITY**

Potential biomarker-driven opportunities in ovarian cancer and other indications

First-in-class potential

**DEVELOPMENT**

Phase 2 read out expected in 2019

# PAIN

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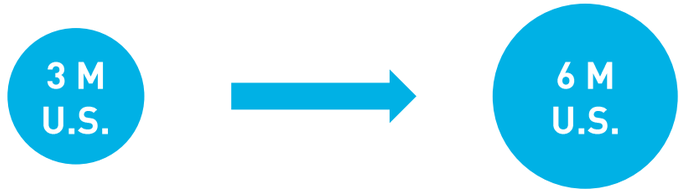
# EMGALITY AND LASMIDITAN
## FOCUSED ON SOLUTIONS FOR BOTH ACUTE AND PREVENTIVE MIGRAINE

## PREVENTIVE TREATMENT

**Currently on Treatment[1]** → **Treatment Eligible[1]**



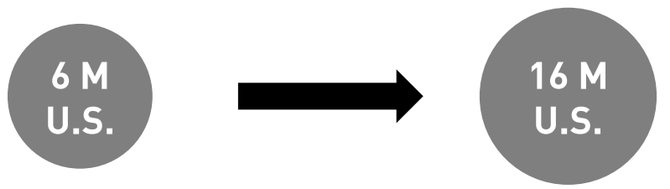

**Emgality: Compelling opportunity to address high unmet need**

**Episodic Cluster Headache**

- First therapy to show benefit in debilitating disease
- Patient population of nearly 400K in U.S. [3]
- Granted breakthrough therapy designation
- Submitted to FDA in Q4 2018

## ACUTE TREATMENT

**Currently on Treatment[1]** → **Diagnosed[1]**




**Unmet need for alternative options as 35-40% of those treating are not receiving an adequate response[2]**

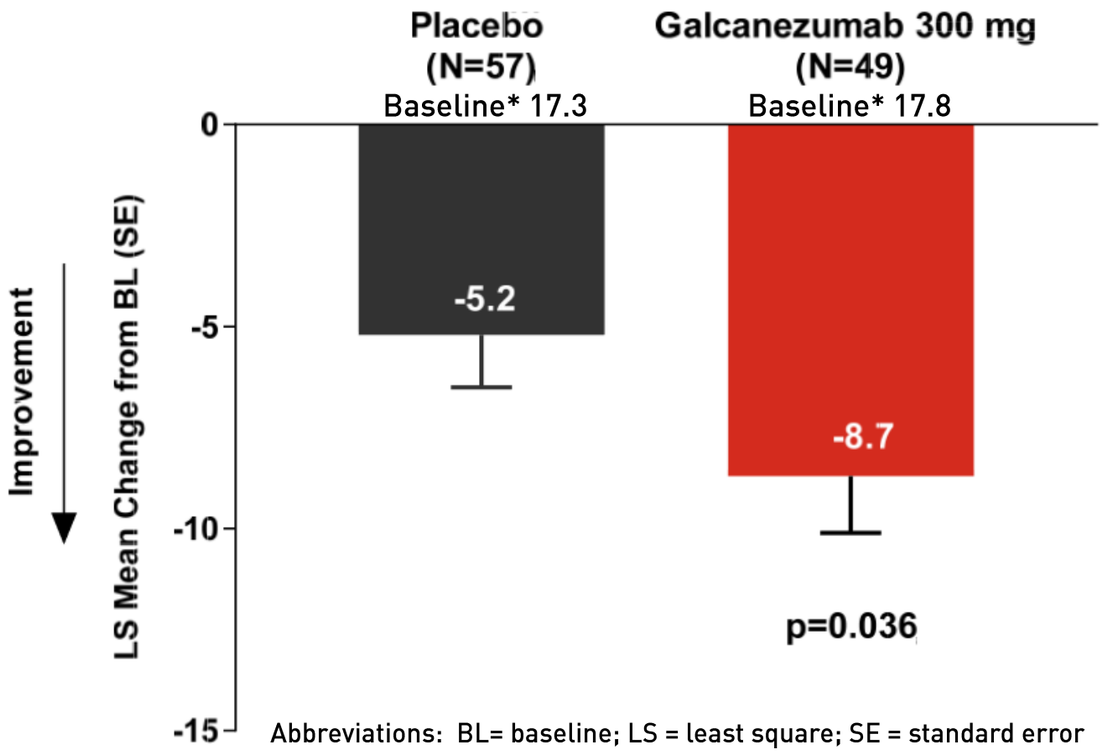
**Lasmiditan: would be first new mechanism approved for acute treatment of migraine in over 20 years**

*(1) Source: American Migraine Prevalence and Prevention Study*
*(2) Lombard et al. A Real-World Analysis of Unmet Needs in Migraine for Responders vs Non-Responders to Acute Treatment. AHS 2018*
*(3) Fischera M., Marziniak M., Gralow I., et al. The incidence and prevalence of cluster headache: a meta-analysis of population-based studies. Cephalalgia 2008; 28:614–18*

# EMGALITY
## EPISODIC CLUSTER HEADACHE

## EFFICACY

Mean Change from Baseline in Weekly Cluster Headache Attack Frequency across Weeks 1-3




Abbreviations: BL= baseline; LS = least square; SE = standard error

*Statistical Methods - mixed-effects model repeated measures analysis*

*Number of weekly cluster headache attacks in the baseline period, mean ± SD: Placebo 17.3 ± 10.1; Galcanezumab 17.8 ± 10.1

## ADVERSE EVENTS

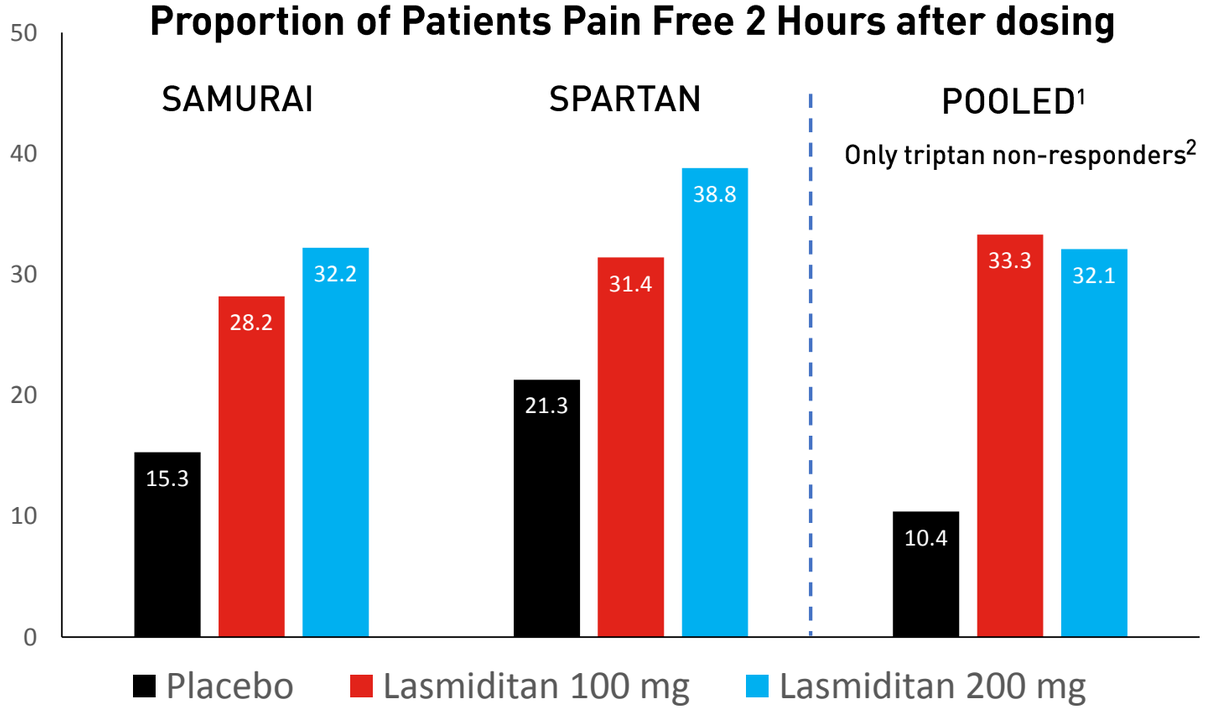
| Category[a] Preferred Term | n (%) Placebo (N=57) | Galcanezumab 300mg (N=49) |
|---|---|---|
| Deaths | 0 | 0 |
| Serious adverse events | 0 | 0 |
| Discontinuation due to adverse events | 1 (2) | 2 (4) |
| Vertigo | 0 | 1 (2) |
| Cluster headache | 1 (2) | 0 |
| Asthma | 0 | 1 (2) |
| TEAE | 19 (33) | 21 (43) |
| Common TEAEs | | |
| Injection site pain | 0 | 4 (8)* |
| Nasopharyngitis | 1 (2) | 3 (6) |
| Injection site swelling | 0 | 2 (4) |
| Pyrexia | 1 (2) | 2 (4) |

Abbreviations: N = number of patients in the safety population; n = number of participants within each specific category.
[a]Participant may be counted in more than one category. *p<.05 vs. placebo

No clinically meaningful differences between treatment groups for laboratory values, vital signs and ECG parameters.
No TE-ADA positive participants.

# LASMIDITAN
## EFFICACY IN PATIENTS WITH PRIOR TRIPTAN THERAPY

## PAIN FREEDOM AT 2 HOURS




1) Data from SAMURAI and SPARTAN pooled together for this subgroup analysis
2) Those patients identified as having triptan use within the past three months prior to SAMURAI or SPARTAN study initiation, who rated themselves as a non-responder to prior triptan treatments when asked by a physician.

