# OX2R AGONISTS FOR THE TREATMENT OF NARCOLEPSY TYPE 1


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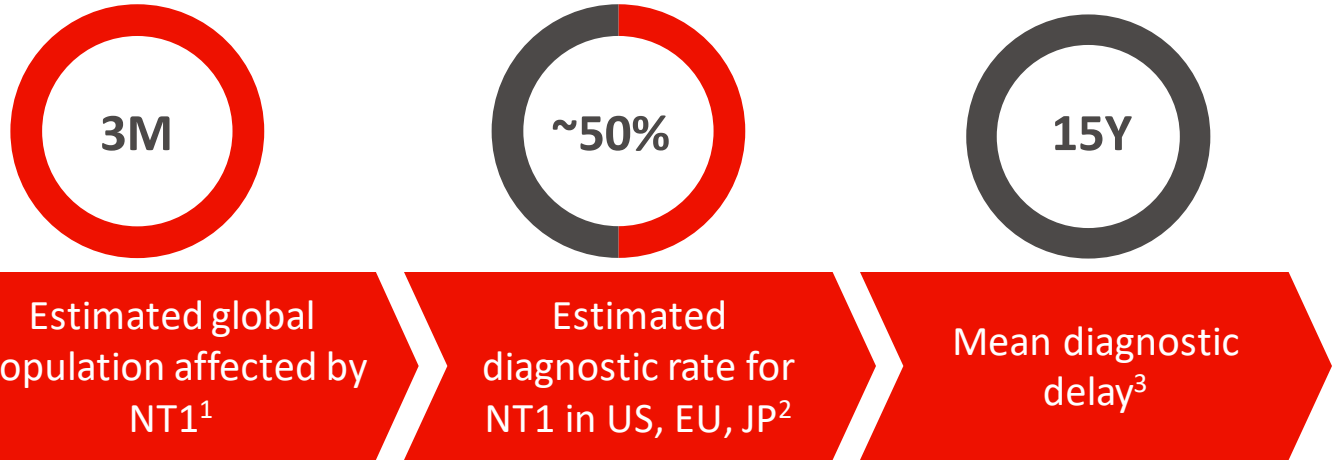
November 14, 2019

Better Health, Brighter Future

# NARCOLEPSY TYPE 1 IS A RARE, ACQUIRED CHRONIC NEUROLOGICAL DISORDER




- Psychosocially devastating effects
- Current treatments are only partially effective
- Polypharmacy is common

*When I'm awake, sleep is constantly intruding on that part of my life. And when I'm asleep, wakefulness is constantly intruding on that part of my life. It's frustrating because no matter how well you regulate your narcolepsy, you're always tired. You're exhausted.*

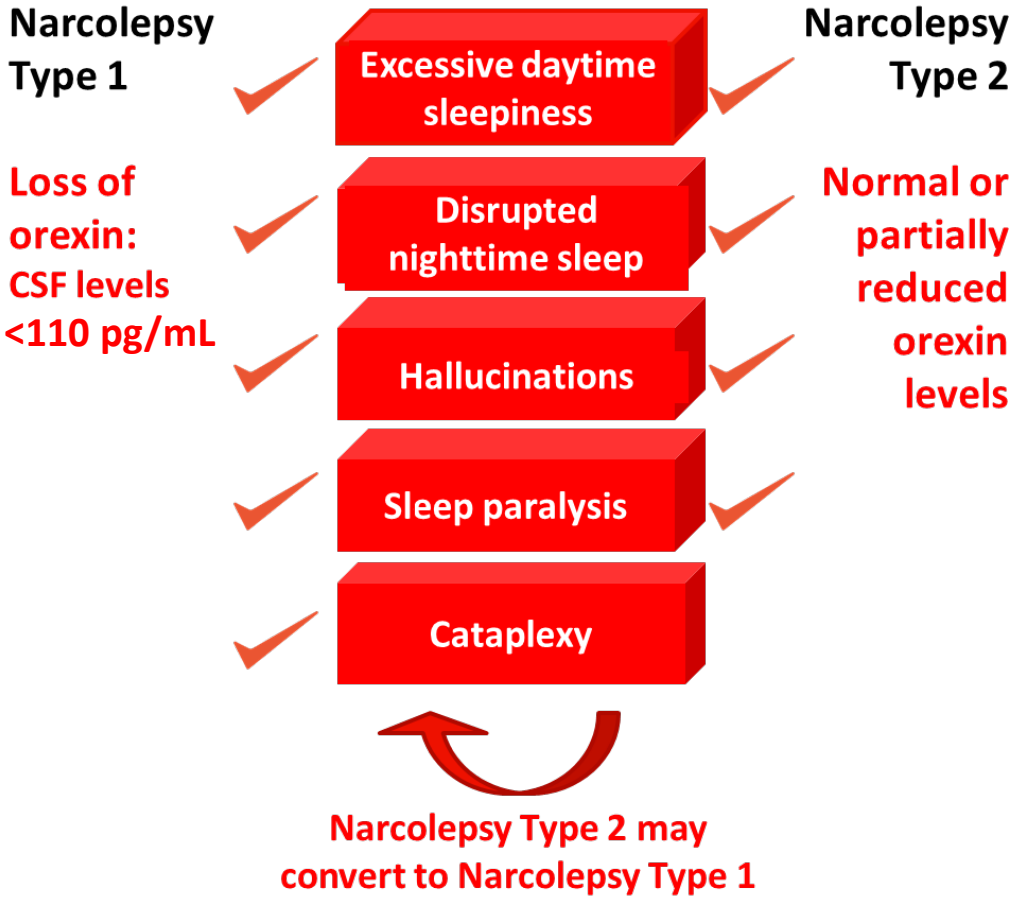
**- Charlie,** adviser with NT1


1. Narcolepsy Network. Narcolepsy Fast Facts. Available at: https://narcolepsynetwork.org/about-narcolepsy/narcolepsy-fast-facts/. Last Updated June 2015. Last Accessed Sept. 2019
2. Thorpy et al. Sleep Med. 2014 May;15(5):502-7
3. Frauscher B, J Clin Sleep Med 2013;9(8):805-12

# NARCOLEPSY TYPE 1 IS DISTINGUISHED BY THE PRESENCE OF CATAPLEXY AND LOW OREXIN LEVELS

*"It's not just about sleep, it's about quality of wakefulness … it's really about partnership with your extended family, your spouse, taking care of your children… it limits my ability to play with my kids."*

**-Sara**, adviser with NT1




**Other hypersomnia disorders**

- Idiopathic Hypersomnia
- Residual Excessive Daytime Sleepiness in Obstructive Sleep Apnea[1]

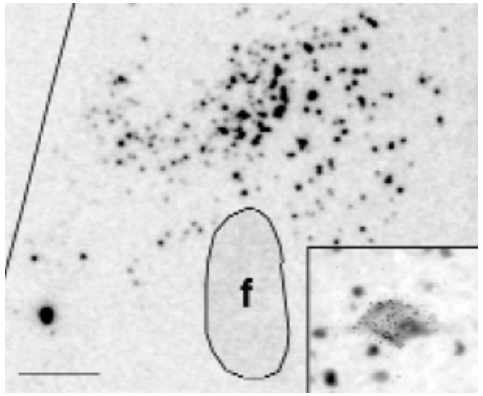
CSF: Cerebral spinal fluid; Orexin also referred to as hypocretin

1. Individuals with Obstructive Sleep Apnea who are compliant with use of continuous positive airway pressure at night

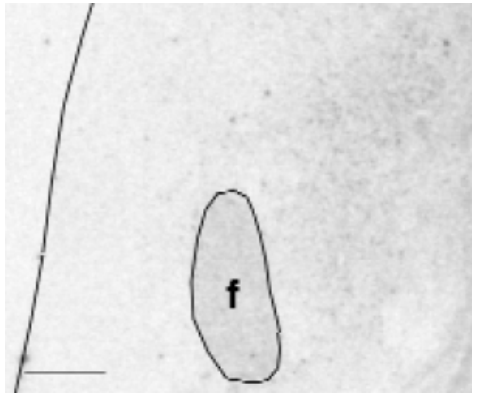
# NARCOLEPSY TYPE I IS CAUSED BY PROFOUND LOSS OF OREXIN-PRODUCING NEURONS

## OREXIN mRNA LABELLING OF POSTMORTEM HYPOTHALAMIC SECTIONS

Healthy control




Narcolepsy Type 1



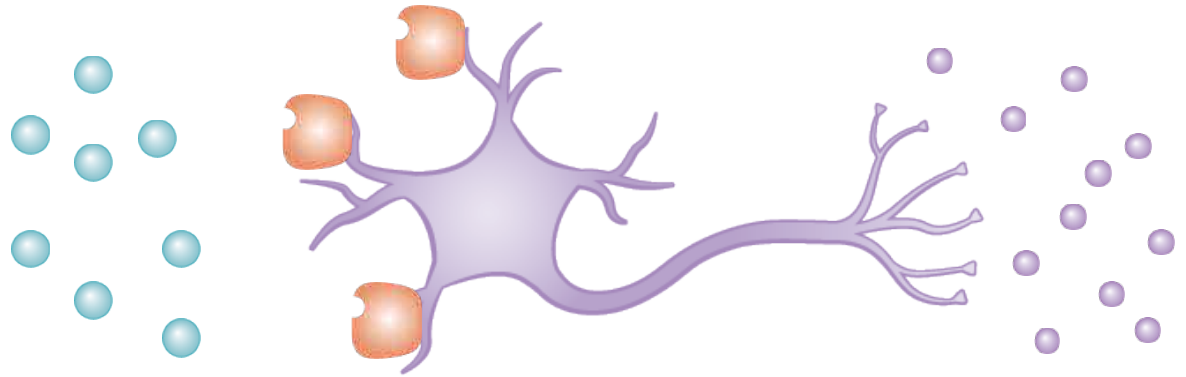

- Individuals with NT1 have >85% less orexin neurons than control, which are located in the hypothalamus[1, 2]

## ACTIVATION OF OREXIN 2 RECEPTOR (OX2R) LEADS TO AROUSAL AND PROMOTES WAKEFULNESS[3]

Orexin neuropeptides A and B

Post-synaptic neurons with orexin 2 receptors

Downstream signalling promoting wakefulness



**THE OREXIN HYPOTHESIS IN NARCOLEPSY TYPE I**

**An orexin 2 receptor agonist may replace the missing endogenous orexin peptide, addressing the underlying orexin deficiency of Narcolepsy Type 1 and reduce disease specific symptoms**

