WAVE 1 PIPELINE MARKET OPPORTUNITY CALL (PART 2)

April 6th, 2021

Takeda Pharmaceutical Company Limited

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FY2021 WILL BE AN INFLECTION YEAR FOR THE PIPELINE

Up to 6 NME **regulatory submissions** anticipated by year-end FY21, with potential for **4 approvals**

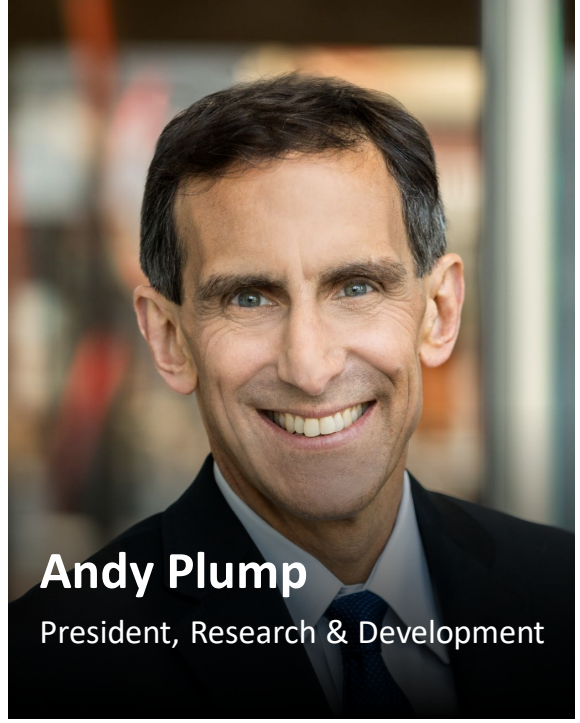
Expect 7 NMEs in **pivotal studies across 10 indications** by the end of FY21

Strong R&D and Commercial partnership to ensure launch excellence and **deliver life transforming treatments to people** worldwide

Takeda intends to increase R&D investment to 500-550 billion JPY in FY2021

AGENDA

TIME (ET)	TIME (JT)	AGENDA
08:00 – 08:05	21:00 – 21:05	**Introduction** *Christophe Weber, President & CEO Takeda*
08:05 – 08:10	21:05 – 21:10	**Delivering an Innovative Pipeline to Our Patients: *Spotlight on Select Wave 1 Programs*** *Andy Plump, President Research & Development*
08:10 – 08:35	21:10 – 21:35	**Maribavir** *Obi Umeh, Global Program Leader Maribavir, Rare Genetic and Hematology* *Claus Jepsen, Head of Global Product and Launch Strategy, Rare Genetic and Hematology*
08:35 – 08:40	21:35 – 21:40	***Break***
08:40 – 09:35	21:40 – 22:35	**Neuroscience Strategy, Soticlestat & Orexin** *Sarah Sheikh, Head of Neuroscience Therapeutic Area Unit* *Elena Koundourakis, Head of Orexin Franchise Development, Neuroscience TA* *Erika Gill, Head of Global Product and Launch Strategy, Neuroscience*
09:35 – 09:40	22:35 – 22:40	**Delivering an Innovative Pipeline to Our Patients: *Spotlight on Select Wave 1 Programs*** *Uthra Sundaram, EVP, Global Product and Launch Strategy*
09:40 – 10:30	22:40 – 23:30	**Panel Q&A Session**



Delivering an Innovative Pipeline to Our Patients

Spotlight on Select Wave 1 Programs

A GLOBAL VALUES-BASED BIOPHARMACEUTICAL COMPANY WITH A PATIENT-DRIVEN AND SCIENCE-FIRST R&D ENGINE

R&D FOCUS

INNOVATIVE BIOPHARMA

- ONCOLOGY
- RARE GENETIC & HEMATOLOGY
- NEUROSCIENCE
- GASTROENTEROLOGY (GI)
- PLASMA-DERIVED THERAPIES
- VACCINES

- CELL THERAPY
- GENE THERAPY
- DATA SCIENCES

INNOVATIVE PIPELINE

- **11 Wave 1 NMEs**
  5 programs with BTD, 3 with FTD and 1 with Sakigake designation
- **~30 Wave 2 NMEs**

ROBUST PARTNERSHIP MODEL

- Takeda's Labs are designed to access innovation wherever it originates
- Investments in novel mechanisms and capabilities for a sustainable future

 | NME: New Molecular Entity; BTD: Breakthrough Therapy Designation; FTD: Fast Track Designation.

TAKEDA LABS IN KEY INNOVATIVE CENTERS

CAMBRIDGE, MA
R&D Center, Oncology, Cell therapy, GI Research

SHONAN, JAPAN
Neuroscience Research, T-CiRA, iPark

SAN DIEGO, CA
Specialized drug discovery technologies, GI and Neuroscience

VIENNA, AUSTRIA
Gene Therapy, Plasma Derived Therapy

WE ARE ACCESSING INNOVATION BY INTEGRATING TAKEDA'S WORLD CLASS LABORATORIES WITH A NETWORK OF PARTNERS

HEMOSHEAR THERAPEUTICS
Fibrotic, Rare Liver Diseases

MD Anderson Cancer Center
TAK-007 & CAR-NK Platform

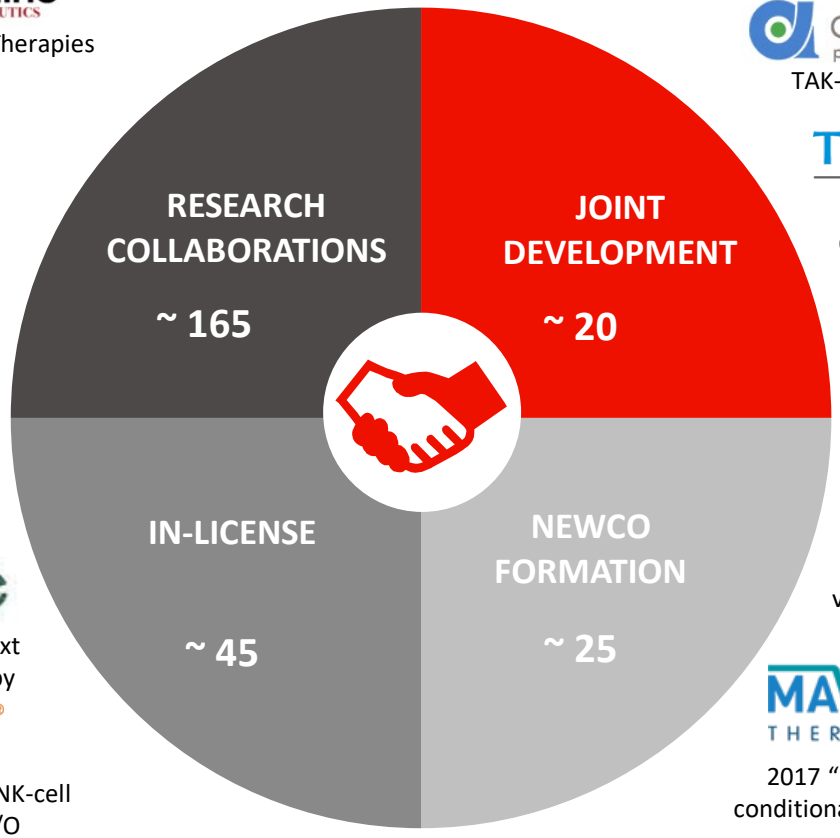
Neurocrine BIOSCIENCES
Psychiatry Partnership

Carmine THERAPEUTICS
Non-Viral Gene Therapies

arrowhead pharmaceuticals
TAK-999, RNAi therapy

SKYHAWK THERAPEUTICS
RNA Splicing Small Molecules Targeting Neurologic Disease

TURNSTONE BIOLOGICS
TAK-605 and Oncolytic Virus Platform



PeptiDream
Peptide-Drug Conjugates for Neuromuscular Diseases

Phathom PHARMACEUTICALS
Newco to develop vonoprazan in the US, EU, CA

evozyne
Synthetic Proteins for Next Generation Gene Therapy

KSQ Therapeutics
Novel T-cell and NK-cell targets for I/O

MAVERICK THERAPEUTICS
2017 "Build to Buy" newco for conditional bispecific T-cell engagers

Select new partnerships from FY19 and FY20

RESEARCH PIPELINE[1]
~80% NON SMALL MOLECULES

- 22% Small Molecule
- 20% Biologic and other
- 21% Peptide/Oligonucleotide
- 37% Cell and Gene Therapy

OUR PIPELINE IS POISED TO DELIVER NOW AND IN THE FUTURE

WAVE 1[1] | CLINICAL-STAGE NMEs | WAVE 2[2]