## ADVERSE EVENTS

| | SAMURAI | | | SPARTAN | | |
|---|---|---|---|---|---|---|
| TEAEs | PBO (n=617) | L 100 mg (n=630) | L 200 mg (n=609) | PBP (n=645) | L 100 mg (n=635) | L 200 mg (n=649) |
| ›1 TEAEs | 16.0% | 36.3% | 42.2% | 11.6% | 36.1% | 39.0% |
| Dizziness | 3.4% | 12.5% | 16.3% | 2.5% | 18.1% | 18.0% |
| Paresthesia | 2.1% | 5.7% | 7.9% | 0.9% | 5.8% | 6.6% |
| Somnolence | 2.3% | 5.7% | 5.4% | 2.0% | 4.6% | 6.5% |
| Fatigue | 0.3% | 4.1% | 3.1% | 0.9% | 4.1% | 4.8% |
| Nausea | 1.9% | 3.0% | 5.3% | 1.2% | 3.3% | 2.6% |
| Lethargy | 0.3% | 1.9% | 2.5% | 0.2% | 1.3% | 2.2% |

# TANEZUMAB
## OSTEOARTHRITIS PAIN, CHRONIC LOWER BACK PAIN AND CANCER PAIN

## UNMET NEED

- **Osteoarthritis (OA) Pain**
  - Progressive disease that results in debilitation and ongoing pain
  - ~27 million people suffer from OA Pain in the U.S.[1]
- **Chronic Lower Back Pain (CLBP)**
  - Leading cause of disability in the U.S.
  - ~33 million people suffer from CLBP in the U.S.[2]
- **Physicians and patients consistently report low satisfaction with current pain treatments**
- **Patients in the tanezumab OA and CLBP studies typically have had pain for several years and have experienced inadequate pain relief or intolerance to at least 3 different classes of analgesics**

## PHASE 3 READOUTS

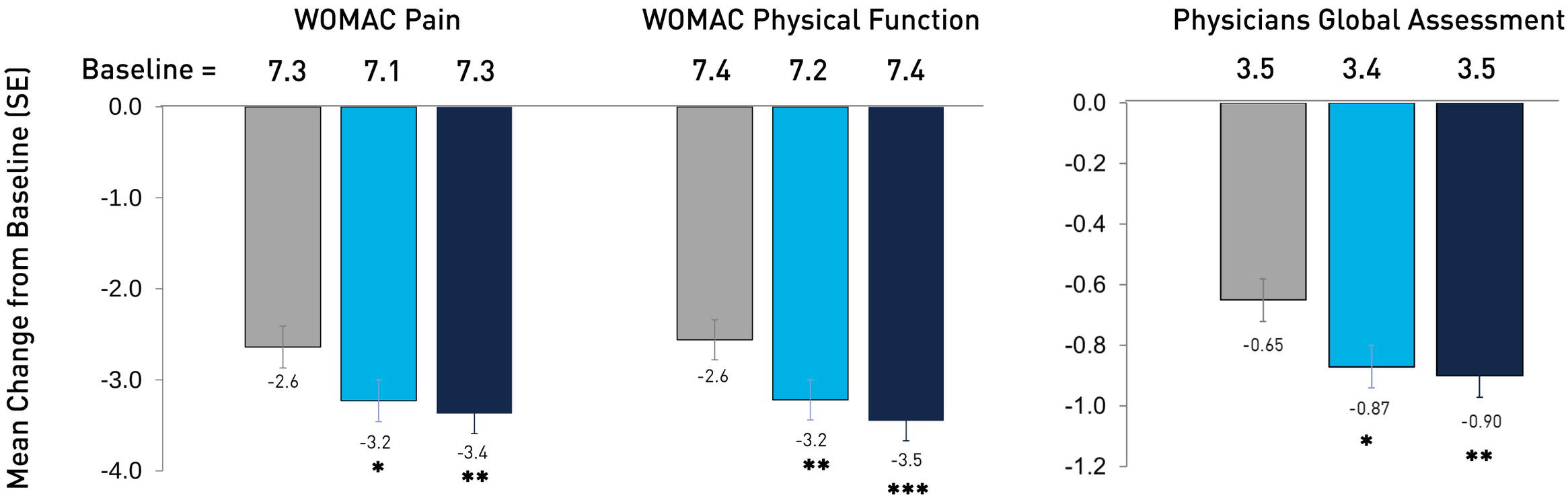
| 2017 | 2018 | 2019 | 2020 |
|---|---|---|---|

| | |
|---|---|
| Study 1056: OA Dose Titration | √ Data presented at American College of Rheumatology (ACR) 2018 |
| Study 1057: OA 24 Week Efficacy and Safety | Topline expected 1H 2019 |
| Study 1058: OA Long-Term Efficacy & Safety | Topline expected 1H 2019 |
| Study 1059: CLBP | Topline expected 1H 2019 |

(1) OA Research Society International, Arthritis Foundation, International Association for the Study of Pain, ACR Lawrence RC et all 2008, Veteran Affairs Department of Defense, Ma et al etc.
(2) Decision Resources

# TANEZUMAB
## STUDY 1056: CO-PRIMARY EFFICACY ENDPOINTS

## Both tanezumab treatment groups met co-primary endpoints for study




*p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001 vs placebo
Intent to Treat population; multiple imputation

placebo (n=232) tanezumab 2.5 mg (n=231) tanezumab 2.5/5 mg (n=233)

WOMAC = Western Ontario & McMaster Universities Osteoarthritis Index

# TANEZUMAB
## STUDY 1056: JOINT SAFETY EVENTS AND TOTAL JOINT REPLACEMENTS

### SUMMARY OF ADJUDICATED JOINT SAFETY EVENTS

| Number (%) of patients | placebo n = 232 | tanezumab 2.5 mg n = 231 | tanezumab 2.5/5 mg n = 233 |
|---|---|---|---|
| Adjudicated joint safety events | 5 (2.2) | 14 (6.1) | 18 (7.7) |
| Normal progression of OA | 5 (2.2) | 8 (3.5) | 17 (7.3) |
| Rapidly progressive OA type 1 | 0 | 3 (1.3) | 1 (0.4) |
| Rapidly progressive OA type 2 | 0 | 2 (0.9) | 0 |
| Primary osteonecrosis | 0 | 0 | 0 |
| Other (pre-existing SIF) | 0 | 1 (0.4) | 0 |

*SIF = subchondral insufficiency fracture*

- Both RPOA-2 events occurred in index joints that were K-L Grade 4 at screening
- All RPOA-1 events occurred in joints with K-L Grade 2-3 OA at screening and 3/4 occurred in index joint
- One patient each with RPOA-1 and RPOA-2 events had a TJR in that joint

### SUMMARY OF TOTAL JOINT REPLACEMENTS

| Number (%) of patients | placebo n = 232 | tanezumab 2.5 mg n = 231 | tanezumab 2.5/5 mg n = 233 |
|---|---|---|---|
| Total joint replacements | 4 (1.7) | 8 (3.5) | 16 (6.9) |
| Knee | 4 | 3 | 9[a] |
| Hip | 0 | 5 | 7 |

In the patients who had TJRs:

- All joints with surgeries were K-L Grade 3 of 4 at screening
- Surgeries were primarily in study index joint (26 / 28 patients; 93%)
- Events were adjudicated as normal OA progression (26 / 28 patients; 93%)
- Surgeries were elective (21 / 28 patients; 75%)
- Occurred after completion of the treatment period (19 / 28 patients; 68%)

**The cause of the treatment imbalance in this study is not known, but it is inconsistent with prior tanezumab studies**

[a]One patient had 2 total knee replacements, both of which were K-L 4 at baseline and adjudicated as normal progression of OA

# NEURODEGENERATION

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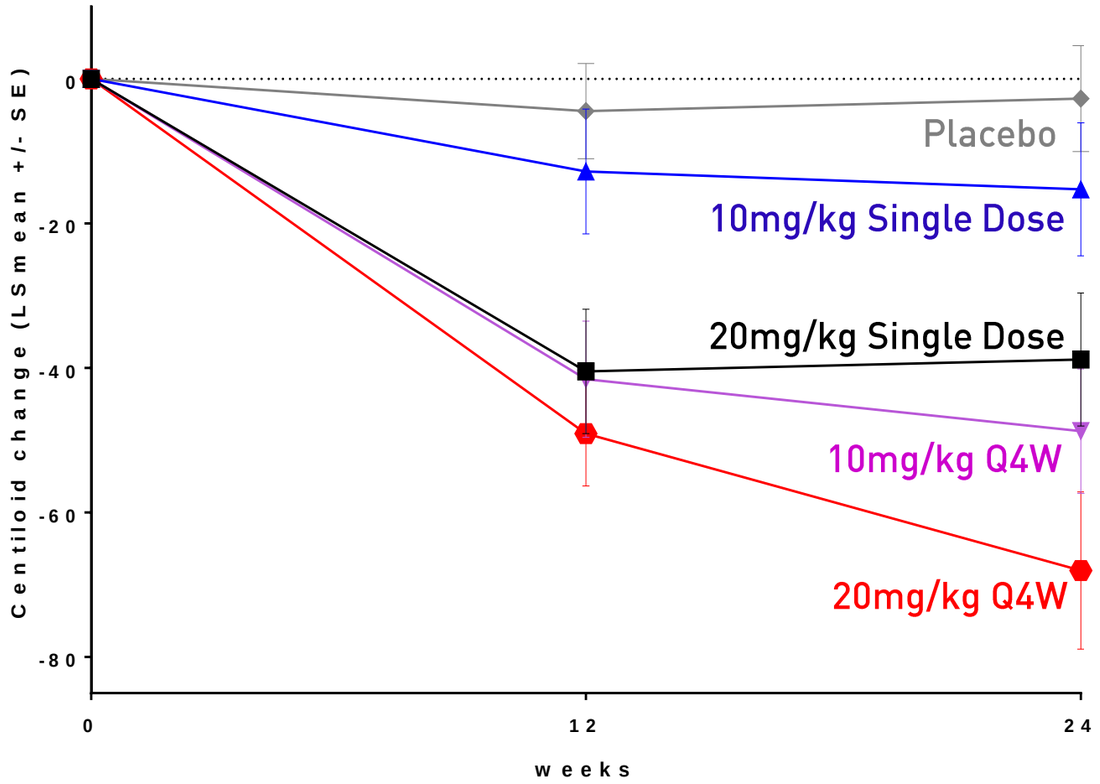
# N3PG Aβ ANTIBODY
## DISEASE MODIFICATIONS FOR ALZHEIMER'S

## PHASE 1 DATA

### Rapid Clearance of Amyloid after N3pG Antibody Treatment




## PHASE 2 DESIGN

**Target Population**
- Early symptomatic Alzheimer's Disease
- Amyloid positive
- Low-medium tau burden

**Enrollment**
- Randomized, placebo-controlled
- Double arm trial, 133 patients/arm
- Complete enrollment targeted for Q1 2019