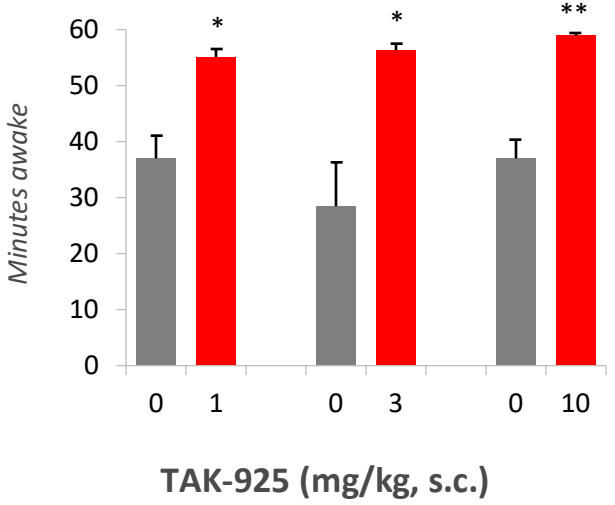
f: fornix


1. Reprinted by permission from Springer Nature. Peyron C, et al. Nat Med. 2000;6:991-997
2. Thannickal TC, et al. *Neuron.* 2000;27:469–474
3. Tsujino N, et al. Pharmacol. Rev. 2009;61(2):162-176

# TAK-925, A SELECTIVE OX2R AGONIST, REDUCES NARCOLEPSY-LIKE SYMPTOMS IN AN OREXIN-DEFICIENT MOUSE MODEL

## TAK-925 FULLY RESTORED WAKEFULNESS

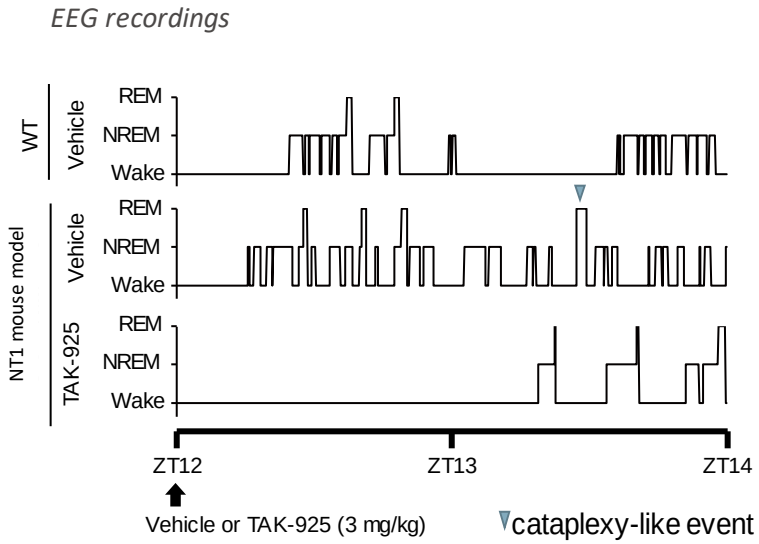
**Wakefulness time of NT1 mouse model in active phase for one hour**




*p<0.05, **p<0.01 vs placebo

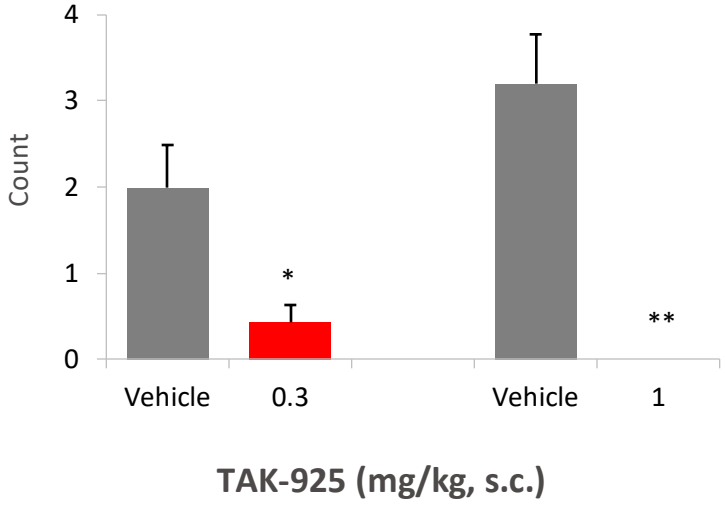
## TAK-925 ELIMINATED SLEEP / WAKE TRANSITIONS

**Hypnogram of sleep/wake transitions in NT1 mouse model**




## TAK-925 ABOLISHED CATAPLEXY-LIKE EPISODES

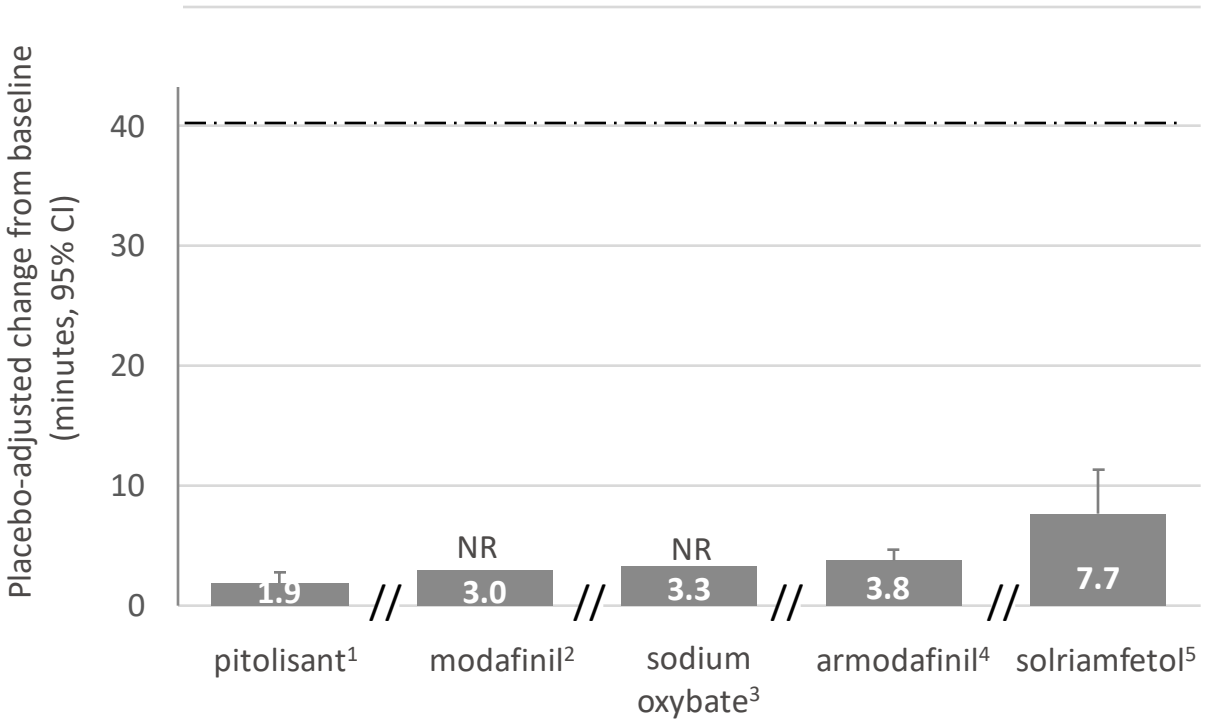
**Cataplexy-like episodes in NT1 mouse model for three hours after chocolate**




*p<0.05, **p<0.01 vs placebo

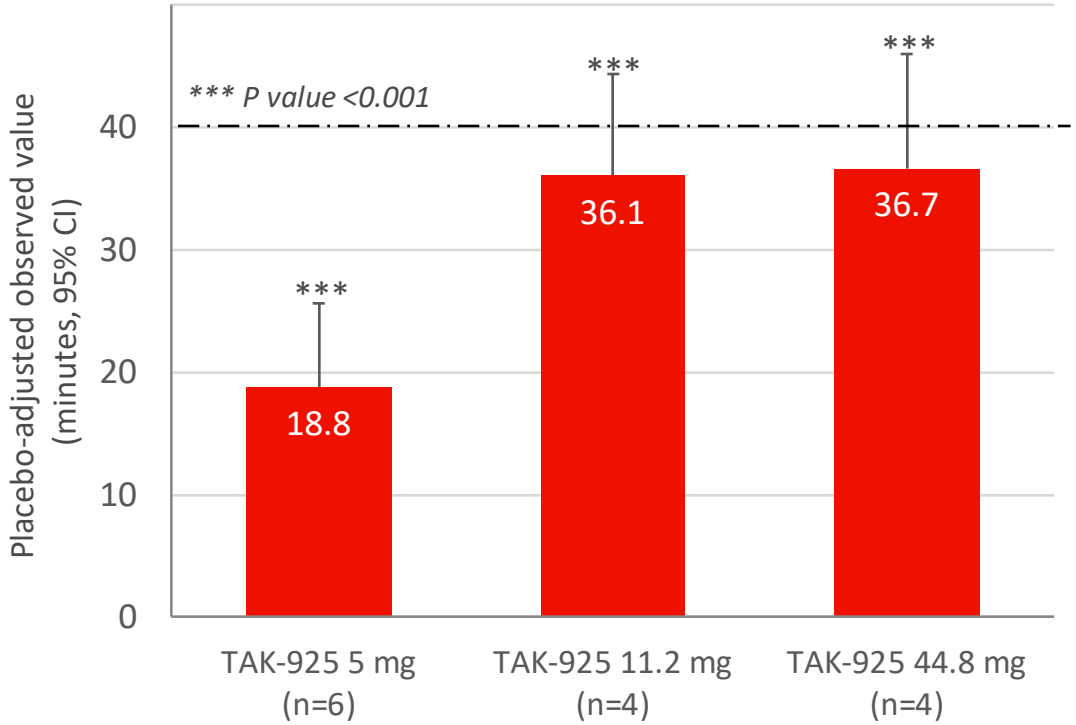
# TAK-925 SHOWED PROMISING ABILITY TO MAINTAIN WAKEFULNESS IN AN EARLY PROOF OF CONCEPT STUDY IN NT1 PATIENTS

## SLEEP LATENCY IN THE MAINTENANCE OF WAKEFULNESS TEST (MWT): CURRENT TREATMENTS




## SLEEP LATENCY IN THE MAINTENANCE OF WAKEFULNESS TEST (MWT): TAK-925 (N=14)

(single dose nine hour continuous IV infusion during the day)[6]




- TAK-925 was well-tolerated; most AEs were mild and no SAEs were observed
- In this TAK-925-1001 study, four 40 minute MWTs were conducted per period
- Direct cross-study comparison can not be made between TAK-925 and treatments due to different studies with different designs