TARGET APPROVAL	FY20	FY21	FY22	FY23	FY24	FY25/26	FY27 AND BEYOND
ONCOLOGY		**mobocertinib** *2L NSCLC with EGFR exon 20 insertion mutation*[3]	**pevonedistat** *HR-MDS*	**mobocertinib** *1L NSCLC with EGFR exon 20 insertion mutation*	**pevonedistat** *Unfit AML* **TAK-007** *CD19+ hematologic malignancies*	**TAK-981** *Multiple cancers* **TAK-573** *R/R MM* **TAK-605** *Multiple cancers*	**TAK-252** *Solid tumors* **TAK-102** *Multiple cancers* **TAK-186** *EGFR Solid Tumor* **TAK-676** *Solid tumors* **TAK-940** *CD19+ hematologic malignancies*
RARE GENETIC & HEMATOLOGY		**maribavir** *R/R CMV infect. in transplant* **TAK-609** *Hunter CNS (IT)*	**maribavir** *1L CMV infect. in HSCT*	**TAK-611** *MLD (IT)* **TAK-755** *cTTP*		**TAK-755** *iTTP, SCD* **mezagitamab** *MG, ITP*	**TAK-607** *Complications of prematurity*
NEUROSCIENCE				**soticlestat** *DS* **soticlestat** *LGS*	**Orexin2R-ag** *(TAK-994/TAK-925) Narcolepsy T1*	**Orexin2R-ag** *Sleep Disorders*	**TAK-341** *Parkinson's Disease* **TAK-071** *Parkinson's Disease* **TAK-041** *Anhedonia in MDD* **TAK-653** *TRD* **TAK-831** *CIAS NS*
GASTRO-ENTEROLOGY		**Eohilia**[4] *EoE Approval date TBD*				**TAK-062** *Celiac Disease* **TAK-101** *Celiac Disease* **TAK-999** *AAT Liver Disease* **TAK-951** *Nausea & vomiting* **TAK-906** *Gastroparesis*	**sibofimloc** *Crohn's Disease (post-op and ileitis)* **TAK-671** *Acute Pancreatitis* **TAK-039** *Hepatic encephalopathy* **TAK-954** *POGD*
VACCINES		**TAK-003** *Dengue Vaccine* **TAK-919** *Moderna COVID-19 Vaccine (JP)* **TAK-019** *Novavax COVID-19 Vaccine (JP)*				**TAK-426** *Zika Vaccine*	**TAK-214** *Norovirus Vaccine*
PDT							

Orphan Potential in at Least One Indication | Breakthrough and/or Fast Track Designations | China Breakthrough and/or Japan SAKIGAKE Designation | Deep Dive Today | New Addition to the Pipeline | COVID-19 Vaccines

1. Projected approval dates depend on data read-outs; some Wave 1 target approval dates assume accelerated approval
2. Certain Wave 2 programs may be accelerated into Wave 1 depending on future data read outs
3. Approval date assumes filing on Phase 2 data
4. In active discussions with the FDA. Projected approval subject to outcome of discussions

Takeda's Fiscal Year ends March 31 of the following year; e.g."FY20" refers to the twelve month period ending March 31, 2021.
All timelines are approximate estimates of April 6, 2021.

TAKEDA'S R&D ENGINE WITH POTENTIAL TO DELIVER A SERIES OF LIFE-TRANSFORMING MEDICINES

11 + 2

WAVE 1 pipeline assets with potential approval by FY2024

- 11 NMEs with best-in-class / first-in-class potential in areas of high unmet need
- 10 target orphan patient populations; 6 have Breakthrough and/or Fast Track Designations
- All 11 Wave 1 pipeline assets have near-term pivotal milestones

FY2021 expected to be an inflection year for the pipeline

- *Up to 6 regulatory submissions anticipated by year-end FY21, with potential for 4 approvals*
- *Expect 7 programs in pivotal studies across 10 indications by year-end FY21*
- *Potential approval of TAK-919 (Moderna) and TAK-019 (Novavax) COVID-19 vaccines in Japan[2] (Partnered programs)*

~30

WAVE 2 programs with transformative or curative potential to support sustainable growth from FY2025. TAK-999 and TAK-981 are on the cusp of Wave 1 with potential to accelerate[1]

15+

Innovative medicines with potential to be approved in China by FY2024, with 6 approvals already received in the past 3 years

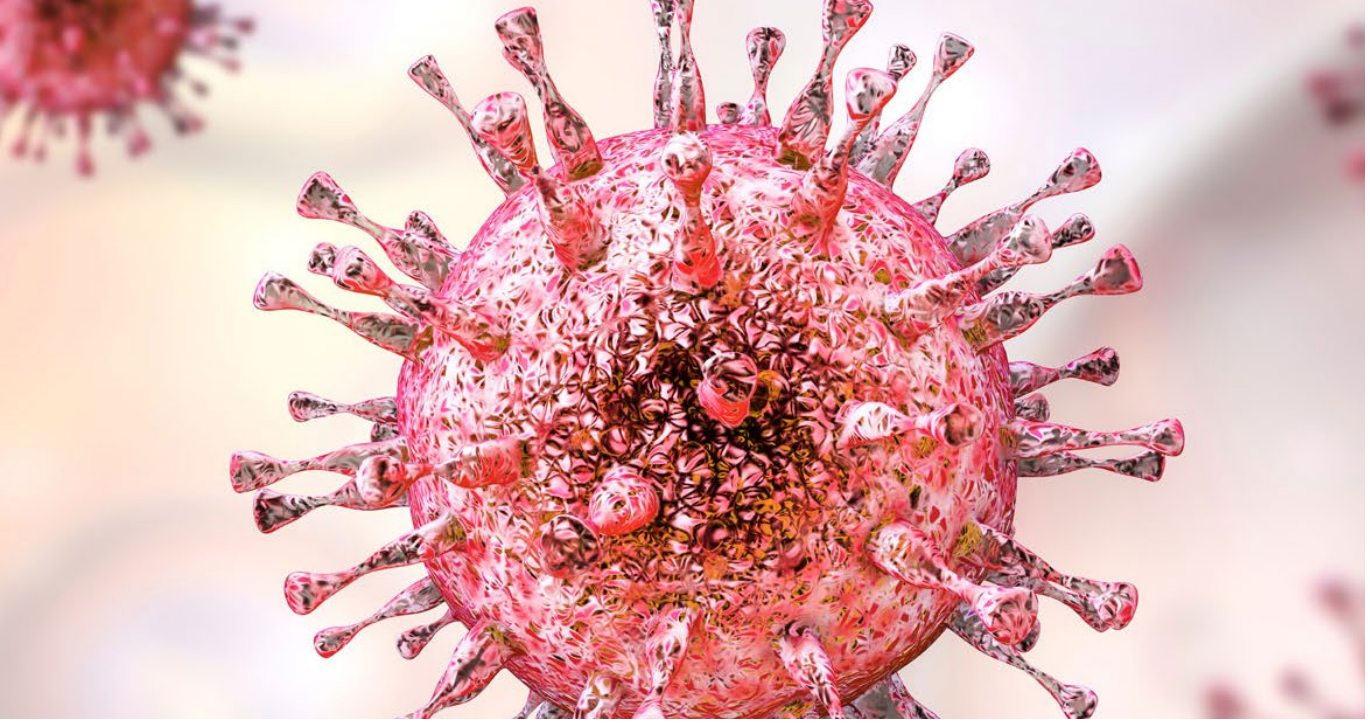
1. Potential to accelerate into Wave 1 dependent on future data readouts.
2. Takeda is supporting global access to three different COVID-19 vaccines: Novavax to develop, manufacture and commercialize 250 million doses of their vaccine in Japan; the Government of Japan's Ministry of Health, Labour and Welfare and Moderna to distribute 50 million doses of their vaccine in Japan; have released capacity at our contract manufacturer, IDT Biologika GmbH, to manufacture Johnson & Johnson's vaccine for three months.

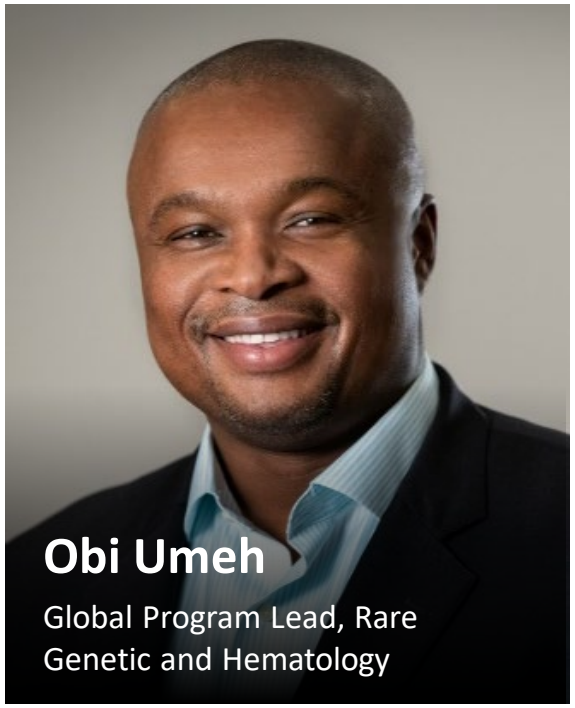
WAVE 1 PIPELINE TO DELIVER LIFE-TRANSFORMING TREATMENTS TO GROWTH EMERGING MARKETS

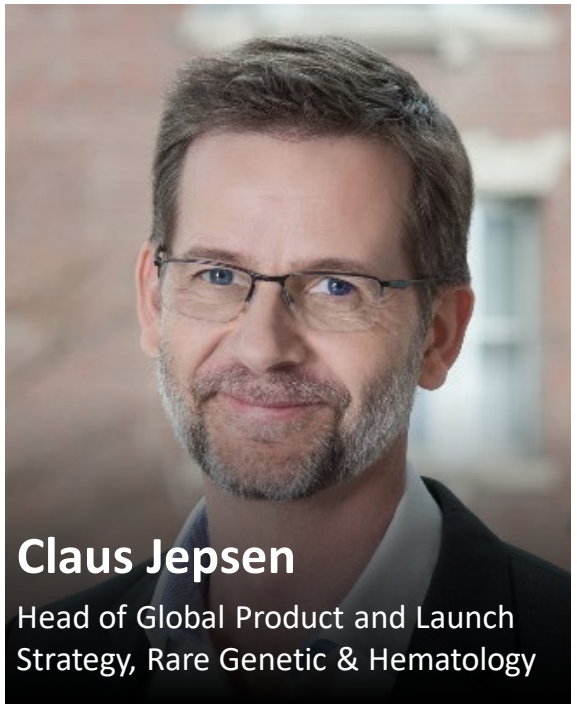
Planned Registrations

Therapeutic Areas	2021				2026+
VACCINES	**TAK-003** Dengue Vaccine				
ONCOLOGY	**Mobocertinib (TAK-788)** Exon 20 NSCLC 2L	**Pevonedistat (TAK-924)** High Risk Myelodysplastic Syndromes		**TAK-007** CD19+ hematologic malignancies	
RARE GENETIC & HEMATOLOGY		**Maribavir (TAK-620)** CMV infection in transplant patients (R/R)	**TAK-609** Hunter Syndrome (intrathecal)	**TAK-755** Thrombotic Thrombocytopenic Purpura	**TAK-611** Metachromatic leukodystrophy (intrathecal)
NEUROSCIENCE				**Soticlestat (TAK-935)** Lennox-Gastaut syndrome and Dravet syndrome	**Orexin** Narcolepsy Type 1
GASTRO-ENTEROLOGY			**Eohilia (TAK-721)** Eosinophilic Esophagitis		

 | Source: Takeda | All timelines are current best estimates and are subject to change due to impact by COVID-19 as of April 6, 2021