**Primary endpoint is integrated Alzheimer's Disease Rating Scale (iADRS) at 18 months**

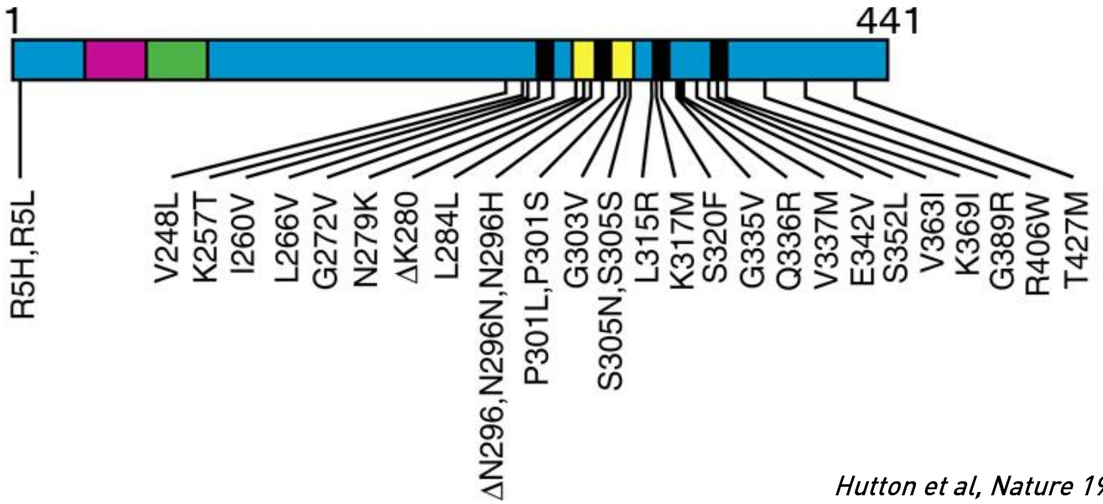
**Expected to readout in 2020**

# TAU PATHOLOGY AS A THERAPEUTIC TARGET

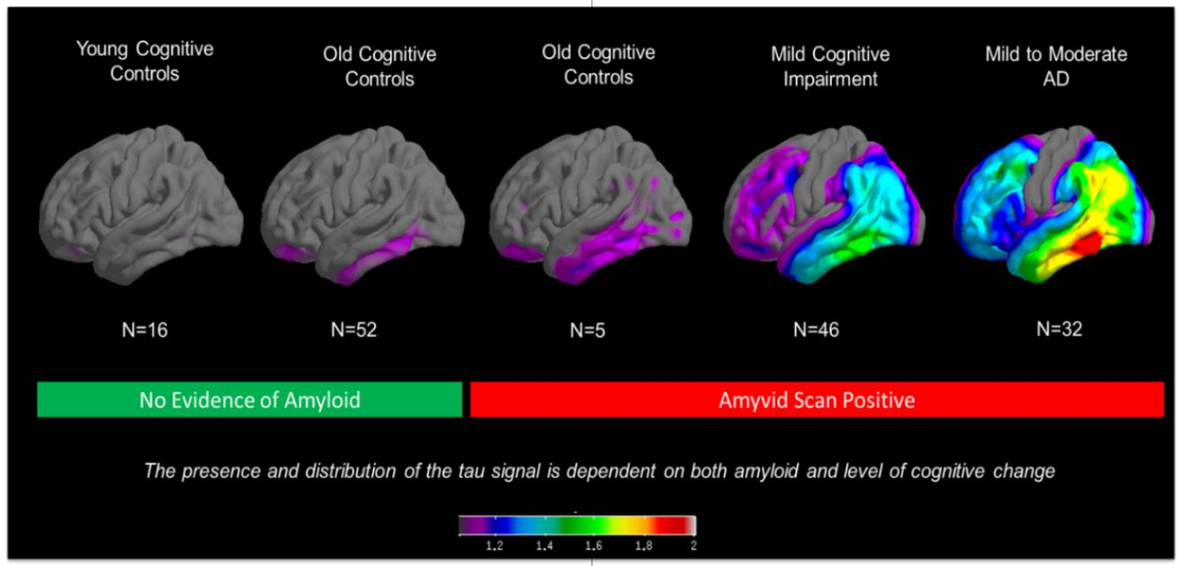
## HUMAN GENETIC, NEUROPATHOLOGICAL AND IMAGING EVIDENCE

## MUTATIONS IN MAPT CAUSE NEURODEGENERATION

(Frontotemporal Dementia linked to Chr17)




## TAU PATHOLOGY CORRELATES WITH AD CLINICAL PROGRESSION

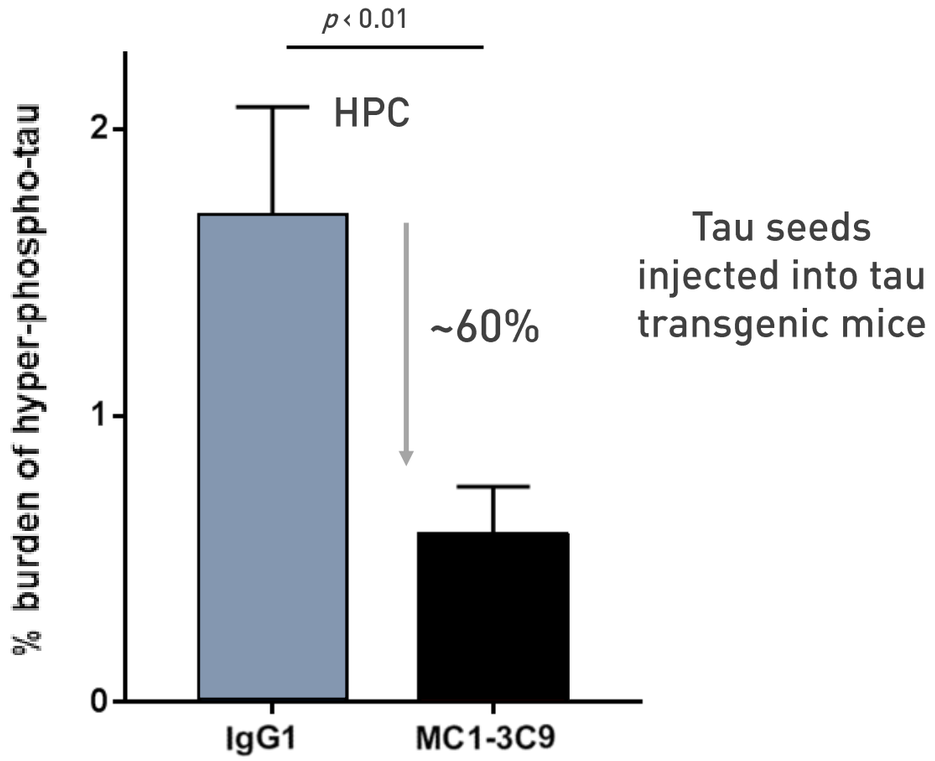



*Hutton et al, Nature 1998; Goedert, Mov. Disord 2005*

# ANTI-TAU ANTIBODY
## DISEASE MODIFICATION FOR ALZHEIMER'S

## PRE-CLINICAL DATA

Tau Spread Model: Reduction of Tau Pathology




Tau seeds injected into tau transgenic mice

*MC1-3C9 is a mouse tau antibody surrogate; HPC = hippocampus*

## PHASE 2 DESIGN

**Target Population**
- Early symptomatic Alzheimer's Disease
- Low-medium tau burden

**Enrollment**
- Randomized, placebo-controlled
- 285 patients, 95/arm
- Studying low and high dose

**Primary endpoint is integrated Alzheimer's Disease Rating Scale (iADRS) at 18 months**

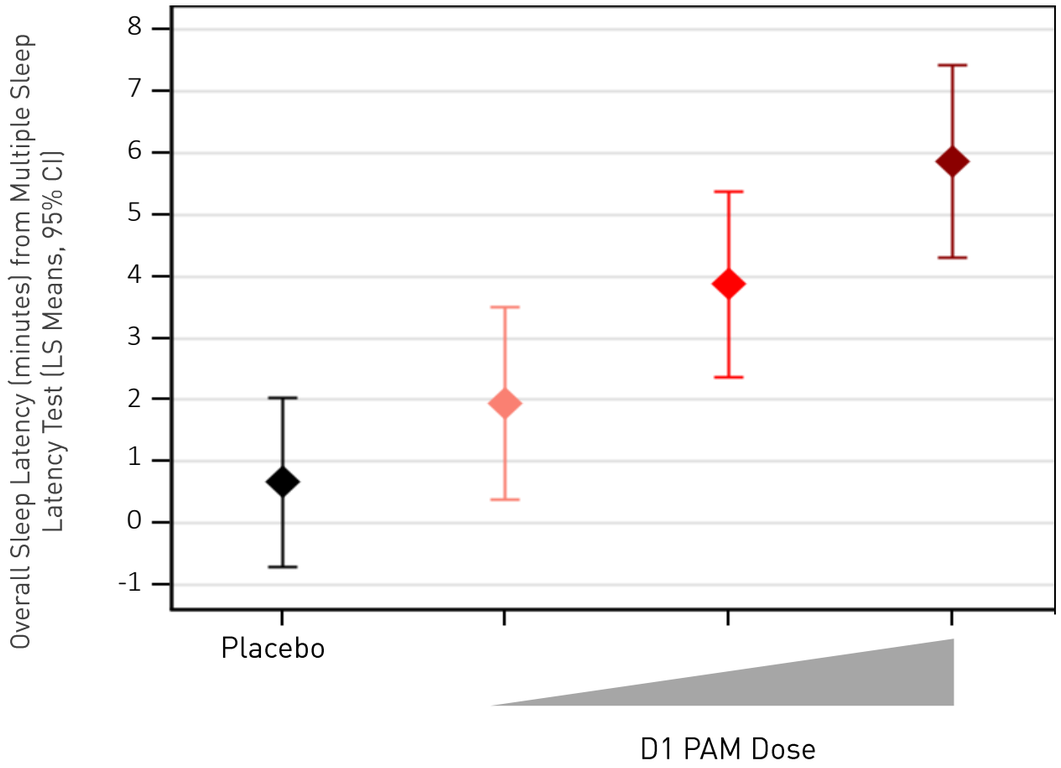
**Expected to readout in 2021**

# D1 POSITIVE ALLOSTERIC MODULATOR (PAM)

## POTENTIAL FIRST-IN-CLASS SYMPTOMATIC TREATMENT FOR DEMENTIAS

## PHASE 1 DATA

D1 PAM increases sleep latency




Evidence of target engagement and central pharmacology

## PHASE 2 DESIGN

**Target Population**

- Mild-to-moderate Parkinson's disease dementia

**Enrollment**

- Randomized, placebo-controlled trial
- Studying low, mid and high dose
- 340 patients, 85 patients/arm

**Primary endpoint is change from baseline in Continuity of Attention (CoA) Composite Score of the Cognitive Drug Research Computerized Cognition Battery at 12 weeks (2 week follow-up period)**

**Expected to readout in 2019**

# IMMUNOLOGY

Lilly

2018 INVESTMENT COMMUNITY MEETING

# OLUMIANT DEVELOPMENT PROGRAM SUMMARY

## Rheumatoid Arthritis

- Launched in EU & Japan in 2017
- Launched in U.S. in May 2018 (2 mg only)