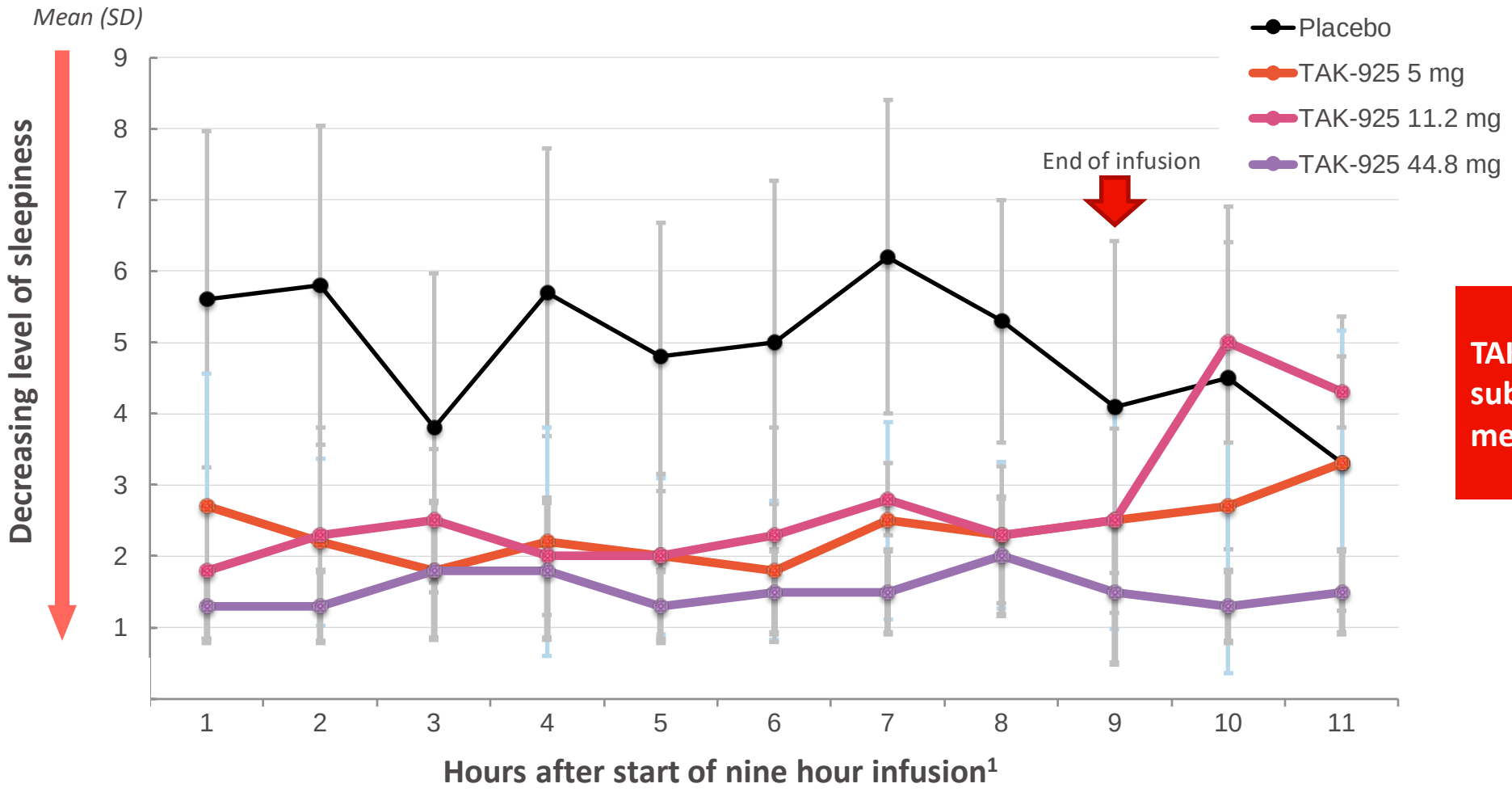
NR: 95% CI rot reported

1. Lancet Neurol. 2017 Mar;16(3):200-207; 2. FDA statistical Review: Page 5, 200 mg; 3. Label/Trial N4; 4. Clinicaltrials.gov (NCT00078377); 5. FDA Statistical Review, Study 14-002, 150 mg
6. Evans R, Tanaka S, Tanaka S, et al. 2019. A phase 1 single ascending dose study of a novel orexin 2 receptor agonist, TAK-925, in healthy volunteers (HV) and subjects with narcolepsy type 1 (NT1) to assess safety, tolerability, pharmacokinetics, and pharmacodynamic outcomes. Abstract presented at World Sleep 2019. Vancouver, Canada. http://www.professionalabstracts.com/ws2019/iPlanner/#/presentation/1832

# TAK-925 ALSO REDUCED SUBJECTIVE SLEEPINESS IN THIS EARLY PROOF OF CONCEPT STUDY IN NT1

## KAROLINSKA SLEEPINESS SCALE VALUES DURING AND AFTER ADMINISTRATION OF TAK-925

(single dose nine hour continuous IV infusion during the day)



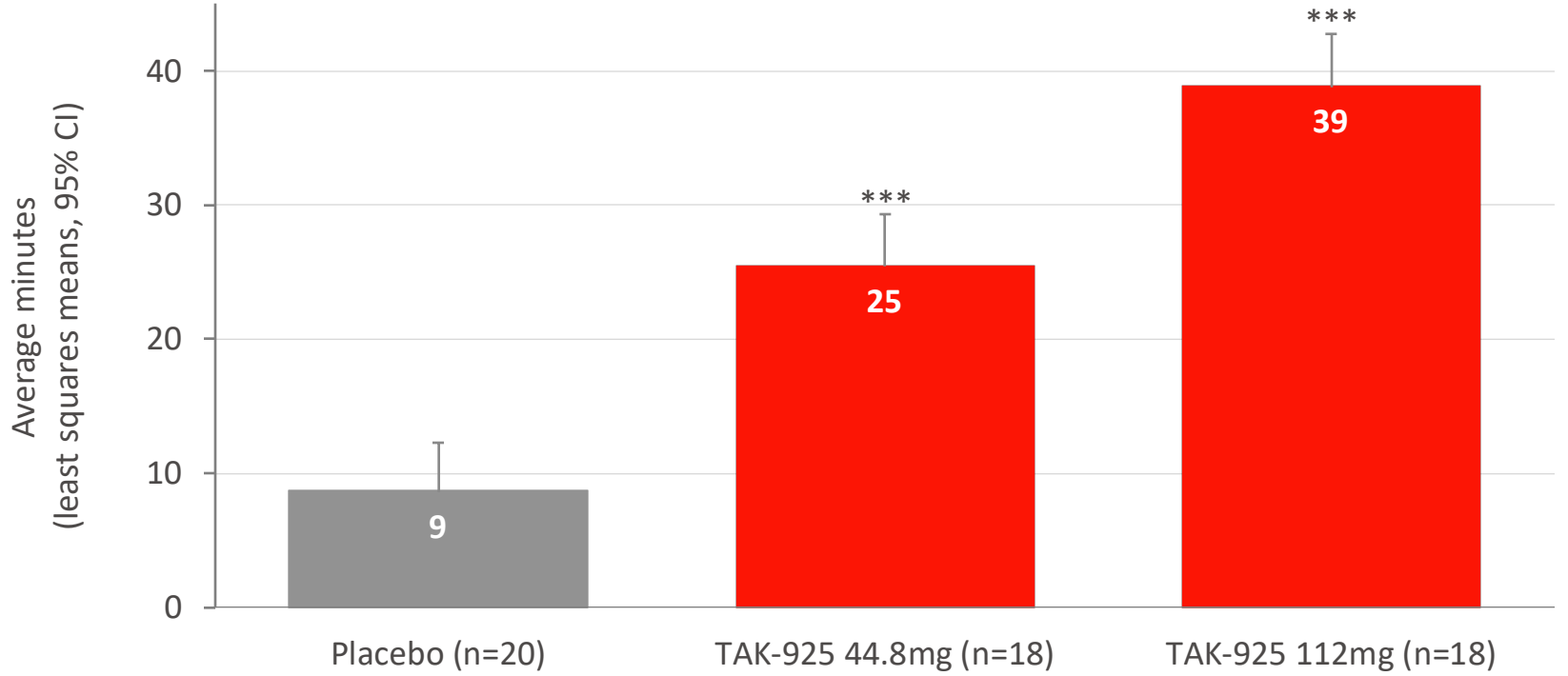

**TAK-925 improved subjective and objective measures of wakefulness**

1. TAK-925 effective plasma half-life <2 hours

Evans R, Tanaka S, Tanaka S, et al. 2019. A phase 1 single ascending dose study of a novel orexin 2 receptor agonist, TAK-925, in healthy volunteers (HV) and subjects with narcolepsy type 1 (NT1) to assess safety, tolerability, pharmacokinetics, and pharmacodynamic outcomes. Abstract presented at World Sleep 2019. Vancouver, Canada. http://www.professionalabstracts.com/ws2019/iPlanner/#/presentation/1832

# TAK-925 MAINTAINED WAKEFULNESS IN SLEEP-DEPRIVED HEALTHY ADULTS IN A SECOND PHASE 1 STUDY

## SLEEP LATENCY IN THE MAINTENANCE OF WAKEFULNESS TEST (MWT) IN SLEEP-DEPRIVED HEALTHY ADULTS[1]



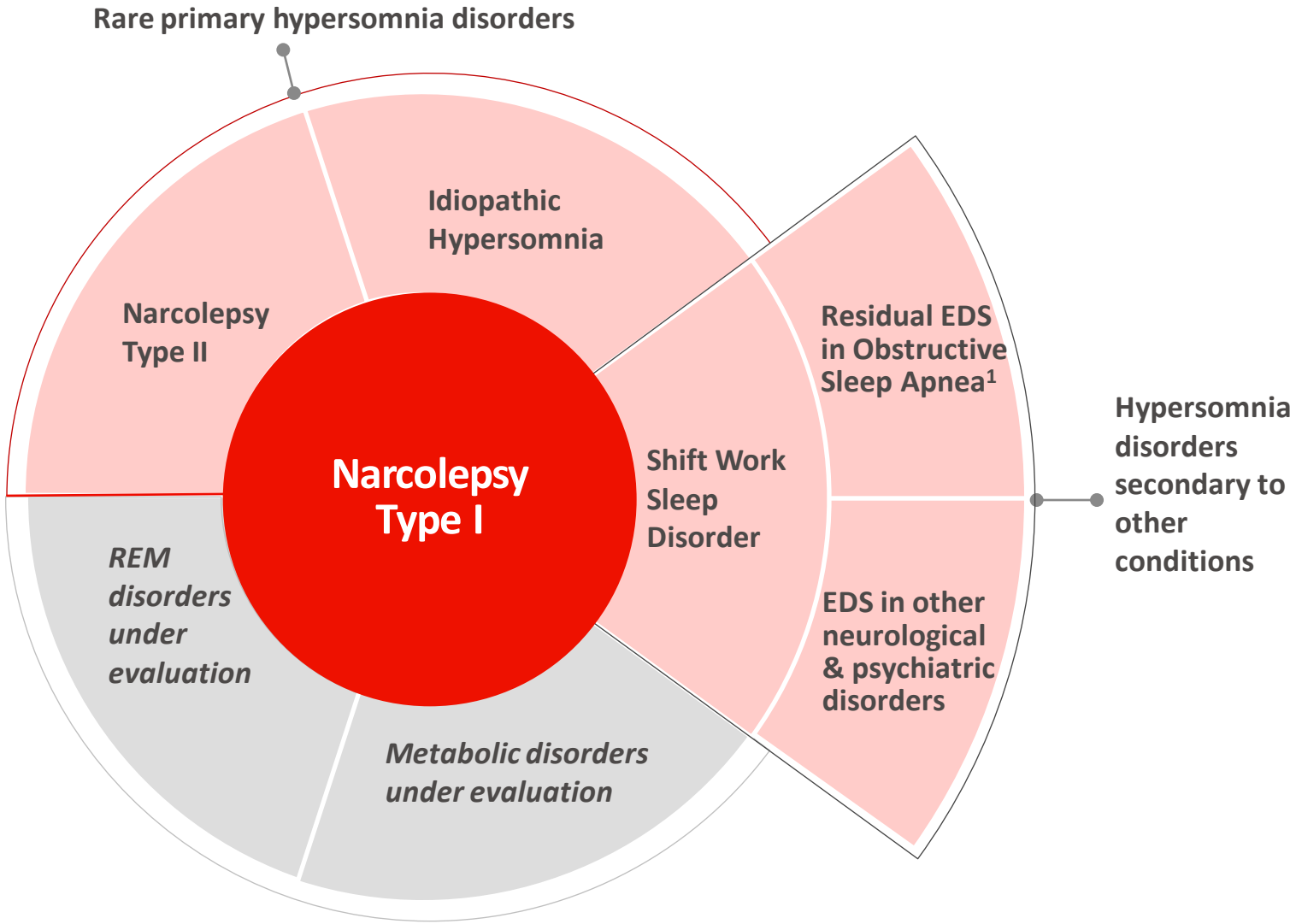

TAK-925 was well-tolerated; most AEs were mild and no SAEs were observed

**Results suggest potential therapeutic use of TAK-925 in other hypersomnia disorders not associated with orexin deficiency**