Maribavir (TAK-620)

Potential Game Changer in the Treatment for Post-Transplant Cytomegalovirus (CMV) Infection

TRANSPLANTS ARE HIGHLY LIMITED, PRECIOUS, LIFE-SAVING TREATMENTS

Transplants

- Are lifesaving
- Save over 190k lives annually[1,2]
- Loss is devastating for patients & costly to society

Cytomegalovirus (CMV)

- Impacts about a quarter of all transplant recipients[3,4]
- Infection can lead to graft loss, morbidity and mortality
- Clearing CMV helps preserve life-saving benefit of transplantation

Maribavir

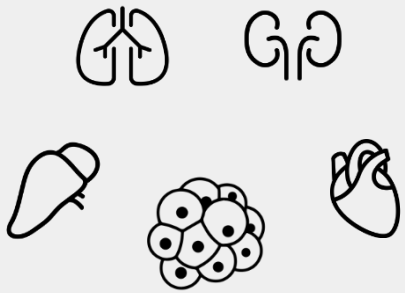
- New, oral anti-viral, with novel MOA & improved safety profile
- Strong clinical data including outstanding phase 3 trial results
- Potential to transform management of post-transplant CMV infection

Takeda plans global filings in 2021 with the goal of bringing Maribavir to patients

1: https://www.who.int/transplantation/gkt/statistics/en/ 2. Niederwieser, D., Baldomero, H., Atsuta Y et al.One and Half Million Hematopoietic Stem Cell Transplants (HSCT). Dissemination, Trends and Potential to Improve Activity By Telemedicine from the Worldwide Network for Blood and Marrow Transplantation (WBMT).Blood (2019) 134 (Supplement_1): 2035. 3. L Stern, B Withers, S Avdic et al.Human Cytomegalovirus Latency and Reactivation in Allogeneic Hematopoietic Stem Cell Transplant Recipients. Front Microbiol. 2019 May 28;10:1186. 4.Poornima Ramanan, Raymund Razonable.Cytomegalovirus Infections in Solid Organ Transplantation: A Review.Infect Chemother. 2013 Sep; 45(3): 260–271.

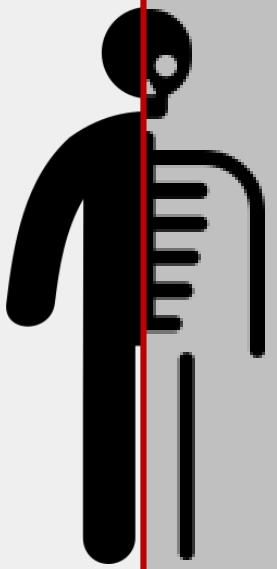
IMMUNOSUPPRESSION IS BOTH NECESSARY AND CHALLENGING

NECESSARY



Prevents Rejection
thus
Protects Transplant

CHALLENGING



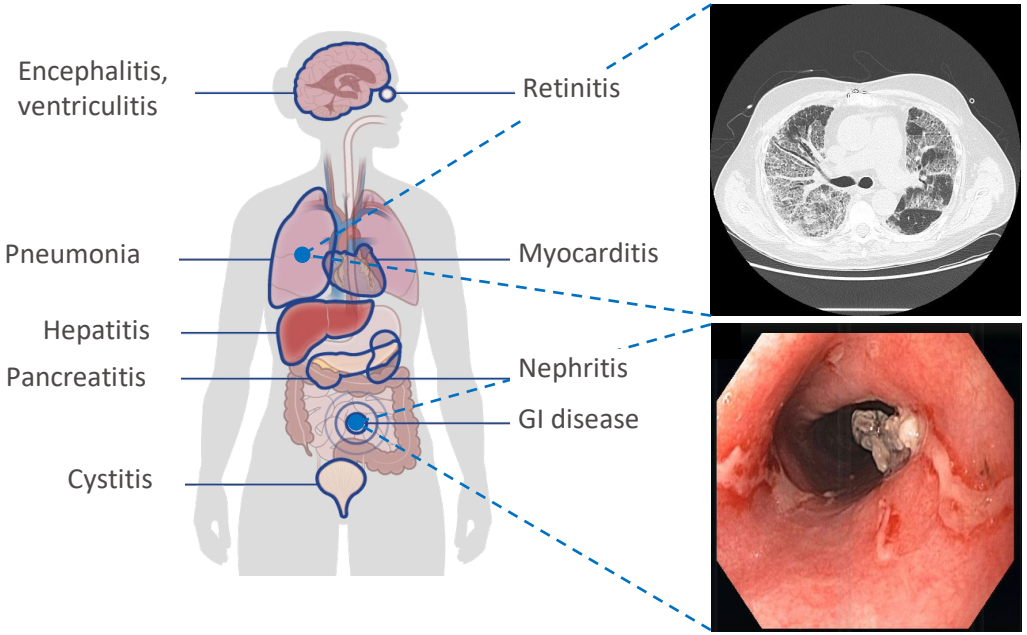
Disables Immune System
► Increased Risk of
Deadly Infections

CMV

- **Common virus, infects most people by adulthood**
- **Infection is dormant (like chickenpox virus) until immune system is compromised**

POST-TRANSPLANT CMV INFECTION *MORE THAN DOUBLES* THE RISK OF *TRANSPLANT LOSS*, MORTALITY AND *TOTAL COST OF TRANSPLANTATION* [1,2,3]

Untreated, CMV Invades Multiple Vital Organs



And Negatively Alters the Immune System

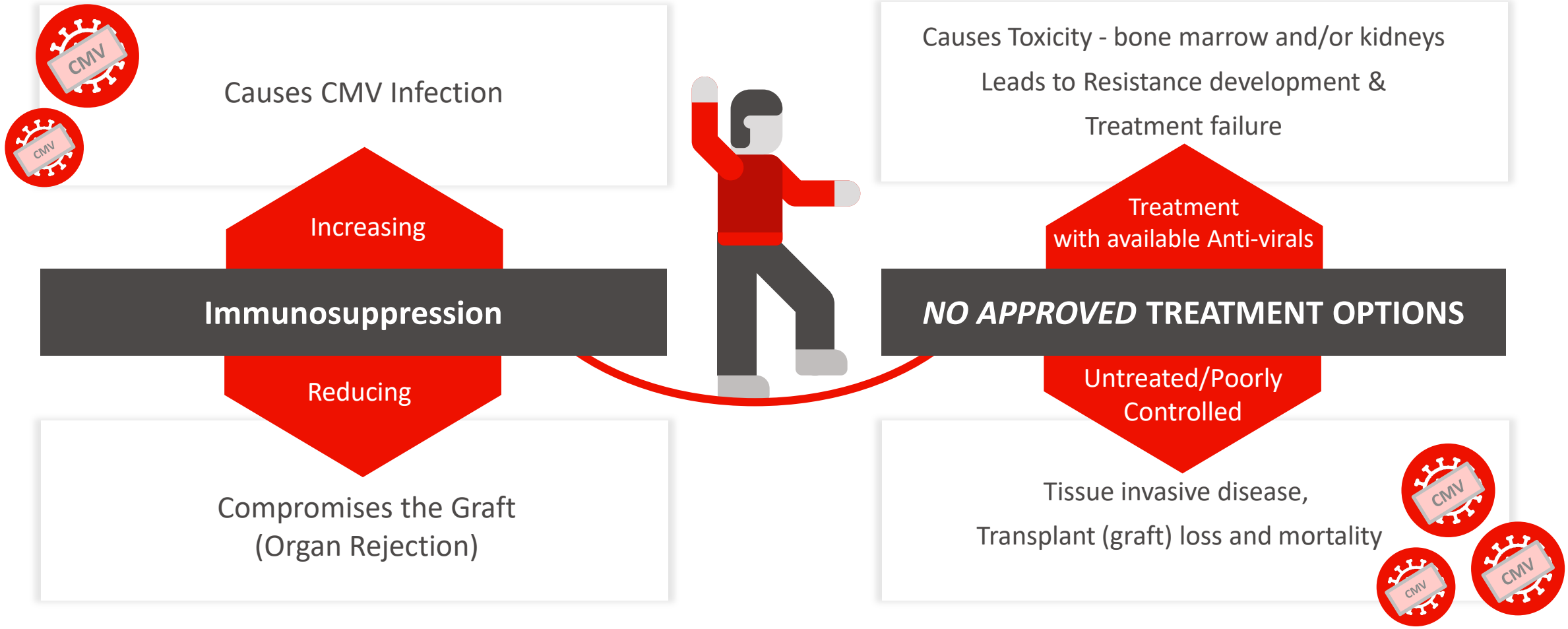
Leading to:

- Graft rejection (SOT)
- Graft-versus-Host Disease (GvHD)
- Immunosuppression
- Fungal/bacterial co-infections

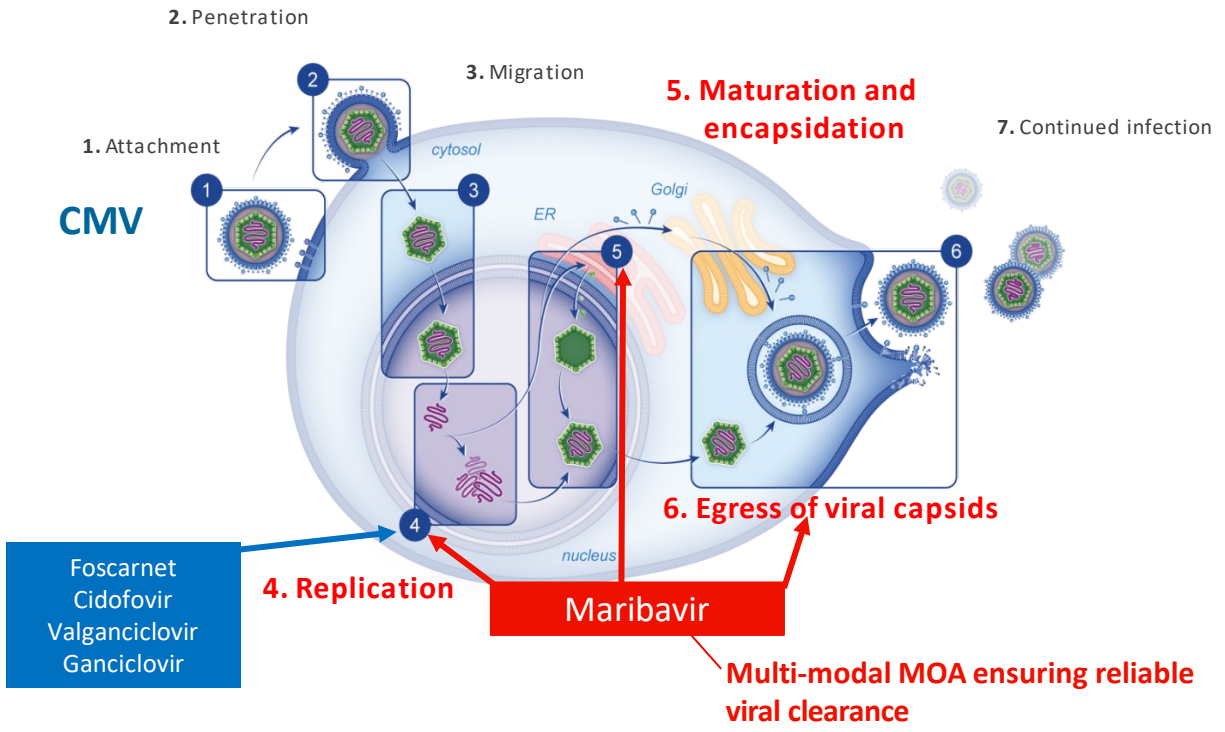
SOT = Solid Organ Transplant

1. Stern M, Hirsch H, Cusini A et al. Cytomegalovirus serology and replication remain associated with solid organ graft rejection and graft loss in the era of prophylactic treatment. Transplantation. 2014 Nov 15;98(9):1013-8
2. MR Jorgenson, JL Descourourez, B Cardinale et al. Risk of opportunistic infection in kidney transplant recipients with cytomegalovirus infection and associated outcomes. Transpl Infect Dis . 2019 Jun;21(3):e13080
3. C Robin, F Hémery, C Dindorf et al. Economic burden of preemptive treatment of CMV infection after allogeneic stem cell transplantation: a retrospective study of 208 consecutive patients.*BMC Infect Dis* **17,** 747 (2017)

A CLEAR UNMET NEED EXISTS FOR AN ANTI-CMV AGENT WITH *STRONG EFFICACY WITHOUT COMPROMISE*



MARIBAVIR HAS THE POTENTIAL TO REDEFINE SUCCESS IN POST-TRANSPLANT CMV DUE TO ITS NOVEL MULTI-MODAL MECHANISM OF ACTION



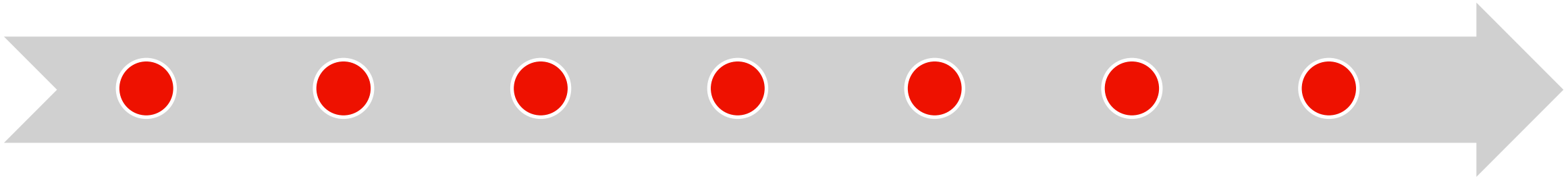
Maribavir:

Works at 3 *different* points (4, 5 & 6) in the viral lifecycle: viral DNA replication, maturation & encapsidation

Only agent that targets pUL97 all other agents inhibit *only* viral replication (#4) at pUL54

Novel MOA permits efficacy against drug resistant CMV

MARIBAVIR, AN ORAL SAFE ANTIVIRAL EXTENSIVELY STUDIED IN MORE THAN 1500 PATIENTS TO DATE



2011

ODD US Granted for Treatment of Post-Transplant CMV

December 2014

Two positive Ph 2 Studies in 1L & 2L (R/R) CMV infection using 400mg bid dose completed

December 2016

Ph 3 Studies in 1L (Study 302) & 2L (Study 303) CMV Infection using 400mg bid dose initiated

December 2017

Breakthrough Therapy Designation (BTD) Granted

November 2020

Positive data readout in 2L (R/R) CMV Infection (Study 303)

1H 2021

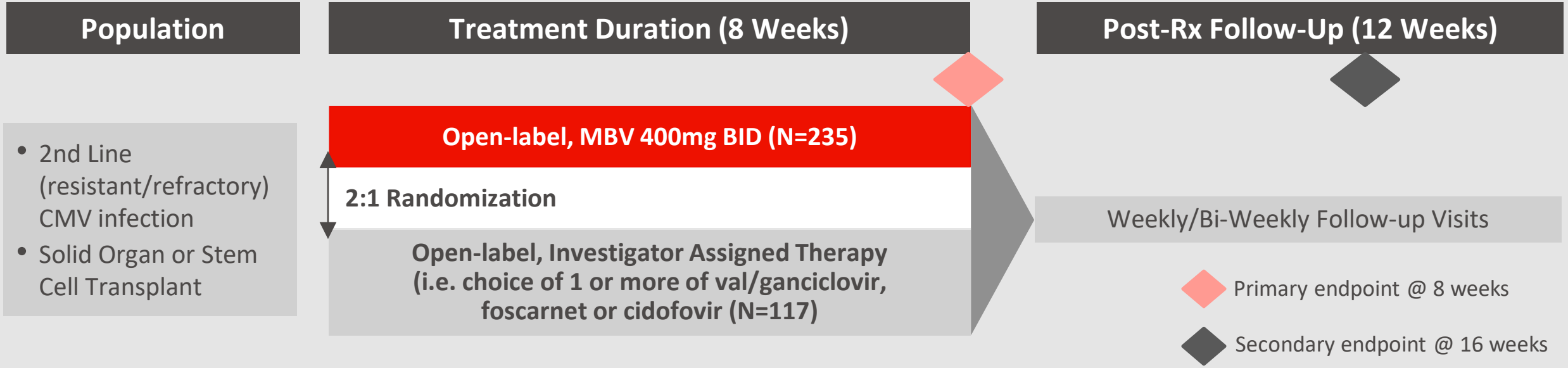
Planned Regulatory Submissions for 2L (R/R) CMV Study

FY 2022

Expected approval for 1L CMV infection (Study 302)

ODD= Orphan Drug Designation, provides up to 7.5* and 12* years of data exclusivity in US & EU respectively

MARIBAVIR MET ITS PRIMARY & SECONDARY ENDPOINTS IN THE PHASE 3 RESISTANT/REFRACTORY CMV INFECTION STUDY (Solstice Trial)



Primary Endpoint (End of Therapy)

Confirmed clearance of plasma CMV DNA (CMV viremia clearance) at the end of Study Week 8

Key Secondary Endpoint (Off-Therapy)

Meet Primary endpoint PLUS

Achieve symptom resolution or improvement, in patients with symptomatic CMV at baseline OR maintain asymptomatic state through Week 16

SOLSTICE 303
Together we can cultivate progress

GLOBAL TRIAL, REPRESENTATIVE OF RESISTANT/REFRACTORY POST-TRANSPLANT CMV PATIENT POPULATION

Large Global Trial

- >140 sites, 12 countries, 3 continents
- N = 352 transplant recipients

Broad Transplant Population

Included adequate numbers of both solid organ and hematopoetic stem cell transplant recipients