## Alopecia Areata

- Phase 2/3 adaptive program initiated Q3 2018
- Top line data expected 2020

## Atopic Dermatitis

- Ongoing Phase 3 program
- Top line data starting 1H 2019

## Systemic Lupus Erythematosus (SLE)

- Ongoing Phase 3 program
- Top line data expected 2021

# OLUMIANT
## ATOPIC DERMATITIS

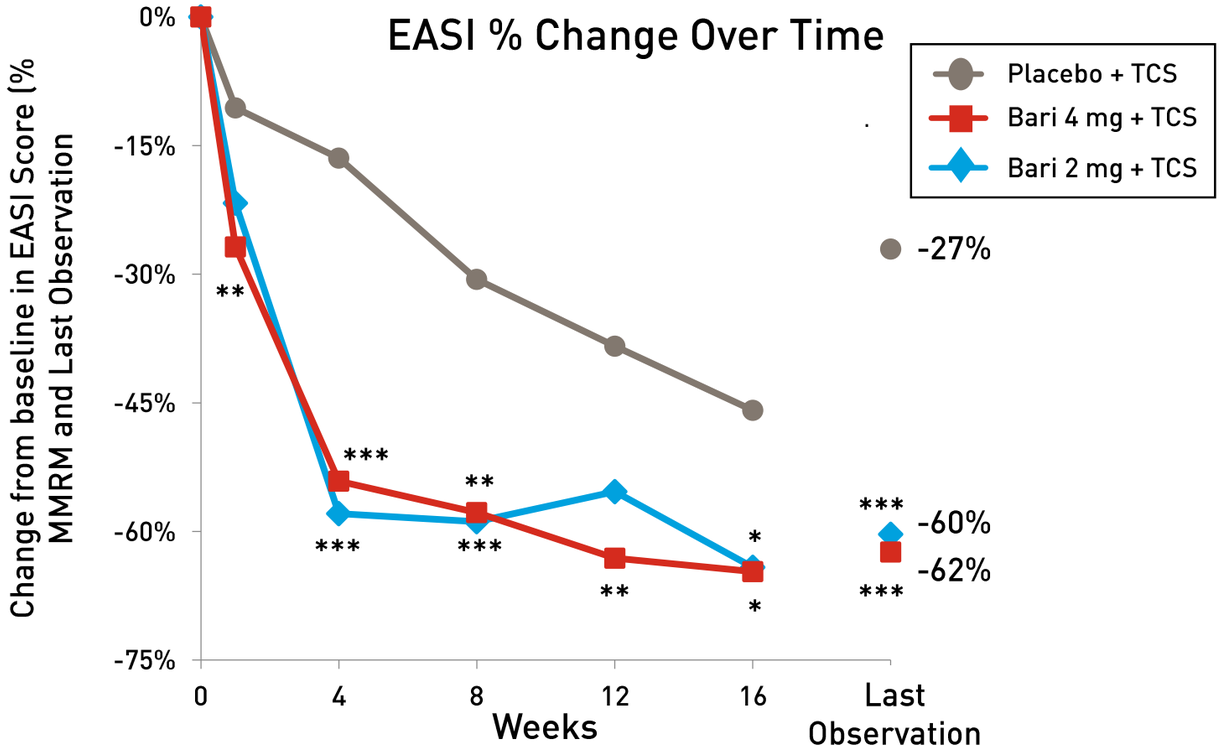
## SIGNIFICANT UNMET NEED

- **Unmet need**
  - Most common inflammatory skin disease in adults and children
  - U.S. population affected by atopic dermatitis estimated to be 18 million (›2x psoriasis)
- **Lack of new therapies**
  - Increased patient and physician awareness as new agent launched in 2017
- **U.S. market growth for new systemic therapies**
  - Atopic dermatitis market projected to grow to $8+ billion by 2027
- **Potential to be first-in-class treatment and first oral treatment available**
  - Top line data expected 1H 2019

Source: LLY Estimates combined w/ external sources (IQVIA, Evaluate Pharma, etc.)

## PHASE 2 DATA

**Robust Phase 2 efficacy with rapid reduction in itch and disease activity with convenience of oral dosing**




Weeks 0-16 analyzed with MMRM; last observation is Week 16 ANCOVA; p-value vs placebo: *p≤0.05, **p≤0.01, ***p≤0.001
ANCOVA=analysis of covariance; EASI=Eczema Area and Severity Index; mMRM=mixed-effects model of repeated measures

# OLUMIANT
## SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

## SIGNIFICANT UNMET NEED

**Unmet need**
- Chronic, multi-organ autoimmune disease that can cause widespread tissue and organ damage
- U.S. population affected by SLE estimated to be 450-670K

**Lack of new therapies**
- Significant unmet need and lack of innovation

**U.S. market growth for new systemic therapies**
- SLE market projected to grow to nearly $4 billion by 2027

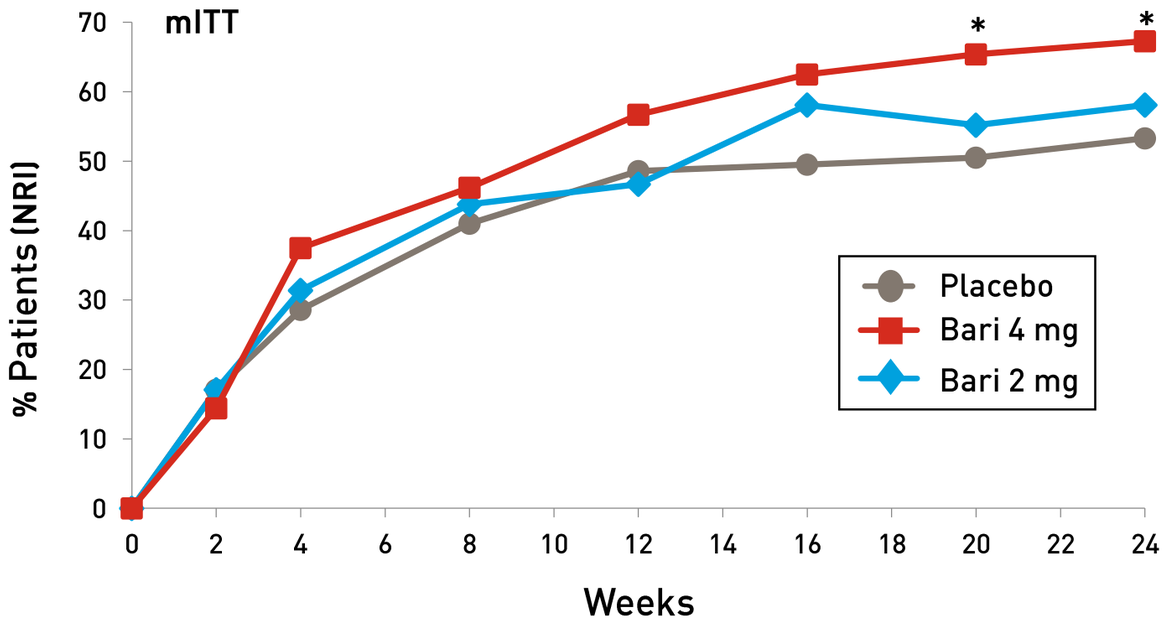
**Potential to be first-in-class treatment and first oral treatment available**
- Top line data expected 2021
- Fast Track designation granted by FDA

Source: LLY Estimates combined w/ external sources (IQVIA, Evaluate Pharma, etc.)

## PHASE 2 DATA

Promising Phase 2 efficacy with convenience of oral dosing

**Remission of Arthritis and/or Rash over time (SLEDAI-2K)**




p-value vs. PBO: *p≤0.05

mITT=modified intention to treat population; NRI=nonresponder imputation; SLEDAI-2K=Systemic Lupus Erythematosus Disease Activity Index 2000;

# OLUMIANT
## SAFETY

## ATOPIC DERMATITIS PHASE 2

| Characteristics, n (%) | Placebo plus TCS N = 49 | Baricitinib 2 mg plus TCS N = 37 | Baricitinib 4 mg plus TCS N = 38 |
|---|---|---|---|
| At least 1 TEAE | 24 (49) | 17 (46) | 27 (71) |
| At least 1 treatment-emergent SAE | 0 | 0 | 1 (3) |
| TEAE resulting in death during treatment & follow-up period | 0 | 0 | 0 |
| TEAE leading to treatment discontinuation | 5 (10) | 1 (3) | 5 (13) |
| **TEAEs in ›5% patients per treatment group** | | | |
| Headache | 0 | 2 (5) | 5 (13) |
| Blood creatine phosphokinase increased | 0 | 1 (3) | 5 (13) |
| Nasopharyngitis | 1 (2) | 1 (3) | 3 (8) |
| Dermatitis atopic | 4 (8) | 1 (3) | 0 |
| Cellulitis | 3 (6) | 1 (3) | 0 |
| Lymphopenia | 3 (6) | 0 | 0 |

TCS=topical corticosteroids; TEAE=treatment-emergent adverse event; SAE = serious adverse event

## LUPUS PHASE 2

| Weeks 0-24[a] | Placebo (N=105) | Baricitinib 2-mg (N=105) | Baricitinib 4-mg (N=104) |
|---|---|---|---|
| SAEs | 5 (4.8) | 11 (10.5) | 10 (9.6) |
| TEAEs | 68 (64.8) | 75 (71.4) | 76 (73.1) |
| Mild | 36 (34.3) | 35 (33.3) | 38 (36.5) |
| Moderate | 29 (27.6) | 35 (33.3) | 31 (29.8) |
| Severe | 3 (2.9) | 5 (4.8) | 7 (6.7) |
| Infections | 41 (39.0) | 47 (44.8) | 47 (45.2) |
| Serious infections | 1 (1.0) | 2 (1.9) | 6 (5.8) |
| Herpes Zoster | 1 (1.0) | 0 | 1 (1.0) |
| Tuberculosis | 0[b] | 0 | 0 |
| Malignancy | 0 | 0 | 0 |
| DVT | 0 | 0 | 1 (1.0)[c] |
| MACE[d] | 0 | 0 | 0 |
| Discontinuation due to AE | 4 (3.8) | 10 (9.5) | 11 (10.6) |
| Treatment interruption due to AE | 11 (10.5) | 7 (6.7) | 21 (20.2) |
| Death | 0 | 0 | 0 |

Data are n (%). AE=adverse event; DVT=deep vein thrombosis; MACE=major adverse cardiovascular event; SAE=serious adverse event; TB=tuberculosis; TEAE=treatment-emergent adverse event. [a]Includes up to 30 days post-treatment. [b]One patient with latent TB (based on a positive QuantiFERON-TB Gold test result after randomization). [c]Patient had pre-existing antiphospholipid antibodies. [d]Non-adjudicated.