1. Evans R, Hazel J, Faessel H, et al. 2019. Results of a phase 1b, 4-period crossover, placebo-controlled, randomized, single dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of TAK-925, a novel orexin 2 agonist, in sleep-deprived healthy adults, utilizing modafinil as an active comparator. Abstract presented at World Sleep 2019. Vancouver, Canada. http://www.professionalabstracts.com/ws2019/iPlanner/#/presentation/2821
2. Int J Neurosci. 1990 May;52(1-2):29-37


***: p-value <0.001 relative to placebo

# WE ARE COMMITTED TO LEADING INNOVATION IN OREXIN BIOLOGY AND EXPANDING THERAPEUTIC INDICATIONS FOR OX2R AGONISTS




- Top priority
- Other hypersomnia disorders
- Additional opportunities for expansion

- **TAK-925-1003** for Narcolepsy Type 2 (NCT03748979)
- **SPARKLE 2001** study for Residual EDS in Obstructive Sleep Apnea (NCT04091425)
- **SPARKLE 2002** study for Idiopathic Hypersomnia (NCT04091438)

REM: Rapid eye movement

1. Individuals with Obstructive Sleep Apnea who are compliant with use of continuous positive airway pressure at night

# TAK-994 IS AN ORAL OX2R AGONIST PROGRESSING TO STUDIES IN NARCOLEPSY TYPE 1

## TAK-994-1501 PROOF OF CONCEPT STUDY IN NARCOLEPSY TYPE 1

SPARKLE
OREXIN INNOVATION

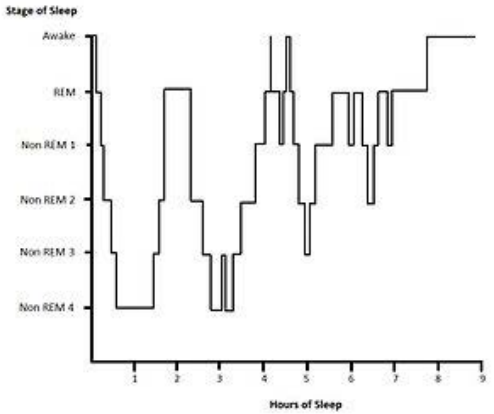
- Multi-center, placebo-controlled trial in North America and Japan
- Enrollment target: 72 adults
- Duration of treatment: 28 days dosing
- Exploratory outcome measures include Maintenance of Wakefulness Test (MWT), Epworth Sleepiness Scale (ESS), and Weekly Cataplexy Rate (WCR)

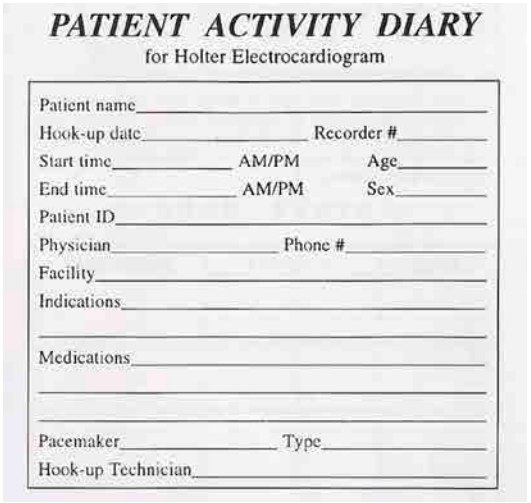
Proof of Concept trial: ClinicalTrials.gov Identifier: NCT04096560

# DIGITAL TECHNOLOGIES ARE ENHANCING THE DEVELOPMENT OF OX2R AGONISTS FOR SLEEP DISORDERS

## TRADITIONAL CLINICAL INSTRUMENTS DO NOT FULLY MEASURE SYMPTOMS OF SLEEP DISORDERS

### Hand-scored polysomnography (PSG)[1]



PATIENT ACTIVITY DIARY

for Holter Electrocardiogram

Patient name_____

Hook-up date_____ Recorder #_____

Start time_____ AM/PM Age_____

End time_____ AM/PM Sex_____

Patient ID_____

Physician_____ Phone #_____

Facility_____

Indications_____

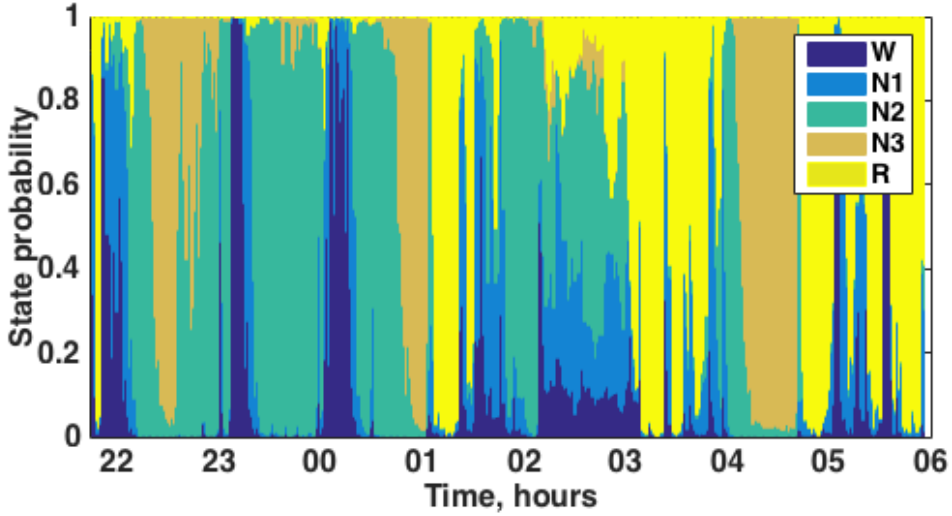
Medications_____

Pacemaker_____ Type_____

Hook-up Technician_____

## DIGITAL MEASURES WILL FURTHER CHARACTERIZE SLEEP ARCHITECTURE AND SUPPORT CLINICAL TRIAL ASSESSMENTS

### Automated analysis of NT1 nPSG[2]




- Real-time data capture to understand disease burden and effects of treatment
- Non-invasive measures to optimize therapy
- Patient stratification using digital fingerprints

nPSG – Night time polysomnography



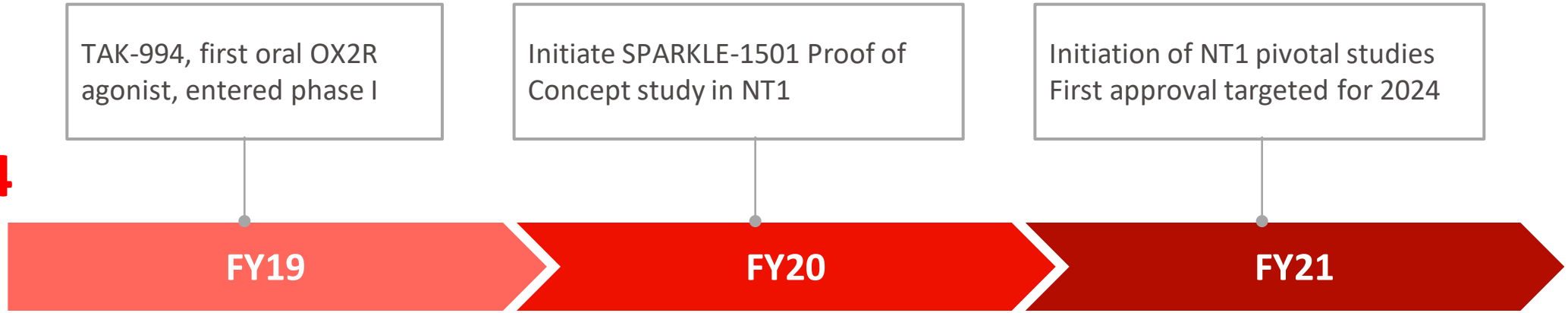
1. Approximately 80% interrater concordance based on Danker-Hopfe et al., J Sleep Res (2009) and Younes & Hanly, J Clin Sleep Med (2016); 2. Analysis shown is based on Stephansen et al., Nature Comm (2018)

# WE ASPIRE TO BRING A POTENTIALLY TRANSFORMATIVE OX2R AGONIST SOLUTION TO INDIVIDUALS WITH NARCOLEPSY TYPE 1

## TAK-925

- Achieved early Proof of Concept for NT1
- Awarded Breakthrough Therapy Designation
- Awarded Sakigake Designation
- Launched formulation development activities

## TAK-994




*Thank you to all the study participants who have enrolled in these early OX2R agonist clinical trials*

# SUMMARY

**1**

TAK-925 has achieved early Proof-of-Concept for OX2R agonists in Narcolepsy Type 1