Resistant & Non-Resistant CMV Patients

Over 50% had CMV resistant to conventional agents at study entry

Well Balanced Treatment Arms

Treatment arms balanced by gender, age groups & various high-risk factors

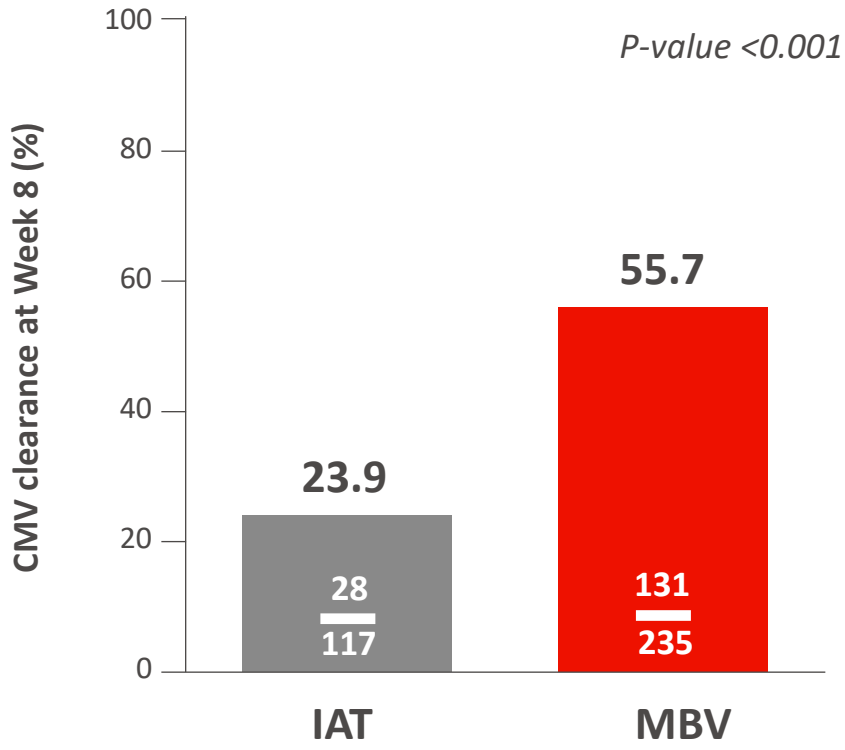
Maribavir better tolerated

>2x more MBV patients completed 8 weeks of treatment vs. conventional antivirals

SOLSTICE 303
Together we can cultivate progress

PRIMARY ENDPOINT: MARIBAVIR SHOWED *CLINICALLY MEANINGFUL*, SUPERIOR VIREMIA CLEARANCE VS. CONVENTIONAL THERAPIES

>2x more efficacy vs comparator
Treatment Difference = 32.8%



Strong Efficacy Across Subgroups of 1° Endpoint

>2x more efficacy across both Solid organ and Stem Cell Transplants

- 30.5% and 36.1% adjusted treatment difference in CMV clearance respectively

>3x more efficacy in patients with resistance

- 44.1% adjusted treatment difference in CMV clearance

>3.8x more efficacy in patients with symptomatic CMV

- 30.6% adjusted treatment difference in CMV clearance

 | Treatment difference was adjusted for baseline CMV viral load (low, intermediate/high) and SOT/HCT, and compared with Cochran-Mantel-Haenszel test. MBV = maribavir.

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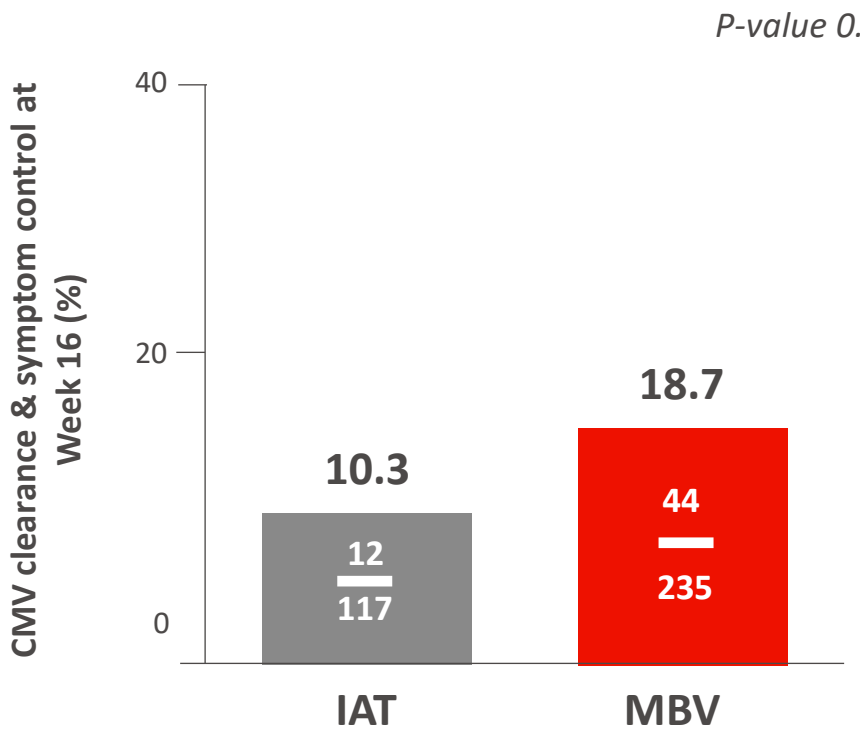
SECONDARY ENDPOINT: MARIBAVIR MAINTAINED SUPERIOR VIREMIA CLEARANCE & SYMPTOM CONTROL THROUGH WEEK 16 (8 WEEKS OFF TREATMENT)

Treatment Difference = 9.5%



Maribavir superior in clearing CMV viremia & Maintaining Symptom Control through Week 16

MBV demonstrated benefit over IAT in CMV viremia clearance & symptom control

- Off-treatment was maintained through Week 16
- 9.5% adjusted treatment difference in CMV clearance & symptom control
- Results provide *internal validation* of the primary endpoint findings

Subgroup analyses of Key 2° endpoint were directionally similar

 IAT = investigator assigned treatment; MBV = maribavir

SOLSTICE 303
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KEY SAFETY FINDINGS

Maribavir was safe & well tolerated without the serious treatment limiting toxicities of existing conventional anti-viral therapies

SAFETY - TOLERABILITY		
Key Treatment-related Adverse Events, %		
Category	**IAT (N=116)**	**MBV (N=234)**
Neutropenia	**(V)GCV, n=56 25.0**	**1.7**
Acute kidney injury	**FOS, n=47 19.1**	**1.7**
Increased immunosuppressant drug levels	0	6.0
Taste disturbance	1.7	44.0

"Neutropenia in ganciclovir recipients after marrow transplantation is an independent risk factor for mortality"[1]

"Acute kidney injury and long-term renal dysfunction are common problems following bone marrow transplantation (BMT) and highly related to mortality"[2]

 1. Salzberger B, et al. Blood. 1997. PMID: 9310503; 2. Kemmner S et al. J Nephrol.2017 Apr;30(2):201-209. doi: 10.1007/s40620-016-0345-y AKI: acute kidney injury

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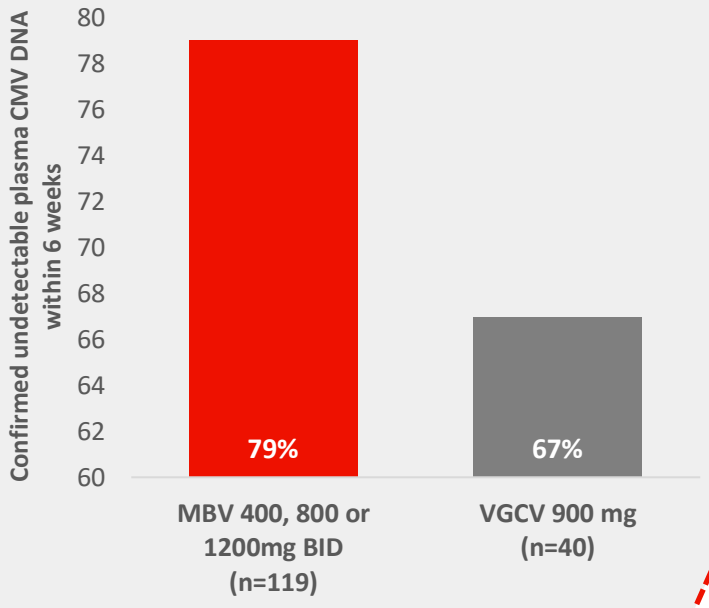
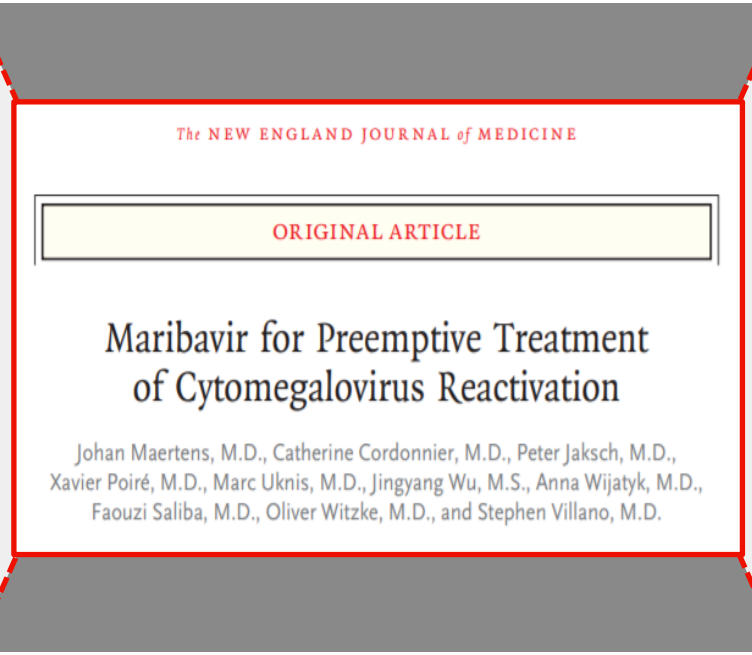
MARIBAVIR HAS A GROWING BODY OF EVIDENCE IN TREATMENT OF FIRST-LINE POST-TRANSPLANT CMV INFECTION