# MIRIKIZUMAB DEVELOPMENT PROGRAM SUMMARY

## Psoriasis

- Initiated Phase 3 program in 2018
- Top line data expected 2020

## Ulcerative Colitis

- Potential first in class
- Initiated Phase 3 program in 2018
- Top line data expected 2021

## Crohn's Disease

- Ongoing Phase 2 program
- Top line Phase 2 data expected 1H 2019
- Potential Phase 3 initiation 2019

# MIRIKIZUMAB
## PSORIASIS

## IL-23 IN DERMATOLOGY

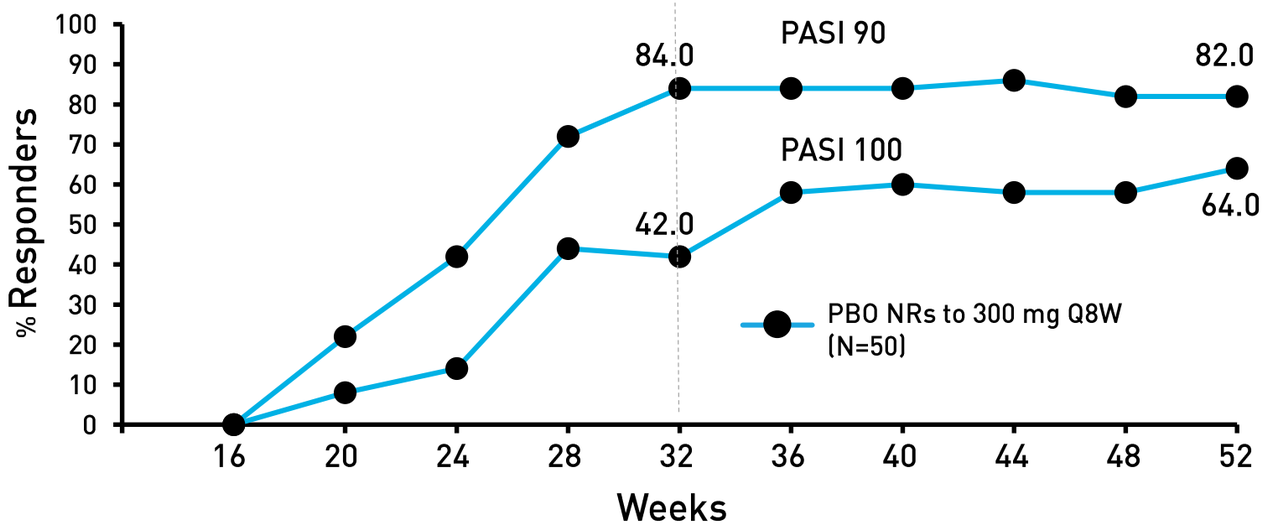
- **Unmet need**
  - Different mechanisms provide patients with flexibility and options
  - Lilly has both an IL-17 and IL-23p 19
- **Sustained efficacy**
  - Mirikizumab could allow patients to get more clearance and maintain clear skin in a stable way over time
- **U.S. market growth for new systemic therapies**
  - U.S. population affected by Psoriasis estimated at more than 7 million
  - Psoriasis market projected to grow to over $16 billion by 2027
- **Top line data expected 2020**

Source: LLY Estimates combined w/ external sources (IQVIA, Evaluate Pharma, etc.)

## PHASE 2 DATA

**Robust Phase 2 efficacy with significant portion of patients achieving PASI 100**

PASI 90 and PASI 100 Response Rates (NRI) Among Patients Initially Assigned PBO Then Receiving Continuous Therapy Beginning Week 16




PASI=Psoriasis Area and Severity Index; PBO=Placebo; NRI=Nonresponder Imputation; Q8W=Every 8 Weeks.

# MIRIKIZUMAB PSORIASIS PHASE 2 SAFETY DATA

## MOST COMMON TEAEs (>5% IN TOTAL 300MG SC Q8W) THROUGH WEEK 52

| Adverse Event | Placebo to Miri 300 mg Q8W (N=50) n (%) | Miri 30 mg Q8W to 300 mg Q8W (N=34) n (%) | Miri 100 mg Q8W to 300 mg Q8W (N=21) n (%) | Miri 300 mg Q8W to 300 mg Q8W (N=15) n (%) | Total Miri 300 mg Q8W (N=120) n (%) |
|---|---|---|---|---|---|
| Nasopharyngitis | 9 (18.0) | 8 (23.5) | 4 (19.0) | 4 (26.7) | 25 (20.8) |
| Upper respiratory tract infection | 7 (14.0) | 2 (5.9) | 2 (9.5) | 1 (6.7) | 12 (10.0) |
| Arthralgia | 2 (4.0) | 2 (5.9) | 3 (14.3) | 1 (6.7) | 8 (6.7) |
| Injection site pain | 3 (6.0) | 2 (5.9) | 2 (9.5) | 0 | 7 (5.8) |
| Urinary tract infection | 2 (4.0) | 1 (2.9) | 1 (4.8) | 2 (13.3) | 6 (5.0) |
| Back pain | 0 | 3 (8.8) | 3 (14.3) | 0 | 6 (5.0) |
| Headache | 3 (6.0) | 2 (5.9) | 1 (4.8) | 0 | 6 (5.0) |
| Hypertension | 3 (6.0) | 2 (5.9) | 0 | 1 (6.7) | 6 (5.0) |

- Four (3.3%) patients experienced SAEs and 6 (5.0%) patients discontinued the study due to AEs in this group of patients during Wks 16-52
- TEAEs= treatment emergent adverse events; SC= subcutaneous; Q8W= every 8 weeks; AEs= Adverse events; SAEs= Serious adverse events
- Papp, K.. et al. Poster presented at the 27th European Academy of Dermatology and Venereology Congress, Sept. 12-16, 2018; Paris.

# MIRIKIZUMAB
## ULCERATIVE COLITIS (UC)

## HIGH UNMET NEED

**Unmet need**
- More effective relief
- Greater maintenance and stability of efficacy over time
- Well tolerated options
- Avoidance of surgery and need for colostomy bags

**U.S. market growth for new systemic therapies**
- Increasing incidence of UC globally
- ~700k affected by UC in the U.S.
- Market projected to be over $6 billion by 2027

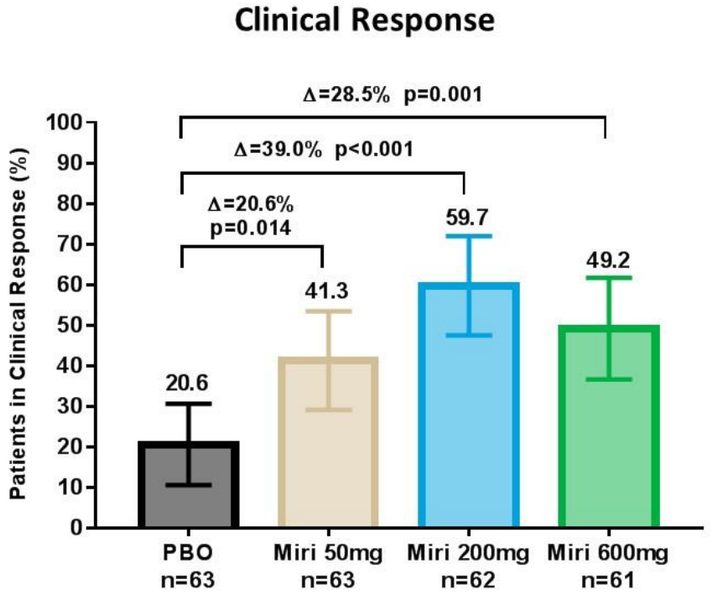
**Potential First-in-Class; topline data expected 2021**

*Source: LLY Estimates combined w/ external sources (IQVIA, Evaluate Pharma, etc.)*

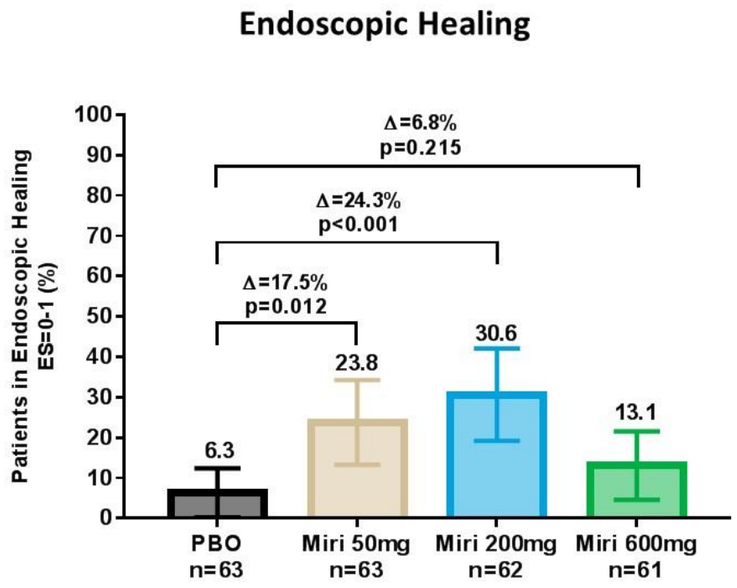
Not for promotional use

## PHASE 2 INDUCTION DATA

Strong Phase 2 efficacy in 12 week induction phase with high level of response




A decrease in the 9-point modified Mayo score (comprised of rectal bleeding, stool frequency and the endoscopic findings) inclusive of >= 2 points and >=35% from baseline with either a decrease of rectal bleeding subscore of >=1 or rectal bleeding subscore of 0 or 1




Mayo modified endoscopic subscore of 0 or 1

- Non-responder Imputation: all patients who discontinued from the study at any time prior to week 12 for any reason or failed to have an adequate week 12 efficacy assessment were considered non-responders at week 12.
- The miri 50mg and miri200mg groups incorporated exposure-based dosing yielding in average induction doses of 100mg and 250mg respectively.