**2**

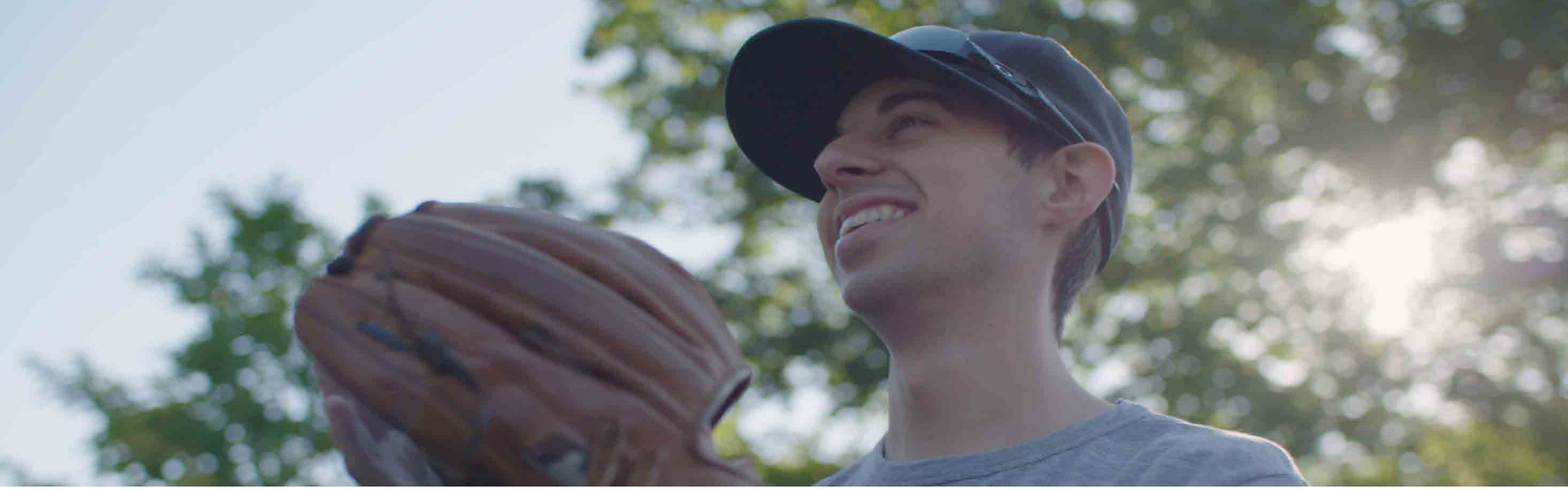
TAK-925 has demonstrated potential of OX2R agonists for treatment of other sleep-related disorders

**3**

TAK-994 is an oral OX2R agonist progressing to studies in Narcolepsy Type 1

# R&D DAY AGENDA – NEW YORK, NOVEMBER 14, 2019

| TIME | AGENDA |
|---|---|
| 12:30 – 12:35 | **Welcome and Opening Remarks**<br>*Sheelagh Cawley-Knopf, Head R&D Global Portfolio Strategy* |
| 12:35 – 12:45 | **Takeda: A Global Values-Based, R&D-Driven Biopharmaceutical Leader**<br>*Christophe Weber, President & CEO Takeda* |
| 12:45 – 13:20 | **Translating Science into Highly Innovative, Life-changing Medicines**<br>*Andy Plump, President R&D* |
| 13:20 – 13:45 | **Oncology and Cell Therapies with Spotlight on CAR-NK**<br>*Chris Arendt, Head Oncology Drug Discovery Unit* |
| 13:45 – 14:05 | **Spotlight on Oncology Opportunities**<br>• **TAK-788** : *Rachael Brake, Global Program Lead*<br>• **Pevonedistat** : *Phil Rowlands, Head Oncology Therapeutic Area Unit* |
| 14:05 – 14:20 | **Break** |
| 14:20 – 14:45 | **Rare Diseases & Gene Therapy**<br>*Dan Curran, Head Rare Disease Therapeutic Area Unit* |
| 14:45 – 15:00 | **Spotlight on Orexin2R agonists**<br>*Deborah Hartman, Global Program Lead* |
| 15:00 – 15:20 | **Therapeutic Area Focus in GI with Spotlight on Celiac Disease**<br>*Asit Parikh, Head GI Therapeutic Area Unit* |
| 15:20 – 16:00 | **Panel Q&A Session** |
| 16:00 | **Drinks reception** |



# THERAPEUTIC AREA FOCUS IN GI WITH SPOTLIGHT ON CELIAC DISEASE


Asit Parikh, MD, PhD

Head Gastroenterology Therapeutic Area Unit

Takeda Pharmaceutical Company Limited

New York, NY

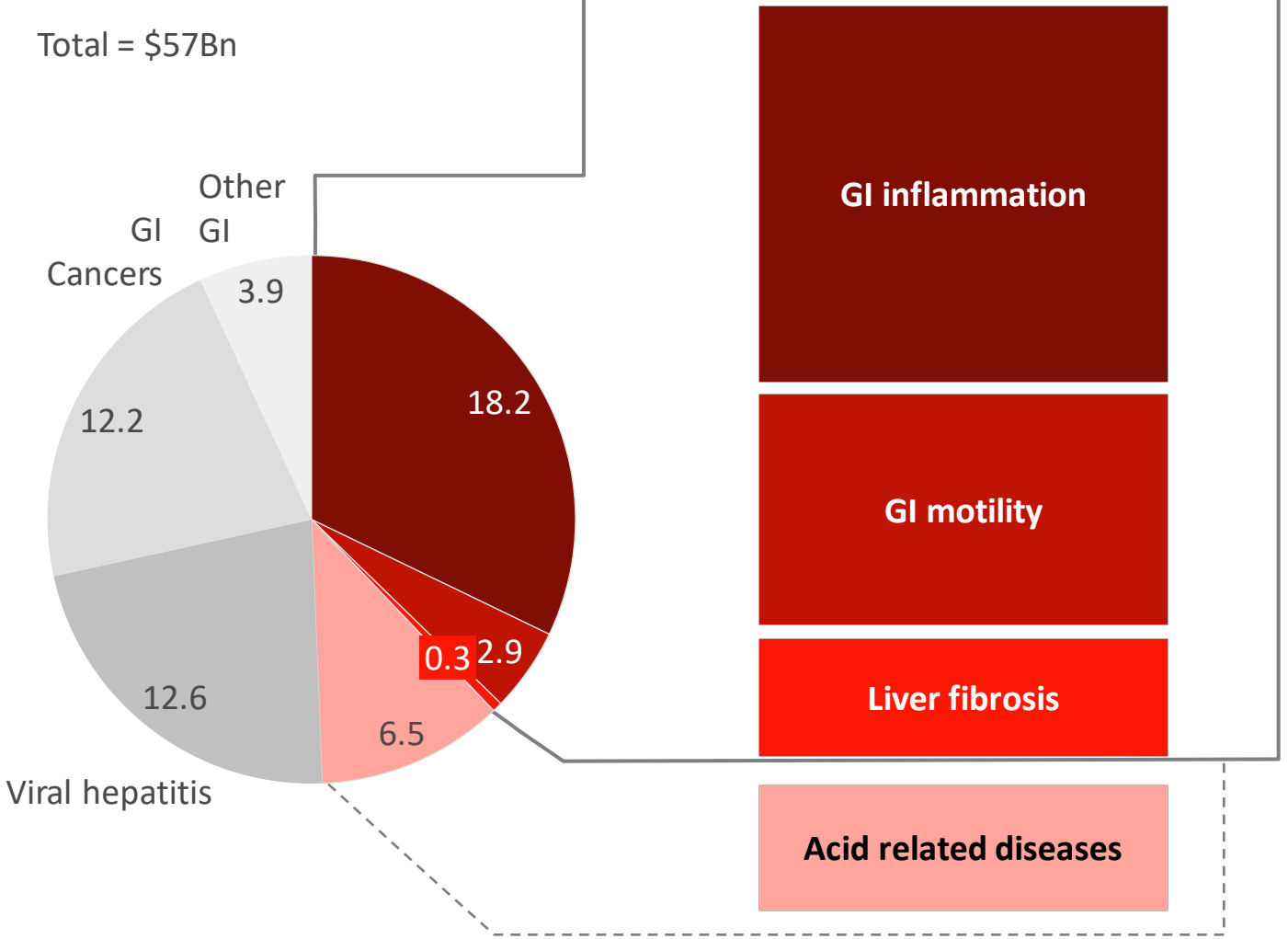

November 14, 2019

# WE TARGET UNMET NEEDS THAT ALIGN WITH OUR STRENGTHS

## AREAS OF FOCUS

- High unmet medical need
- Potential to advance SoC through innovative science – by being first or best in class
- Fit with internal strengths
- Ability to create a commercially - viable path

## GI WW RX SALES 2018 (USD BN)




## TAKEDA GI DISEASE AREAS

- GI inflammation
- GI motility
- Liver fibrosis
- Acid related diseases

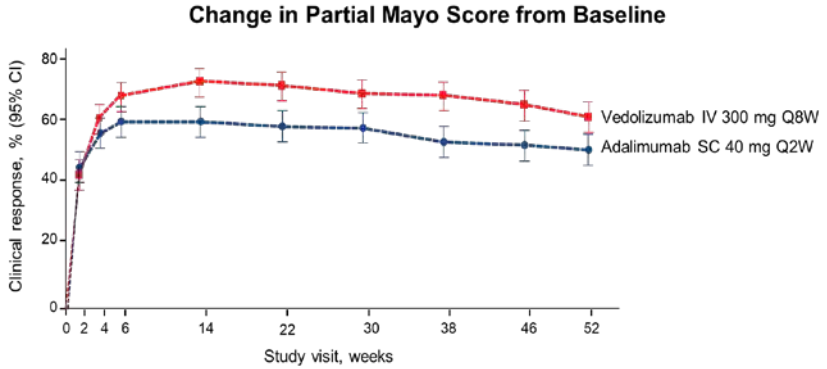
SOURCE: Evaluate Pharma indication specific sales, accessed May 29, 2019. Other GI includes: pancreatic insufficiency, hepatic encephalopathy, diarrhea, bowel clearance, gallstones, hemorrhoids

# WE STRENGTHEN ENTYVIO BY CONTINUOUSLY IMPROVING VALUE FOR PATIENTS

## COMPETITIVE POSITIONING

### VARSITY: 1st Head-to-Head study in IBD (UC)

- Vedolizumab was superior to adalimumab on the primary endpoint of clinical remission at wk 52
- Onset of action as rapid as anti-TNF



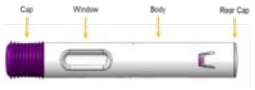

## EXPANDED PATIENT POPULATIONS

### Entyvio Subcutaneous Development

- Positive VISIBLE UC and CD trials
- Subject to regulatory approval, on track to launch exclusive, digital, needle-free jet-injector by 2022

**Prefilled syringe**

**Autoinjector pen**



**Portal jet-injector**

### Gut GvHD prophylaxis

- Could **transform SoC** for cancer patients undergoing allo stem-cell transplants

## GEOGRAPHIC EXPANSION

### Entyvio IV

- Approved in **68 countries**
- Launched in Japan (UC: Nov 2018, CD: May 2019)

**EXPECTED MILESTONES (FY)**

| 2019 | 2020 | 2021 |
|---|---|---|
| Entyvio (SC UC) US approval | Entyvio (SC CD) US, EU approval<br>Entyvio (SC UC) EU, JP approval<br>Entyvio (IV) CN approval | Entyvio GvHD Ph3 readout |

Source: Sands *et al*. Vedolizumab versus Adalimumab for Moderate-to-Severe Ulcerative Colitis. N Engl J Med 2019; 381:1215-1226