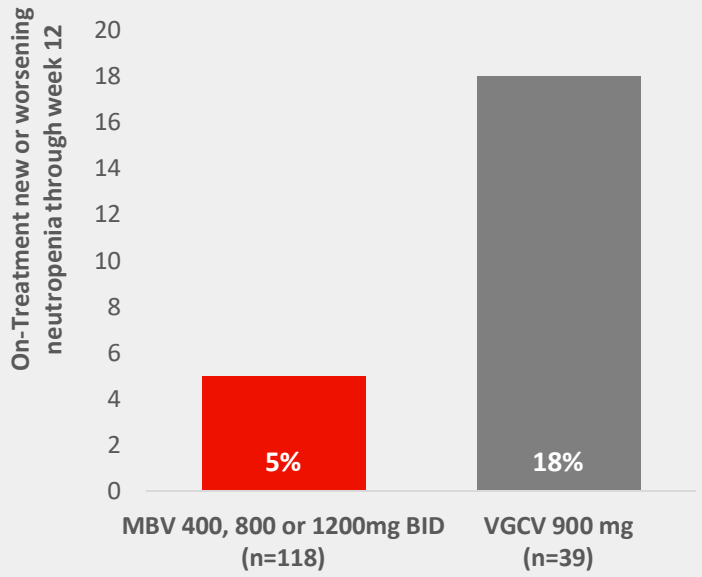
Positive Phase 2 Study In Treatment of 1st Line Post-Transplant CMV Infection in SOT & HSCT Recipients

MBV *compared favorably* to VGCV in CMV viremia clearance



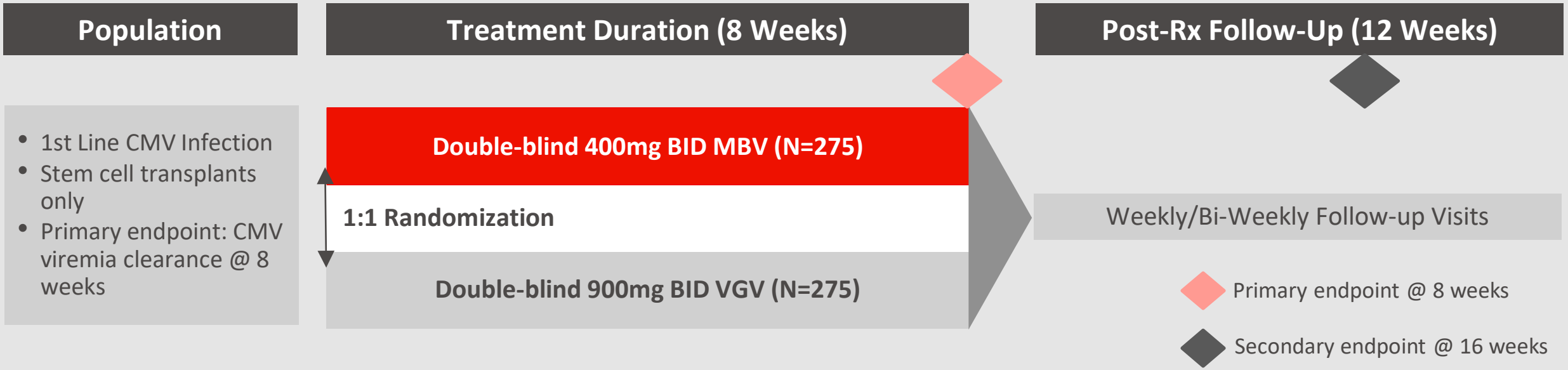


Neutropenia was *lower* with MBV vs VGCV



 BID: twice daily; CMV: cytomegalovirus; HCT: hematopoietic cell transplant; MBV: maribavir; SOT: solid organ transplant; VGCV: valganciclovir

ONGOING PHASE 3 TRIAL IS INVESTIGATING MARIBAVIR IN THE FIRST-LINE POST-TRANSPLANT CMV INFECTION SETTING IN HSCT RECIPIENTS



Potential Approval in FY2022

AURORA 302

SUMMARY

1. Transplants are **extremely precious** life-saving treatments

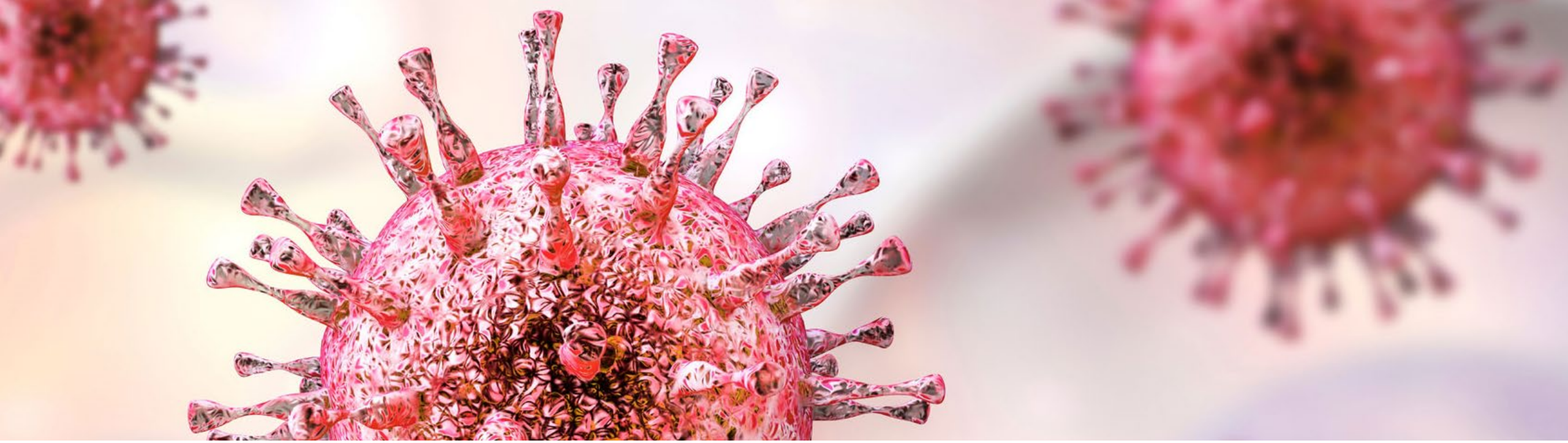
2. CMV infections **threatens survival of transplant** with **devastating consequences** for **the patient** and high cost for society

3. Currently available antivirals for treatment of CMV **are toxic, develop resistance** leading to **treatment failure** and have a **high treatment burden.** Physicians managing CMV are forced to make **difficult and risky tradeoffs**

4. Maribavir is an **exciting** new oral anti-CMV agent with a **novel multimodal MOA**, an **improved safety profile** and **strong clinical data** across a broad spectrum of patients with Post-Transplant CMV Infection

Maribavir has the potential to be a game changer in the management of post-transplant CMV

NEXT STEPS: Worldwide regulatory submissions on track, US & EU first, with plans for Japan, China & ROW



Maribavir – Market Opportunity

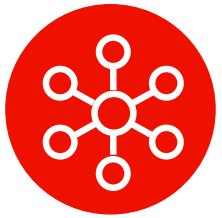
ORGAN TRANSPLANT RECIPIENTS CELEBRATE A UNIQUE SECOND CHANCE AT LIFE

“This is me on my one year lungiversary. Happy Breath Day. Here I am in the wilderness, enjoying life. I think a lot about how to honor my donor. It’s just about giving back, be happy in my career, caring for my friends and family. Simply being a good person”

Jane married & mother of two

CMV IS THE MOST CHALLENGING INFECTION POST-TRANSPLANT - AND AFFECTS TENS OF THOUSANDS OF PATIENTS WORLDWIDE

~190K Globally[1]
~60K USA[2]
(HSCT & SOT transplants)



~ 1/4
of transplant patients experience CMV infections[3]

leaves patients **vulnerable to potentially deadly infections**

2.0-6.2x

Higher risk of ***transplant/graft failure[4]***

2.6x

Higher ***Mortality[5]***

20-30%

Direct transplant ***cost increase[6]***

1) Niederwieser D, Baldomero H, Atsuta Y, et al. One and Half Million Hematopoietic Stem Cell Transplants (HSCT). Dissemination, Trends and Potential to Improve Activity By Telemedicine from the Worldwide Network for Blood and Marrow Transplantation (WBMT).Blood (2019) 134 (Supplement_1): 2035. ; https://www.who.int/transplantation/gkt/statistics/en/ 2) OPTN (SOT) and CIBMTR (HSCT) 3) L Stern, B Withers, S Avdic et al.Human Cytomegalovirus Latency and Reactivation in Allogeneic Hematopoietic Stem Cell Transplant Recipients. Front Microbiol. 2019 May 28;10:1186. Poornima Ramanan, Raymund Razonable.Cytomegalovirus Infections in Solid Organ Transplantation: A Review.Infect Chemother. 2013 Sep; 45(3): 260–271 4) Stern M, Hirsch H, Cusini A et al. Cytomegalovirus serology and replication remain associated with solid organ graft rejection and graft loss in the era of prophylactic treatment. Transplantation. 2014 Nov 15;98(9):1013-8 5) MR Jorgenson, JL Descourourez, B Cardinale et al. Risk of opportunistic infection in kidney transplant recipients with cytomegalovirus infection and associated outcomes. Transpl Infect Dis . 2019 Jun;21(3):e13080 6) C Robin, F Hémery, C Dindorf et al. Economic burden of preemptive treatment of CMV infection after allogeneic stem cell transplantation: a retrospective study of 208 consecutive patients. BMC Infect Dis. 2017;17(1):747.