# MIRIKIZUMAB
## ULCERATIVE COLITIS PHASE 2 SAFETY DATA

| | Placebo IV Q4W (n=63) | Miri IV Q4W 50 mg (n=63) | Miri IV Q4W 200 mg (n=62) | Miri IV Q4W 600 mg (n=60) |
|---|---|---|---|---|
| TEAEs, n (%) | 32 (50.8) | 36 (57.1) | 32 (51.6) | 32 (53.3) |
| Serious adverse event, n (%) | 2 (3.2) | 0 (0) | 2 (3.2) | 3 (5.0) |
| Discontinuations due to adverse event, n (%) | 3 (4.8) | 0 (0) | 1 (1.6) | 2 (3.3) |
| Most common TEAEs (≥5% in any dose group)* | | | | |
| Nasopharyngitis | 6 (9.5) | 5 (7.9) | 3 (4.8) | 5 (8.3) |
| Worsening of ulcerative colitis | 6 (9.5) | 2 (3.2) | 2 (3.2) | 2 (3.3) |
| Anemia | 3 (4.8) | 4 (6.3) | 2 (3.2) | 2 (3.3) |
| Headache | 3 (4.8) | 3 (4.8) | 1 (1.6) | 4 (6.7) |
| Nausea | 4 (6.3) | 2 (3.2) | 2 (3.2) | 3 (5.0) |
| Cough | 4 (6.3) | 0 | 0 | 2 (3.3) |
| Gastroenteritis | 1 (1.6) | 0 | 2 (3.2) | 3 (5.0) |

*presented as most to least frequent among all treatment groups combined

# MIRIKIZUMAB
## CROHN'S DISEASE

## HIGH UNMET NEED

**Unmet need for:**
- More effective relief
- Greater maintenance and consistency of efficacy
- Well tolerated options
- Avoidance of surgery and need for colostomy bags

**U.S. market growth for new systemic therapies**
- U.S. population affected by Crohn's disease estimated to be ~700k
- Crohn's disease market projected to grow to over $12 billion by 2027

*Source: LLY Estimates combined w/ external sources (IQVIA, Evaluate Pharma, etc.)*

## PHASE 3 EFFICACY HURDLE

**Seeking Remarkable, Durable Efficacy**

**Phase 3 Decision**
- High bar for moving to Phase 3
- Similar to UC, looking for efficacy above competition, approved or Phase 3 data

**Key Measures of Efficacy**
- Symptomatic Remission at week 12 (Stool Frequency + Abdominal Pain)
- Endoscopic Response at week 12

**Phase 2 readout expected in 2019**

# DIABETES

Lilly

2018 INVESTMENT COMMUNITY MEETING

# INSULINS: MOLECULE INNOVATION

## NEW MEALTIME INSULINS

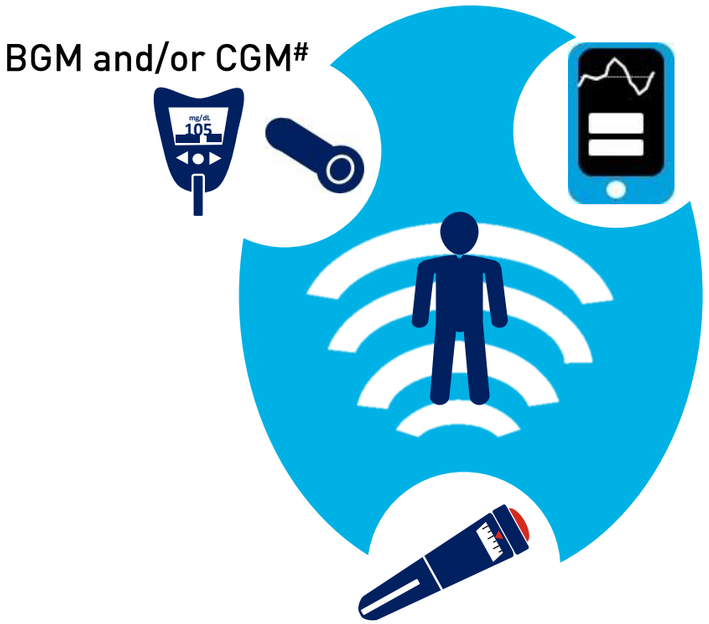
- **Improved control with comparable or lower risk of hypoglycemia**
  - Post-prandial glucose, time in range, and potentially A1c
- **Dosing and administration allow better fit into life**
- **Ultra-Rapid Lispro (URLi)**
  - Positive Phase 3 readouts in 2018
  - Continued development in pediatrics/pump in 2019
  - Submission planned for 2019

## NEW BASAL INSULINS

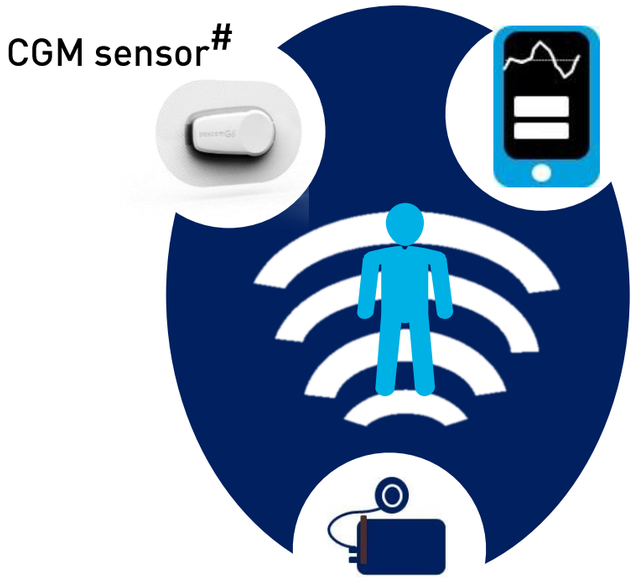
- **Improved patient experience leading to improved outcomes**
- **Basal Insulin-Fc**
  - Convenience and simplicity of once weekly dosing
  - Initiated Phase 2 in Q4 2018
- **Basal Insulin Acylated**
  - Best-in-class insulin analog for once daily dosing
  - Improved PK/PD profile with reduced hypoglycemia profile
  - Initiated Phase 1 in Q4 2018

# INSULINS: DELIVERY & DEVICE INNOVATION

## CONNECTED PENS




## CONNECTED PUMPS




**Connected Care portfolio expected to launch in stages over 3 years starting in 2019**

BGM = blood glucose monitor
CGM = continuous glucose monitor

*Exclusive partnership with DEKA
#Non-exclusive partnership with Dexcom

# TRULICITY AND CV OUTCOME TRIAL RESULT

## REWIND TRIAL KEY ASPECTS

- **Majority of participants did not have established cardiovascular (CV) disease**
  - Mean baseline A1C of 7.3%
  - Median follow-up period of 5.4 years
- **9901 participants with Type 2 Diabetes**
  - Randomized, double-blinded, placebo-controlled study of Trulicity conducted at 370 sites in 24 countries

## REWIND TOP-LINE RESULTS

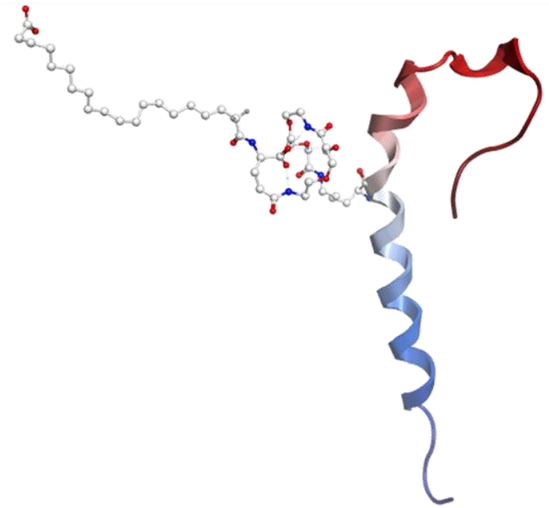
- **Trulicity significantly reduced MACE-3**
- **First T2D medicine to demonstrate MACE-3 reduction in a trial with a majority who did not have established CV disease**
- **Safety profile generally consistent with the GLP-1 RA class**

**Full results to be disclosed at ADA 2019**
**Regulatory submissions in 1H 2019**

**Trulicity demonstrates superiority in reduction of CV events for broad range of people with type 2 diabetes**

REWIND defined established CV disease as including at least one of the following conditions: myocardial infarction (MI), ischemic stroke, unstable angina, revascularization, hospitalization for ischemia related events and/or documented myocardial ischemia.

# TIRZEPATIDE
## DUAL GIP/GLP-1 RECEPTOR AGONIST



**Next generation once-weekly dual incretin designed to strengthen Lilly's leadership in the first injectable space.**

**Innovation** prioritized for speed with goal of 7 years from first human dose to approval

## What We Aim to Do:

**Exceed expectations** for glycemic control and weight reduction

**Replicate** Trulicity's injection experience

**Launch first** with multi-year lead in new class of GIP and GLP-1 receptor dual agonists

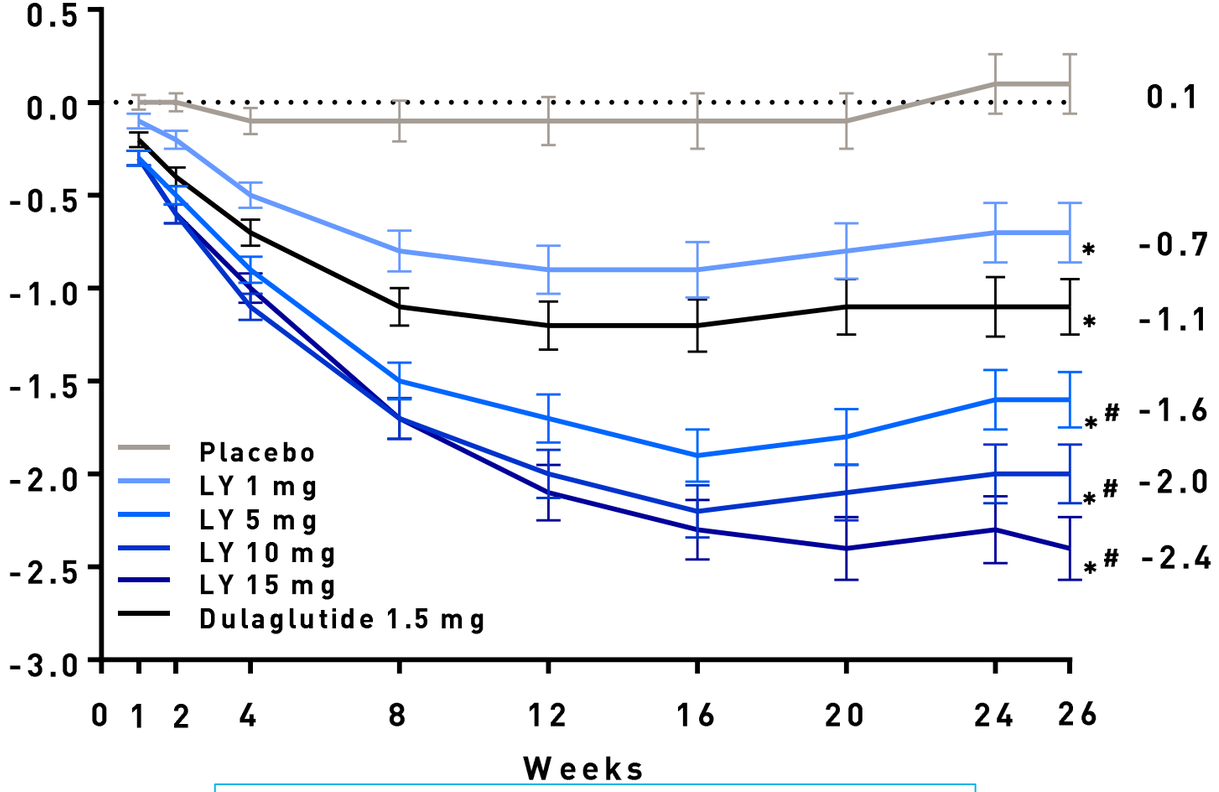
**Deliver** meaningful CV benefit

T2DM **Phase 3** start 2018
Obesity **Phase 3** start 2019
NASH **Phase 2** start 2019