IBD: Inflammatory Bowel Disease; UC: ulcerative colitis; CD: Crohn's Disease; IV=intravenous; SC=subcutaneous; TNF=tumour necrosis factor; SoC: standard of care; CN: China; JP: Japan; GvHD: graft versus host disease; Clinical remission: Complete Mayo score of ≤2 points and no individual subscore >1 point

# WE ARE POSITIONED TO DELIVER NEAR-TERM & SUSTAINED GROWTH

| TARGET APPROVAL → | WAVE 1[1] | | | | | WAVE 2[2] | | | | | PLATFORMS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | CLINICAL-STAGE NMEs | | | | | | | | | | |
| | FY20 | FY21 | FY22 | FY23 | FY24 | FY25 AND BEYOND | | | | | |
| **ONCOLOGY** | | **TAK-788**[3] *2L NSCLC* | | **TAK-007** *Hematologic malignancies* | **TAK-924** *AML* | **TAK-164** *GI malignancies* | **TAK-252** *Solid tumors* | | | | CELL THERAPY AND IMMUNE ENGAGERS; TARGETED INNATE IMMUNE MODULATION; NEXT-GEN CHECKPOINT MODULATORS |
| | | **TAK-924**[3] *HR-MDS* | | **TAK-788** *1L NSCLC* | | **TAK-573** *R/R MM* | **TAK-981** *Multiple cancers* | | | | |
| **RARE DISEASES** *Immunology Hematology Metabolic* | | **TAK-620** *CMV infect. in transplant* | | **TAK-611** *MLD (IT)* | **TAK-607** *Complications of prematurity* | **TAK-079**[4] *MG, ITP* | **TAK-754** *HemA* | **TAK-755** *iTTP, SCD* | | | GENE THERAPY |
| | | **TAK-609** *Hunter CNS (IT)* | | **TAK-755** *cTTP* | | **TAK-531** *Hunter CNS* | | | | | |
| **NEUROSCIENCE** | | | | **TAK-935** *DEE* | **Orexin2R-ag** *(TAK-925/994) Narcolepsy T1* | **TAK-341** *Parkinson's Disease* | **Orexin2R-ag** *Sleep Disorders* | **TAK-041** *CIAS NS* | | | GENE THERAPY; OTHER PLATFORMS *RNA Modulation Antibody Transport Vehicle* |
| | | | | | | **TAK-418** *Kabuki Syndrome* | **TAK-653** *TRD* | **TAK-831** *CIAS NS* | | | |
| | | | | | | **WVE-120101** *Huntington's Disease* | **WVE-120102** *Huntington's Disease* | | | | |
| **GASTRO-ENTEROLOGY** | **TAK-721** *EoE* | | | | | **Kuma062** *Celiac Disease* | **TAK-101** *Celiac Disease* | **TAK-018** *Crohn's Disease (post-op and ileitis)* | **TAK-671** *Acute Pancreatitis* | | GENE THERAPY; MICROBIOME; CELL THERAPY |
| | | | | | | **TAK-954** *POGD* | **TAK-906** *Gastroparesis* | **TAK-951** *Nausea & vomiting* | | | |
| **VACCINES** | | **TAK-003** *Dengue Vaccine* | | | | **TAK-214** *Norovirus Vaccine* | **TAK-426** *Zika Vaccine* | **TAK-021** *EV71 vaccine* | | | |

1. Projected timing of approvals depending on data read-outs; some of these Wave 1 target approval dates assume accelerated approval
2. Some Wave 2 assets could be accelerated into Wave 1 if they have breakthrough data
3. Projected approval date assumes filing on Phase 2 data
4. TAK-079 to be developed in Rare Diseases indications myasthenia gravis (MG) and immune thrombocytopenic purpura (ITP) (FPI projected in each indication in 2H FY19)

Orphan potential in at least one indication
Estimated dates as of November 14, 2019

# TAK-721: ON TRACK TO BE THE FIRST FDA APPROVED AGENT TO TREAT EOSINOPHILIC ESOPHAGITIS (EOE)

## ADDRESSES SIGNIFICANT UNMET NEED

- Chronic, allergic, inflammatory condition of the esophagus that results in swallowing dysfunction
- Diagnosed prevalence is expected to increase significantly

No approved US medication
SOC is food elimination, off-label use[1]

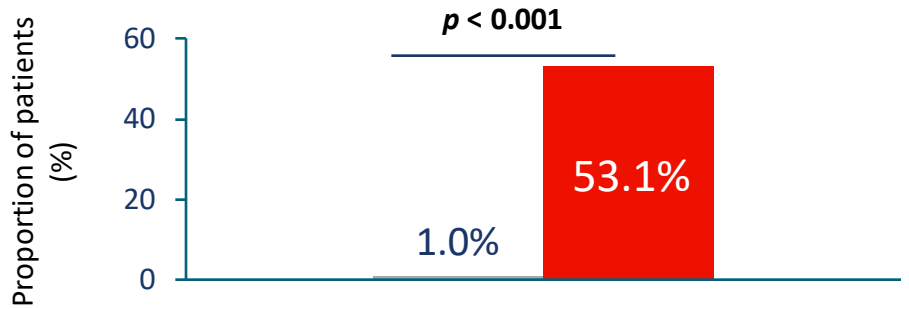
TAK-721 granted breakthrough therapy designation by FDA in 2016

| EXPECTED MILESTONES (FY) | 2019 | 2020 | 2021 |
|---|---|---|---|
| | Q4: Maintenance TL results | Q2: NDA filing<br>Q4: Approval | Q1: Launch |

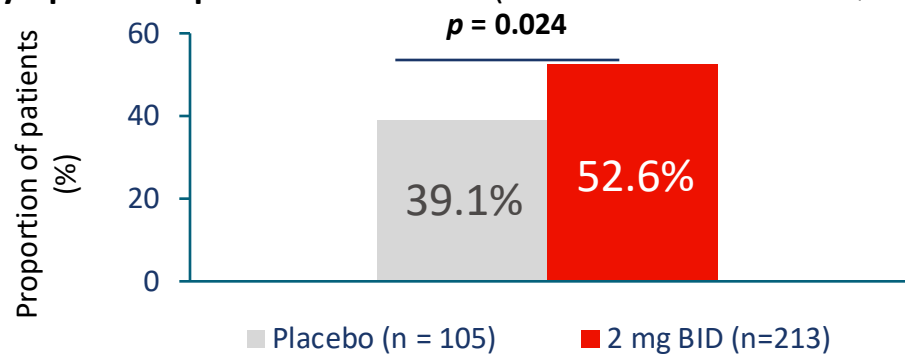
## INDUCTION DATA SHOWS SIGNIFICANT HISTOLOGIC AND SYMPTOM RESPONSE

Results presented at presidential plenary at ACG, Texas, Oct 2019

**Histologic Response at 12 Weeks** (peak ≤ 6 eosinophils/hpf on biopsy)



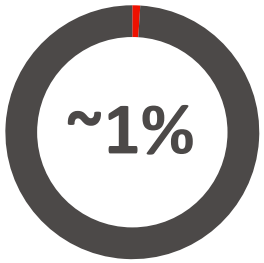

**Symptom Response at 12 Weeks** (≥ 30% reduction in DSQ score)




1. Swallowed use of glucocorticoids intended for asthma (e.g., home or compounded thickening of budesonide solution, or swallowing fluticasone aerosol).

DSQ score: Dysphagia Symptom Questionnaire patient reported outcome score eos/hpf: peak eosinophils per high-powered field from endoscopic biopsies
Eos/hpf: eosinophils per high-power field; BID: Twice daily; SOC: Standard of care; NDA: new drug application

# CELIAC DISEASE IS AN EXAMPLE OF A HIGH UNMET NEED AREA WITH NO THERAPIES




Global population affected by celiac[1]


Patients still suffer from symptoms despite being on a gluten-free diet


Estimated global, eligible patient population[2]

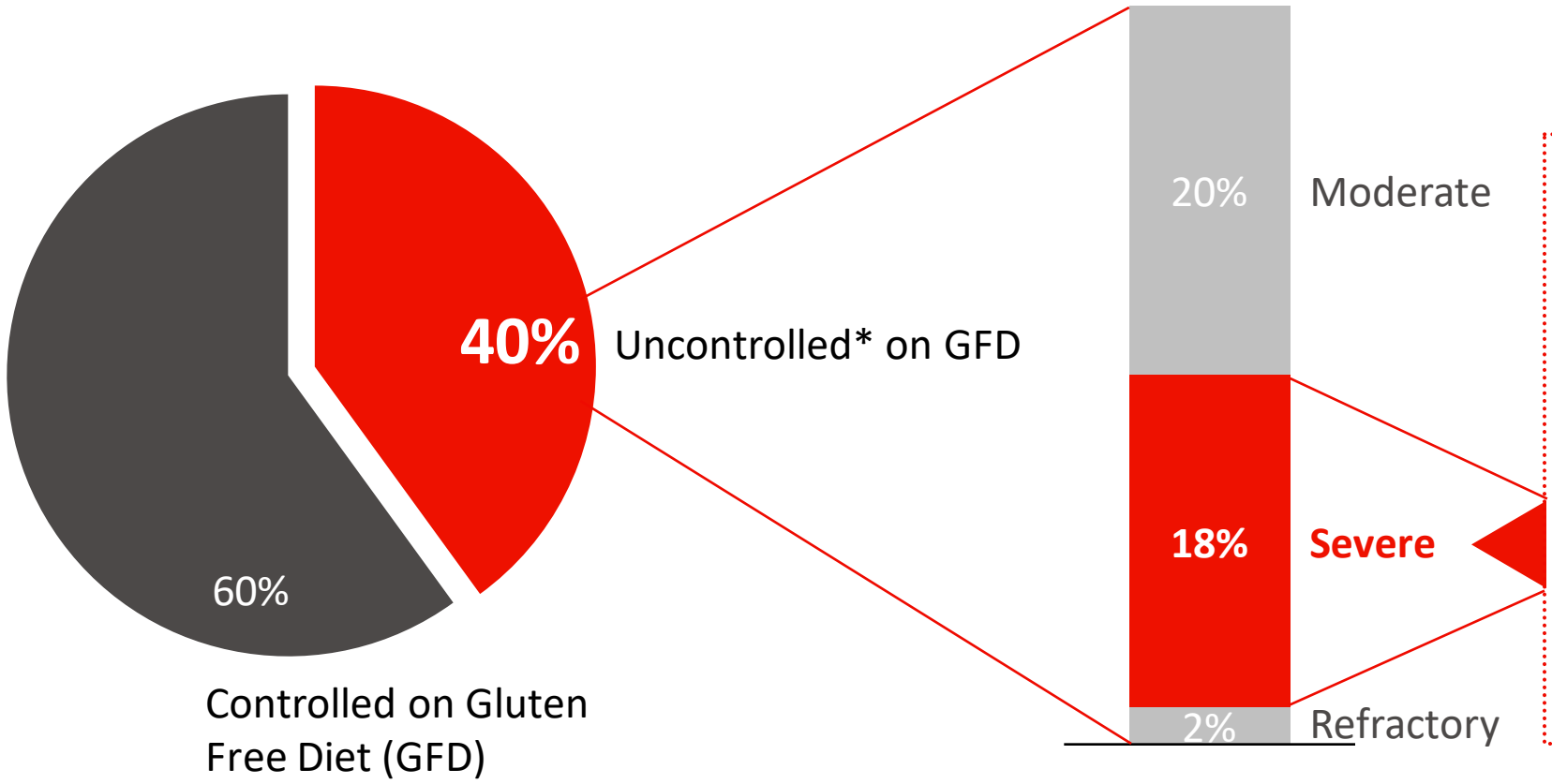
- Overlooked disease, growing prevalence
- Chronic symptoms
- Higher risk of certain cancers
- High treatment burden affecting the whole family
- No current pharmacologic therapies