NOT ONLY DOES CMV INFECTIONS PLACE A HIGH VALUE PROCEDURE AT RISK CMV INFECTIONS ALSO RISK WASTING ORGANS THAT CANNOT BE "RE-ORDERED"

Costly Procedure

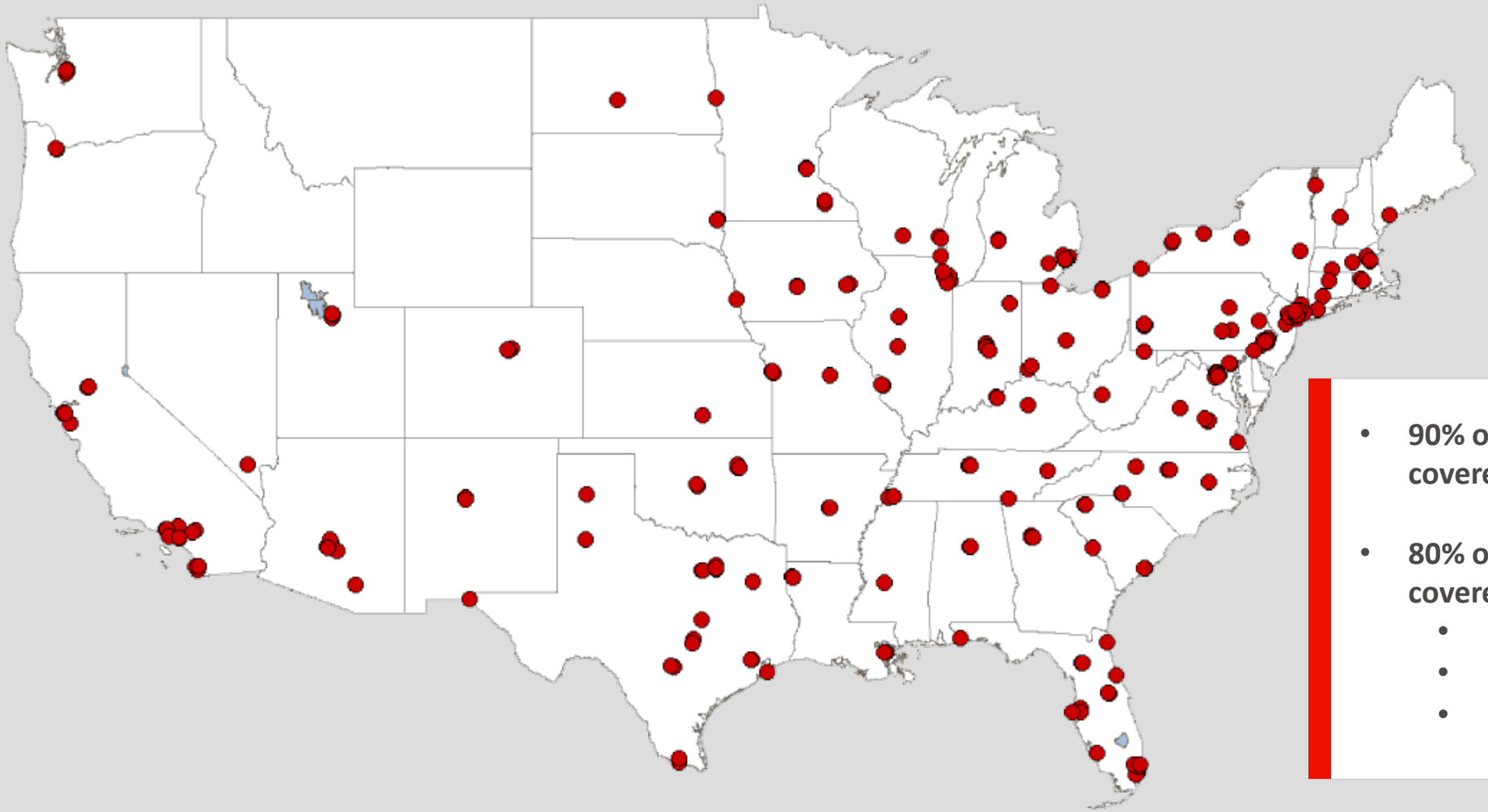
Cost of Kidney Transplant	$443K[1]
Cost of Liver Transplant	$878K[1]
Cost of Allogenic HSCT	$1.1m[1]
Est. annual cost of a transplant patient with CMV infection.	$750-900K[2]

Short Supply

Number of patients on the transplant waiting list	114,000[3]
Number of people dying every day from the lack of available organs for transplant.	20[3]

1) Milliman Research Report: Milliman Research Report: 2017 US Organ and tissue transplant cost estimates and discussion 2) Takeda internal analysis 3) https://www.americantransplantfoundation.org/about-transplant/facts-and-myths/#:~:text=Almost%20114%2C000%20people%20in%20the,of%20available%20organs%20for%20transplant.

BOTH ORGAN AND HCST TRANSPLANT PROCEDURES ARE HIGHLY SOPHISTICATED AND TAKES PLACE IN FEW HIGHLY SPECIALIZED CENTERS

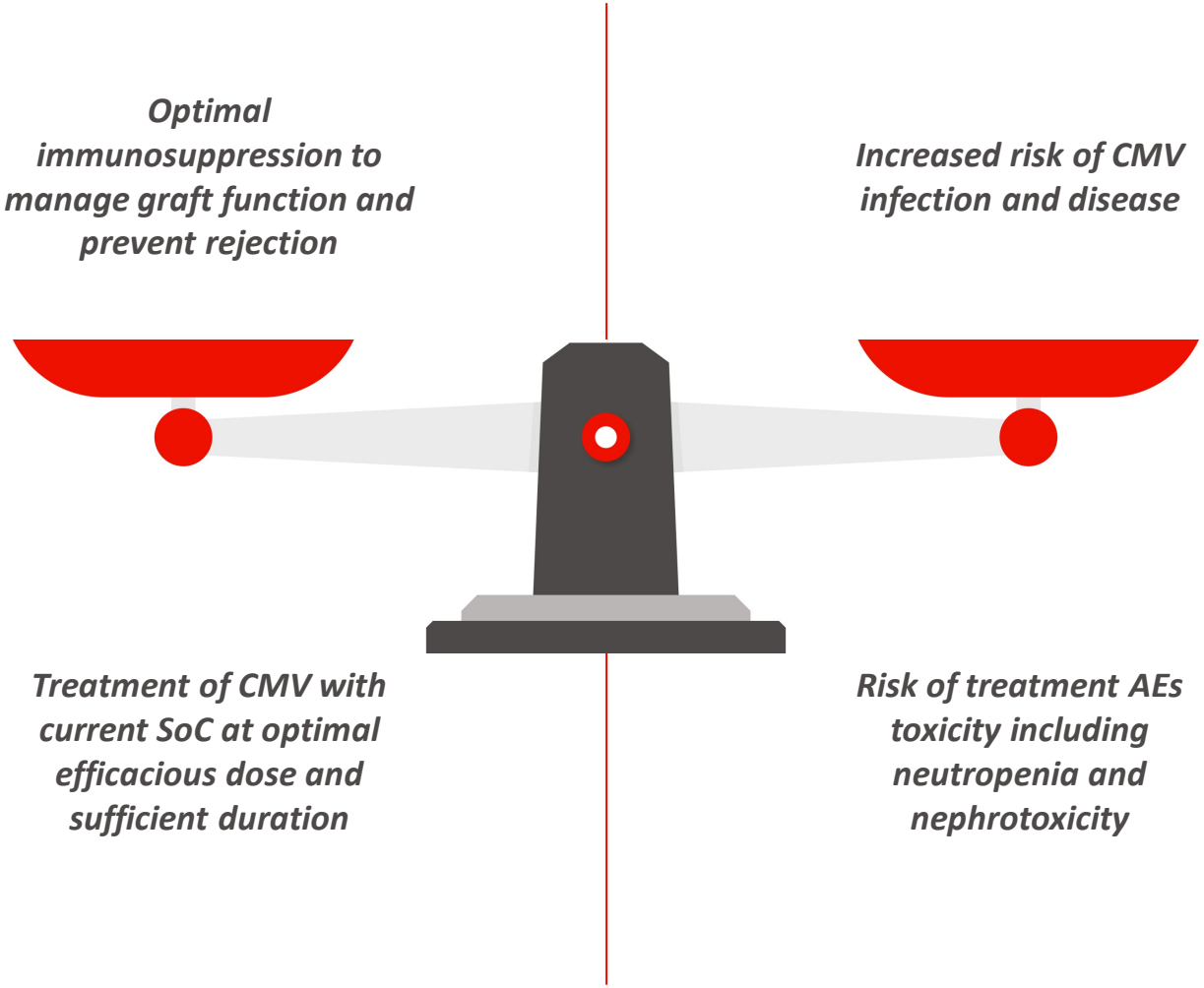


- **90% of allogenic HSCT (adult only) covered at ~80 centers[1]**
- **80% of specific organ transplants covered at a combined ~125 centers[1]**
  - Kidney 101 centers
  - Heart 72 centers
  - Lung 32 centers

THE CURRENT WORLD OF TREATING CMV INFECTIONS IS FULL OF COMPROMISES

Optimal immunosuppression to manage graft function and prevent rejection

Increased risk of CMV infection and disease



Treatment of CMV with current SoC at optimal efficacious dose and sufficient duration

Risk of treatment AEs toxicity including neutropenia and nephrotoxicity

1. **Addresses** Efficacy compromises that threaten CMV clearance
2. **Tackles** Safety compromises that threaten the graft & patient survival
3. **Alleviates** Hospitalization compromises that threaten patients' QoL & well being
4. **Maribavir has the potential to be a CMV game changer**