# TIRZEPATIDE PHASE 2

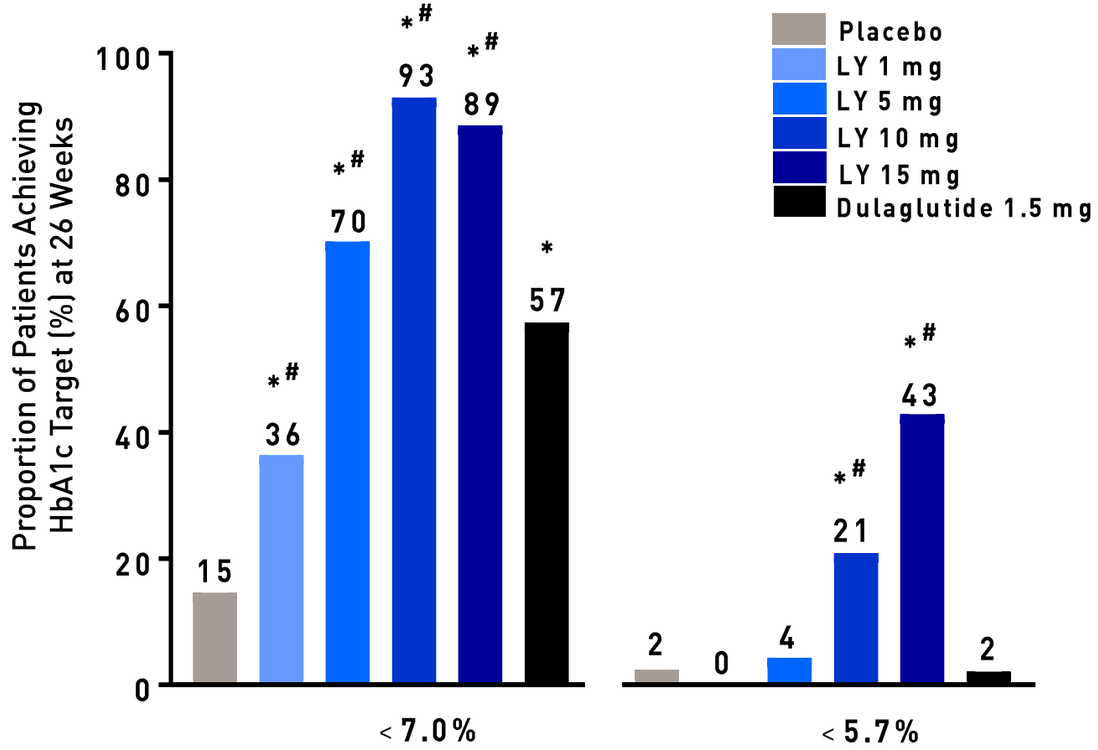
## ACHIEVED POSITIVE RESULTS IN HBA1C REDUCTIONS (ON TREATMENT ANALYSIS)

## HbA1C (%)




Observed significant and dose-related decreases in HbA1c

## HbA1C (%) TARGET




43% of 15 mg dose patients achieve <5.7% HbA1c, a mark of normal glucose level

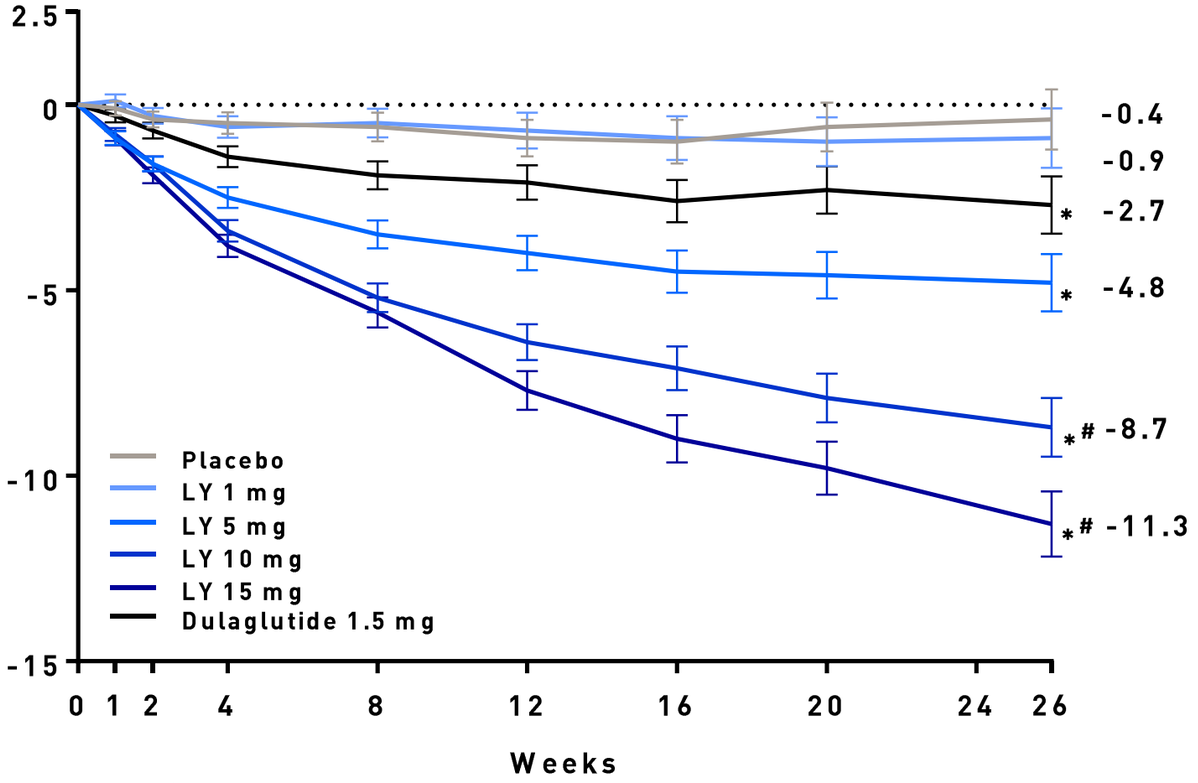
HbA1c (%) data presented are LS mean ± SE. MMRM on treatment analysis
Trial Description: 26 week randomized trial; 1mg, 5mg, 10mg: 2 week titration, 15mg: 6 week titration, dulaglutide 1.5mg
Baseline Characteristics: Mean age 57, weight 91.5 kg, BMI 32.6, A1c 8.1%, 90% on metformin

HbA1c (%) target data are logistic regression, on treatment analysis
*, #p<.05 vs placebo and vs. dulaglutide 1.5 mg, respectively

# TIRZEPATIDE PHASE 2

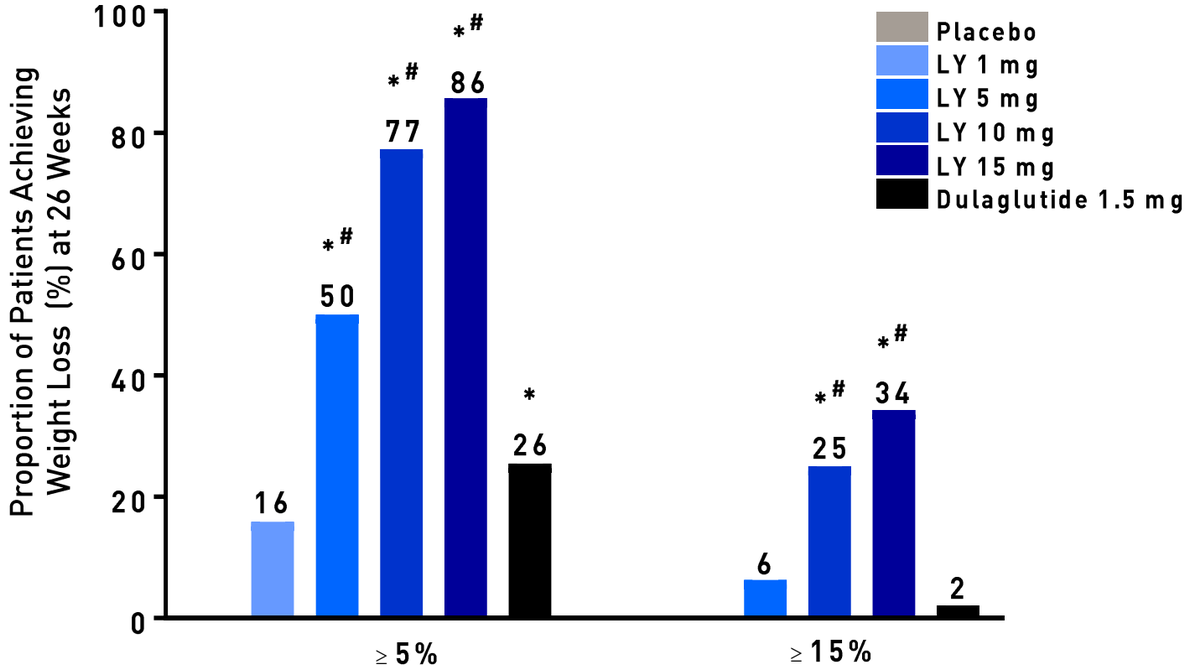
## ACHIEVED POSITIVE RESULTS IN WEIGHT LOSS (ON TREATMENT ANALYSIS)

## WEIGHT LOSS (KG)




Observed significant and dose-related decreases in body weight (kg)

## WEIGHT LOSS (%) TARGET




34% of 15 mg dose patients achieve ≥15% body weight reduction

Data presented are LS mean ± SE. MMRM on treatment analysis.
Trial Description: 26 week randomized trial; 1mg, 5mg, 10mg: 2 week titration, 15mg: 6 week titration, dulaglutide 1.5mg
Baseline Characteristics: Mean age 57, weight 91.5 kg, BMI 32.6, A1c 8.1%, 90% on metformin

HbA1c (%) target data are logistic regression, on treatment analysis
*, #p<.05 vs placebo and vs. dulaglutide 1.5 mg, respectively