*“Some of us are so extremely sensitive that one little crumb will make us extremely sick. I'm one of those people, and there is really nothing I can do about it”*

– **Delisi**, Celiac disease patient

1. Pooled global prevalence; Clin Gastroenterol Hepatol. 2018 Jun;16(6):823-836
2. Estimated number of patients projected eligible for treatment, in markets where the product is anticipated to be commercialized, subject to regulatory approval

# WE ARE FOCUSING ON THE NARROWEST POPULATION WITH HIGH UNMET NEED



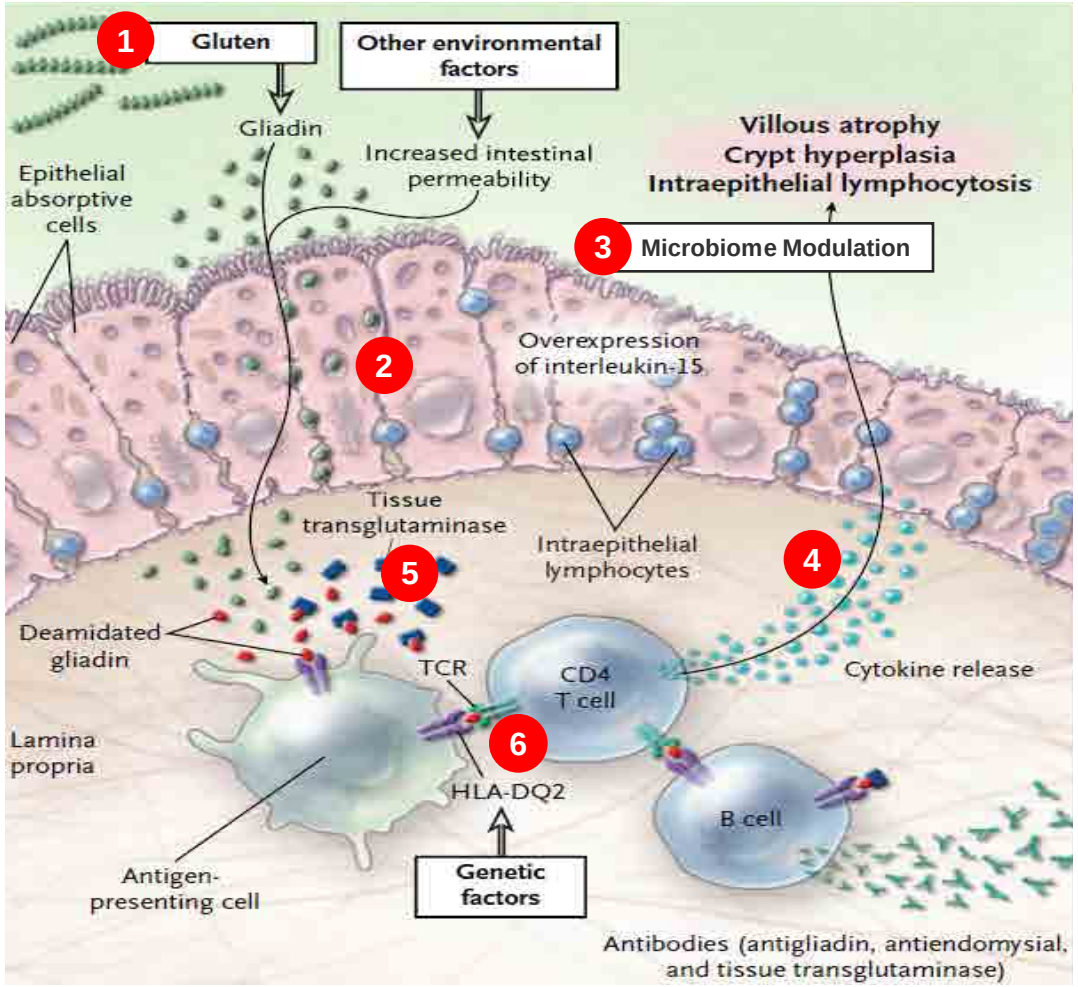

**Our focus:**

- Niche patient segment with the highest unmet need
- Severe symptoms with villous atrophy
- Continue to suffer despite the GFD and are highly likely to take a therapy

*Uncontrolled defined as ongoing chronic moderate to severe symptoms with villous atrophy

# OUR APPROACH TO TREATING CELIAC DISEASE

## TREATMENT OPPORTUNITIES FOR CELIAC DISEASE




1. Enzymatic digestion of gluten
2. Reduce intestinal permeability
3. Microbiome modulation
4. Cytokine inhibition
5. Transglutaminase inhibition
6. Promote Immune tolerance

PVP BIOLOGICS

Kuma062 promises greatly increased enzymatic efficiency and improved formulation over predecessors

COUR

TAK-101 (TIMP-GLIA) has the potential to be a first in class, tolerizing immune therapy for celiac disease

*Source: Green and Cellier, 2007*

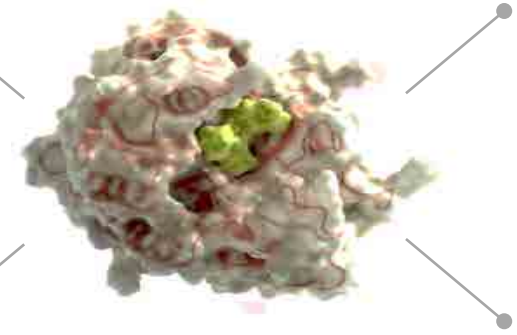
# KUMA062: A HIGHLY POTENT ORAL GLUTENASE THAT COULD CHANGE THE STANDARD OF CARE IN CELIAC DISEASE

## ABOUT KUMA062

- Kuma062 is an oral, computationally-engineered super glutenase
- Enhanced catalytic activity compared to other glutenases

**Optimal activity at the pH range of the stomach after a meal**

**Resistance to common digestive proteases**

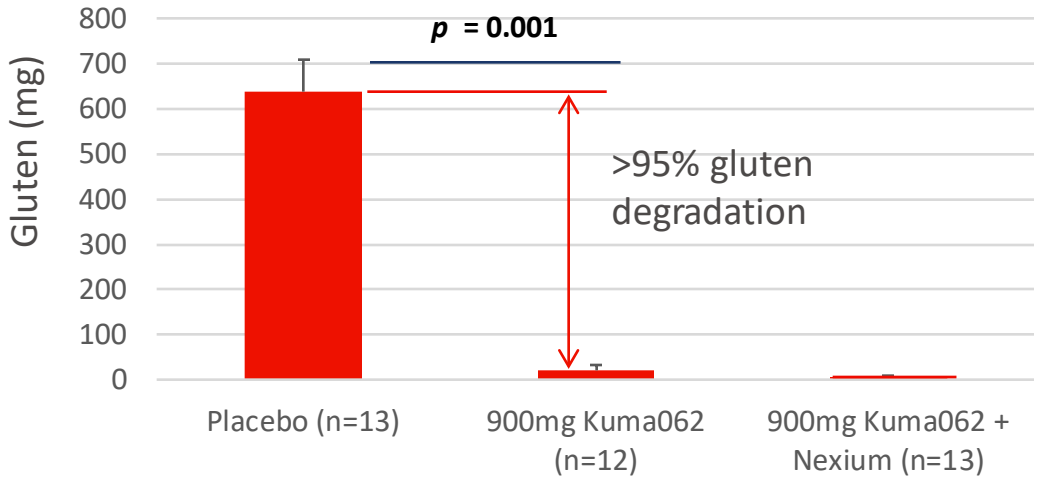


**Specificity for peptides with immunogenic regions of gliadin**

**Eliminates ex vivo T cell response to all 3 major gliadin families**

## CLINICAL DATA SHOWS KUMA062 CAN DEGRADE >95% OF INGESTED GLUTEN

Gluten recovery in gastric contents aspirated 30mins after meal containing 3g of gluten

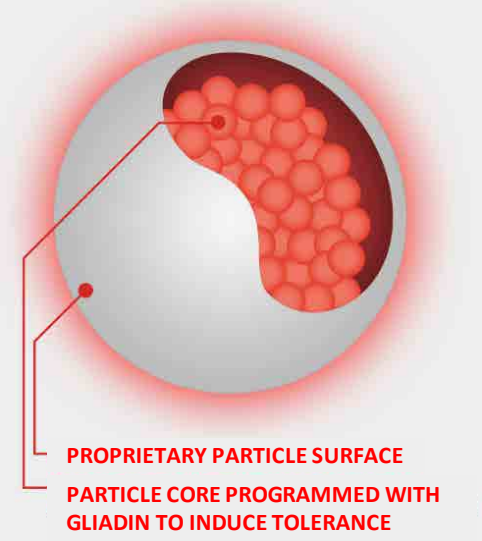



- Kuma well-tolerated, no identified safety concern
- Decision to acquire PVP Biologics expected Q3 FY2019

# TAK-101: POTENTIAL BEST-IN-CLASS, INTRAVENOUS THERAPY FOR CELIAC DISEASE DESIGNED TO MODIFY T CELL RESPONSE

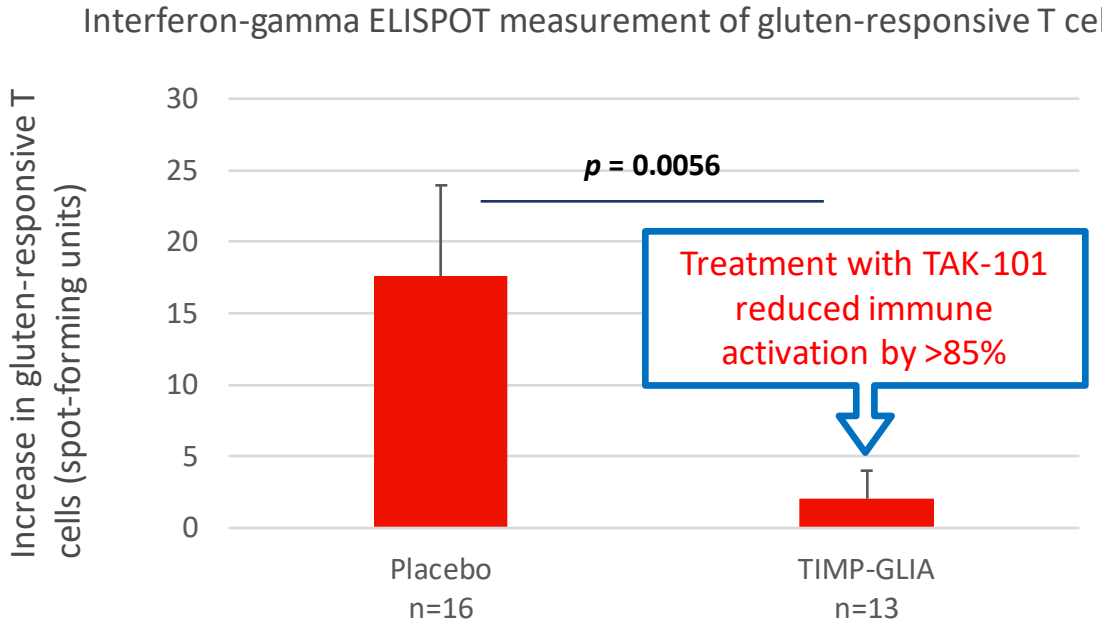
## ABOUT TAK-101*

- Biodegradable polymer encapsulating antigen
- Designed to induce tolerance to gluten, reduce T cell responses to gliadin




- Expected to provide durable (3 months or longer) down regulation of T cell responses to immunogenic gliadin peptides

## TAK-101 REDUCES IMMUNE ACTIVATION AFTER GLUTEN EXPOSURE



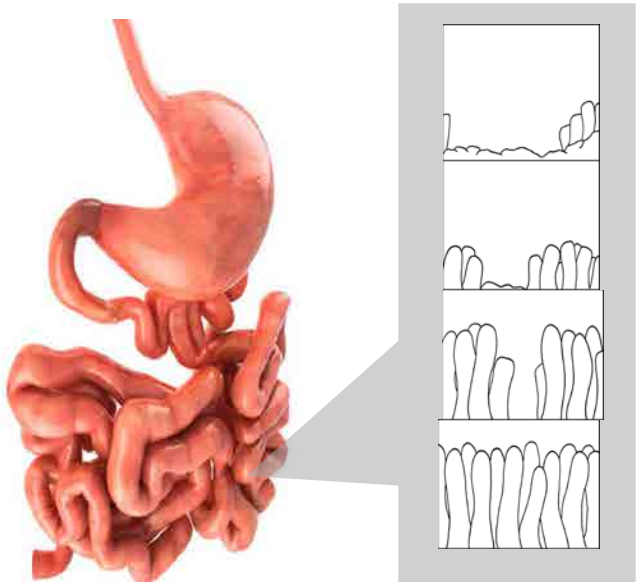

## TAKEDA ACQUIRED EXCLUSIVE GLOBAL LICENSE TO TAK-101


*Formerly TIMP-GLIA
Source: https://www.courpharma.com/our-technology/

# WE ARE LEADING THE SCIENCE IN CELIAC DISEASE WITH A NEW AI - BASED TOOL AND INGESTIBLE DEVICE

## PIONEERING AT BOUNDARIES OF CLINICAL MEDICINE

- Innovative, non-invasive, patented method of measuring total burden of intestinal disease

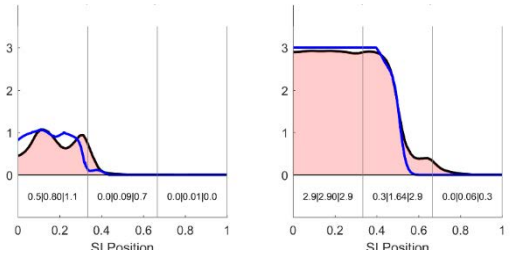


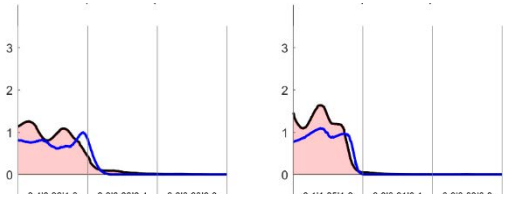
## INNOVATIVE USE OF TECHNOLOGY

- Ingestible high resolution camera pill
- Modern machine-learning/ AI based image processing


## PRECISION MEASUREMENT USING AI

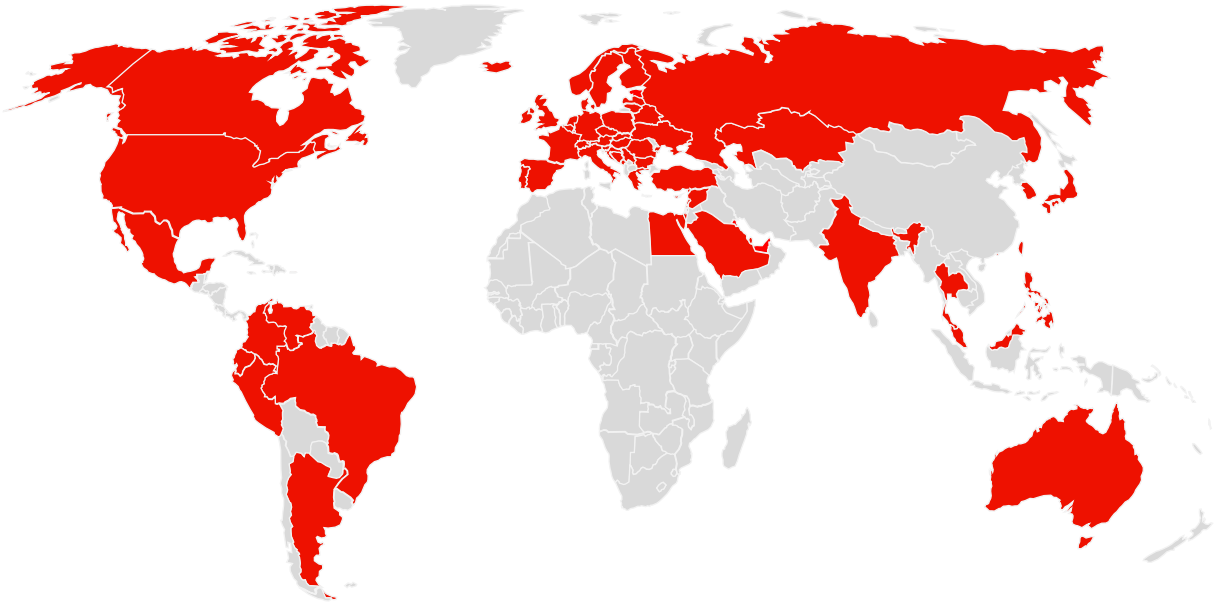
- Pioneering Automated Image assessment quantifies disease burden



# TAKEDA IS THE BEST COMPANY TO BRING CELIAC THERAPIES TO PATIENTS

**World-class, fully connected GI commercial infrastructure across 65+ countries that supports $6bn+ revenues**



- Extensive GI clinical footprint
- Strong reputation for scientific excellence
- Lauded for calculated risk-taking by the GI community
- Experience with redefining guidelines and treatment paths

# NME MILESTONES ACHIEVED IN FY19 AND LOOKING AHEAD TO OTHER POTENTIAL MILESTONES[1] THROUGH FY20

## PIVOTAL STUDY STARTS, APPROVALS

### 1H FY 2019

- ☑ TAK-611 — MLD — Ph 2 start[2]
- ☑ TAK-755 — cTTP — Ph 3 start
- ☑ TAK-925 — Narcolepsy — POC
- ☑ TAK-721 — EoE — Ph 3 data (induction)
- ☑ TAK-101 — Celiac Disease — POC

### 2H FY 2019

- ☑ PEVONEDISTAT TAK-924 — AML — Ph 3 start
- TAK-788 — 1L NSCLC — Ph 3 start
- ☑ PEVONEDISTAT TAK-924 — HR-MDS — Ph 2 Overall Survival
- ☑ TAK-007 — Hem. Malignancies — POC
- TAK-609 — Hunter (IT) — Ph 3 data 2yr extension
- mHTT ASO — Huntington's Disease — POC
- TAK-721 — EoE — Ph 3 data (maintenance)

### 1H FY 2020

- TAK-788 — 2L NSCLC — Ph 2 Pivotal
- TAK-573 — R/R MM, Solid Tumor — POC
- TAK-721 — EoE — Approval
- mHTT ASO — Huntington's Disease — Pivotal start

### 2H FY 2020

- TAK-620 — R/R CMV SOT & HSCT — Ph 3 data
- TAK-755 — iTTP — POC
- TAK-935 — DEE — POC
- TAK-906 — Gastroparesis — POC
- TAK-951 — Nausea & Vomiting — POC

**Oncology**

**Rare Disease**

**Neuroscience**

**Gastroenterology**

☑ Denotes milestones that have been achieved.

## KEY DATA READOUTS

1. Potential key milestone dates as of November 14, 2019. The dates included herein are estimates based on current data and are subject to change
2. Potentially registration enabling

# SUMMARY

**1**

We have built an industry-leading portfolio rooted in unparalleled scientific excellence and outstanding global commercial strength

**2**

We are well positioned to bring the first therapies to celiac patients that could change the standard of care

**3**

We have multiple milestones, including expected key approvals in the next 2 years that will be transformative for patients

# R&D DAY AGENDA – NEW YORK, NOVEMBER 14, 2019

| TIME | AGENDA |
|---|---|
| 12:30 – 12:35 | **Welcome and Opening Remarks**<br>*Sheelagh Cawley-Knopf, Head R&D Global Portfolio Strategy* |
| 12:35 – 12:45 | **Takeda: A Global Values-Based, R&D-Driven Biopharmaceutical Leader**<br>*Christophe Weber, President & CEO Takeda* |
| 12:45 – 13:20 | **Translating Science into Highly Innovative, Life-changing Medicines**<br>*Andy Plump, President R&D* |
| 13:20 – 13:45 | **Oncology and Cell Therapies with Spotlight on CAR-NK**<br>*Chris Arendt, Head Oncology Drug Discovery Unit* |
| 13:45 – 14:05 | **Spotlight on Oncology Opportunities**<br>• **TAK-788** : *Rachael Brake, Global Program Lead*<br>• **Pevonedistat** : *Phil Rowlands, Head Oncology Therapeutic Area Unit* |
| 14:05 – 14:20 | **Break** |
| 14:20 – 14:45 | **Rare Diseases & Gene Therapy**<br>*Dan Curran, Head Rare Disease Therapeutic Area Unit* |
| 14:45 – 15:00 | **Spotlight on Orexin2R agonists**<br>*Deborah Hartman, Global Program Lead* |
| 15:00 – 15:20 | **Therapeutic Area Focus in GI with Spotlight on Celiac Disease**<br>*Asit Parikh, Head GI Therapeutic Area Unit* |
| 15:20 – 16:00 | **Panel Q&A Session** |
| 16:00 | **Drinks reception** |

# Panel Q&A Session