# TIRZEPATIDE PHASE 2
## SAFETY AND TOLERABILITY

## SAFETY & TOLERABILITY

| | LY 5mg | LY 10mg | LY 15mg | Dula 1.5mg |
|---|---|---|---|---|
| Adverse Events (AE) (%) | 72.7 | 78.4 | 84.9 | 74.1 |
| Serious AEs (%) | 1.8 | 5.9 | 3.8 | 5.6 |
| Discontinued Treatment due to AE (%) | 9.1 | 5.9 | 24.5 | 11.1 |
| Nausea (%) | 20.0 | 21.6 | 39.6 | 29.6 |
| Diarrhea (%) | 23.6 | 23.5 | 32.1 | 16.7 |
| Vomiting (%) | 7.3 | 15.7 | 26.4 | 9.3 |
| Hypoglycemia* (%) | 7.3 / 1.8 | 9.8 / 5.9 | 7.5 / 5.7 | 3.7 / 3.7 |
| Pancreatitis (n) | 2 | 0 | 0 | 0 |
| Cholecystitis (n) | 0 | 1 | 0 | 1 |

* Hypoglycemia (≤70 mg/dL) reported as total / documented symptomatic. There were no reports of severe hypoglycemia.
[a] study identifier NCT03311724

## SUMMARY

- Most common AEs were gastrointestinal (nausea, vomiting, diarrhea); majority were mild to moderate and transient.
- Treatment discontinuations in the higher dose groups primarily occurred during the titration phase.
- A separate study[a] evaluated slower, step-wise titration, enabling Phase 3 design. Discontinuation due to AE was <5% (including 15mg) over the 12 week study period.
- Treatment-emergent ADA in LY3298176-treated patients (titers generally low, no PK/PD correlation).
- Heart rate and blood pressure effects comparable to dulaglutide.

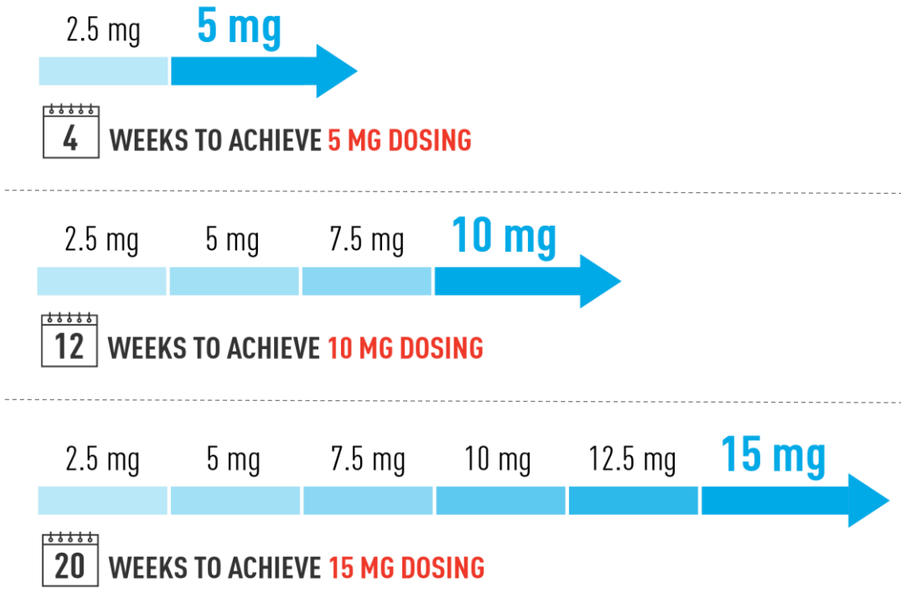
Frias JP et al. *The Lancet.* 2018.

# TIRZEPATIDE
## PHASE 3 DOSING

## Goal: Deliver a Trulicity-like patient experience with single-dose pen at launch

**Step through doses (2.5mg increments) allows gradual introduction and improved tolerability profile**

Informed by Phase 2 studies and exposure modeling

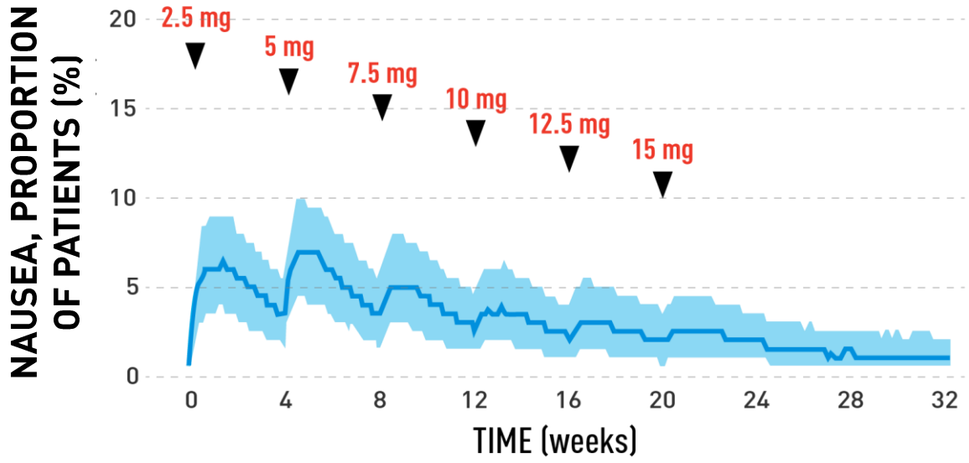



**Phase 3 doses** 5 mg 10 mg 15 mg

### Simulation of Dose Escalation

**Model predicts incidence of nausea with slow, step-wise titration**

Supports improved tolerability profile from Phase 2 to Phase 3



# TIRZEPATIDE PHASE 3

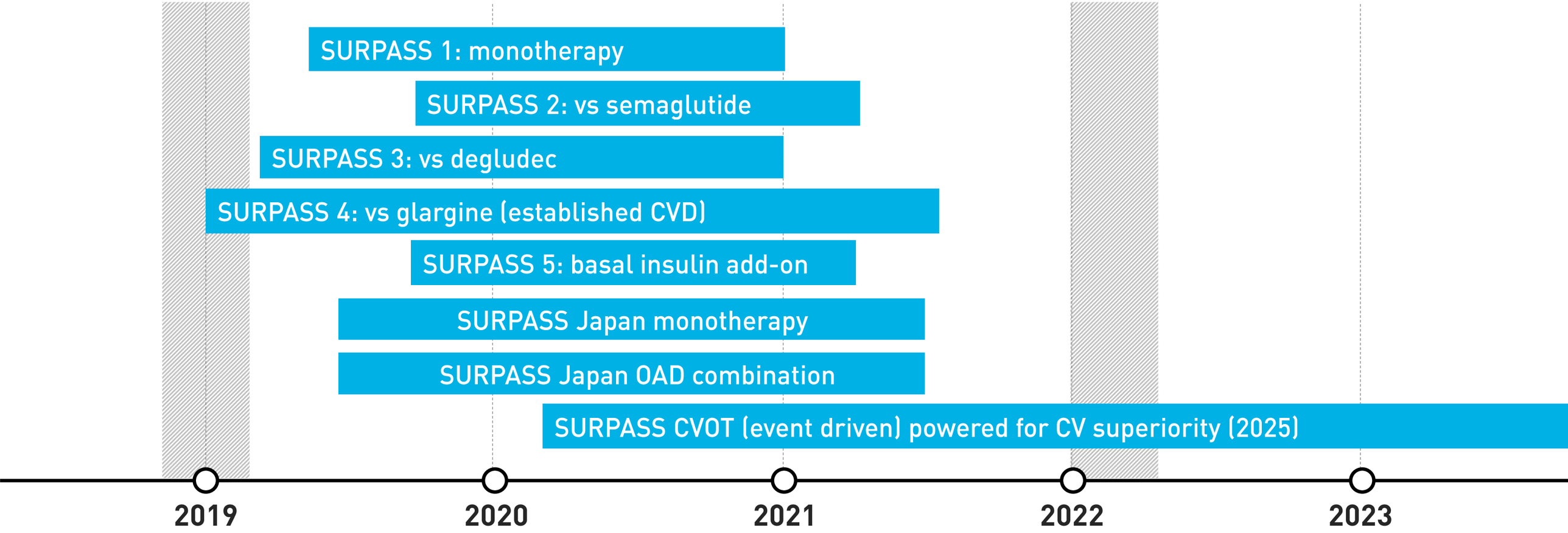
## TYPE 2 DIABETES CLINICAL PROGRAM

**DEC 2018**

**SURPASS PROGRAM INITIATION**

**2022**

**POTENTIAL GLOBAL SUBMISSIONS**



# TIRZEPATIDE
## INITIATING RESEARCH IN ADDITIONAL INDICATIONS

2019

### Obesity Phase 3 Initiation

- Weight loss in obese/overweight patients
- Weight loss in obese/overweight T2DM patients
- Maximizing weight loss
- Maintenance of weight loss

Obesity is increasing in prevalence and is associated with significant co-morbidities and cardiovascular complications (Type 2 Diabetes, Cardiovascular Disease)

2019

### Nonalcoholic Steatohepatitis Phase 2 Initiation

- NASH biopsy study

NASH is increasing in prevalence and associated with risk of cirrhosis, liver transplantation, and cardiovascular complications

# Summary

We have transformed our **development engine** and are rebooting our **discovery engine**

**Neuroscience** is the next wave of growth joining recent launches in Diabetes, Oncology and Immunology

With 2 submissions and 3 Phase 3 starts in 2018, we are continuing our **unprecedented period of productivity**, building towards delivering 20 launches in 10 years

**Dan Skovronsky**
Chief Scientific Officer

**Levi Garraway**
Sr. VP Oncology R&D

**Lotus Mallbris**
VP Immunology Development

**Gudarz Davar**
VP Neurology Development

**Marie Schiller**
VP Connected Care/Insulins

**Brad Woodward**
Incretins Platform Leader

Lilly

2018 **INVESTMENT COMMUNITY MEETING**

# DAVID A. RICKS

Chairman and Chief Executive Officer

Lilly

2018 **INVESTMENT COMMUNITY MEETING**


# THANK YOU, PHIL JOHNSON!

2018 **INVESTMENT COMMUNITY MEETING**

# Summary

## Diverse and durable revenue growth

Expect minimum annual pharma revenue growth of 7% from 2015 to 2020; newest products expected to yield >45% of global pharma revenue in 2019.

## Strong commercial launch capabilities

Lilly is successfully launching into fast-growing therapeutic areas, even against larger companies that often launched earlier.

## Replenishing our pipeline

Lilly moved three assets into Phase 3 in 2018, all with potential to improve the standard of care; more coming.

## Transforming R&D

Lilly's development times often lead the industry. We intend a similar transformation of early-stage R&D.

Lilly

# 2018 INVESTMENT COMMUNITY MEETING


Lilly