No therapies are currently approved for post-transplant treatment of CMV

MARIBAVIR – A POTENTIAL CMV GAME CHANGER

1

CMV is the most common infection post-transplant

- 190K transplants/year WW[1]
- 25% CMV infections[2]
- No currently approved treatment for CMV

2

Current options are sub optimal & require compromises

- Compromises need to be made between patient health, graft-survival and CMV clearance

3

Maribavir has the potential to be a game changer in post-transplant CMV

- Superior efficacy (RR) 55.7% vs 23.9% for CMV clearance
- Favorable tolerability and safety profile

4

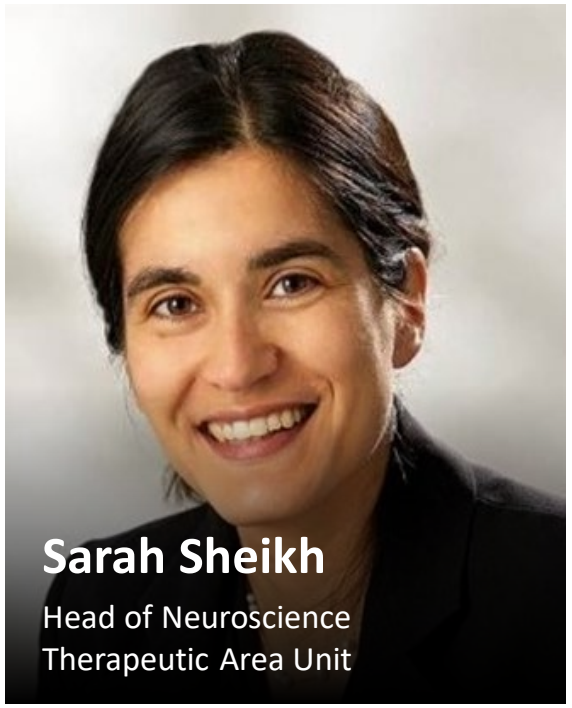
Takeda has the ability to capture the full potential

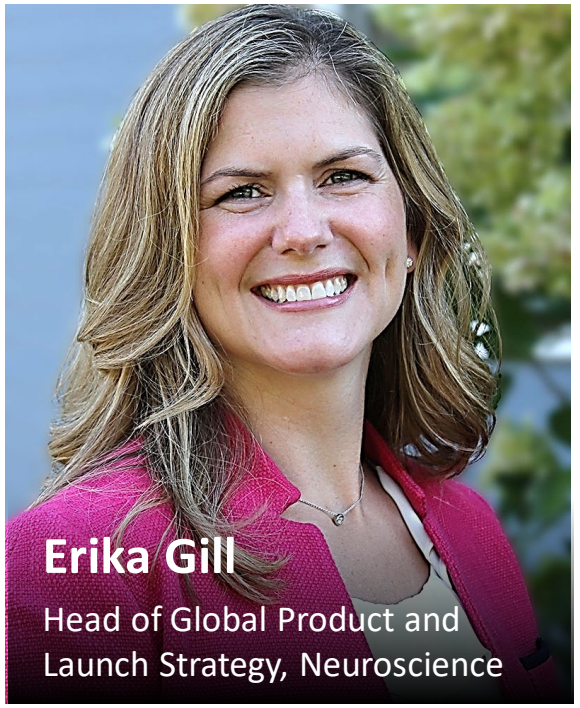
- Submission to FDA is on track 1H 2021
- Submission to EMA on track for 1H 2021
- Detailed in-market preparations underway

1) Niederwieser D, Baldomero H, Atsuta Y, et al. One and Half Million Hematopoietic Stem Cell Transplants (HSCT). Dissemination, Trends and Potential to Improve Activity By Telemedicine from the Worldwide Network for Blood and Marrow Transplantation (WBMT).Blood (2019) 134 (Supplement_1): 2035. ; https://www.who.int/transplantation/gkt/statistics/en/ 2) L Stern, B Withers, S Avdic et al.Human Cytomegalovirus Latency and Reactivation in Allogeneic Hematopoietic Stem Cell Transplant Recipients. Front Microbiol. 2019 May 28;10:1186. Poornima Ramanan, Raymund Razonable.Cytomegalovirus Infections in Solid Organ Transplantation: A Review.Infect Chemother. 2013 Sep; 45(3): 260–271

AGENDA

TIME (ET)	TIME (JT)	AGENDA
08:00 – 08:05	21:00 – 21:05	**Introduction** *Christophe Weber, President & CEO Takeda*
08:05 – 08:10	21:05 – 21:10	**Delivering an Innovative Pipeline to Our Patients: *Spotlight on Select Wave 1 Programs*** *Andy Plump, President Research & Development*
08:10 – 08:35	21:10 – 21:35	**Maribavir** *Obi Umeh, Global Program Leader Maribavir, Rare Genetic and Hematology* *Claus Jepsen, Head of Global Product and Launch Strategy, Rare Genetic and Hematology*
08:35 – 08:40	21:35 – 21:40	***Break***
08:40 – 09:35	21:40 – 22:35	**Neuroscience Strategy, Soticlestat & Orexin** *Sarah Sheikh, Head of Neuroscience Therapeutic Area Unit* *Elena Koundourakis, Head of Orexin Franchise Development, Neuroscience TA* *Erika Gill, Head of Global Product and Launch Strategy, Neuroscience*
09:35 – 09:40	22:35 – 22:40	**Delivering an Innovative Pipeline to Our Patients: *Spotlight on Select Wave 1 Programs*** *Uthra Sundaram, EVP, Global Product and Launch Strategy*
09:40 – 10:30	22:40 – 23:30	**Panel Q&A Session**





Soticlestat (TAK-935) Deep Dive:

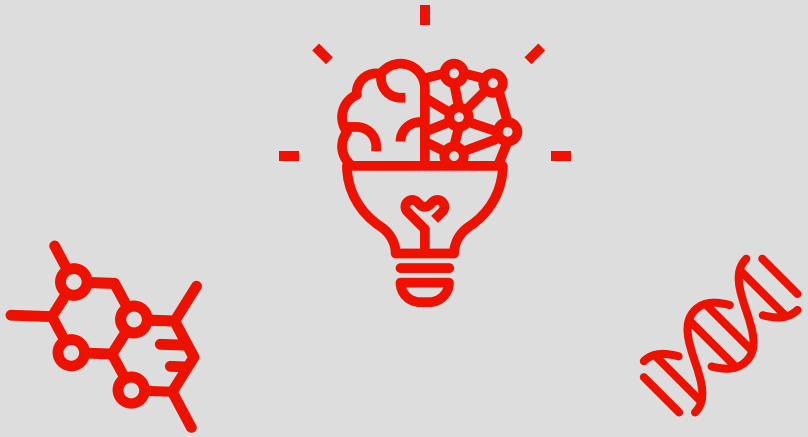
Novel MoA for Treatment of Dravet Syndrome and Lennox-Gastaut Syndrome

THE 2020s AS THE DECADE OF NEUROLOGY

Increasing ability to address devastating neurological diseases

Patient with SMA type 1

Innovation landscape



TAKEDA NEUROSCIENCE ROADMAP

Wave 1 (thru FY2024)

First launches of potentially transformative therapies in rare Neurology

Soticlestat (DS and LGS)

Potential approval in FY23

Orexin (Narcolepsy Type 1)

Potential approval in FY24

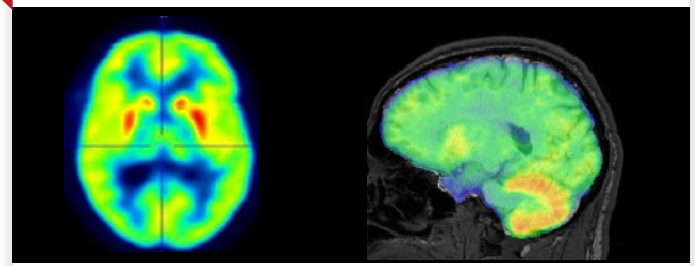
Wave 2 (FY2025+)

Capitalizing on the next wave of innovation

- **Other sleep disorders**
- **Huntington's Disease / Ataxia**
- **Neuromuscular Diseases**
- **Neurodegeneration**

KEY INFLECTIONS SET OUR FUTURE IN NEUROSCIENCE

Science & Innovation



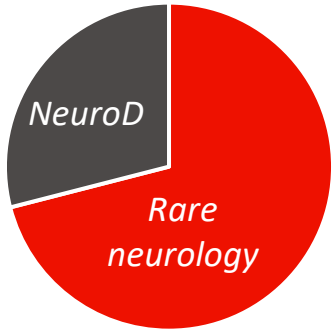
Focus on Rare Neurology

Evaluate Vantage June 17, 2020

Neurocrine picks Takeda's brain

Neurocrine BIOSCIENCES

Portfolio: Programs per Disease Cluster



Execution of Wave 1 programs

BIOPHARMADIVE

Takeda takes full control of drug for rare epilepsies

Soticlestat

SPARKLE
OREXIN INNOVATION

KEY TAKEAWAYS FOR SOTICLESTAT IN DRAVET SYNDROME AND LENNOX-GASTAUT SYNDROME

1

Potential first-in-class therapy

- Novel mechanism of action that may reduce seizure susceptibility and improve seizure control

2

Promising option for patients and caregivers

- Demonstrated efficacy in double-blind, placebo-controlled, POC study (ELEKTRA)[1]
- Promising emerging safety and tolerability profile
- Complementary approach to other AEDs with different mechanisms

3

Takeda leveraging capabilities to develop & commercialize globally[2]

- Global capabilities and local footprint will enable worldwide development program
- Regulatory approval in US, Europe, Japan, China, and other global markets expected to start in FY2023

 [1] Hahn et al. AES 2020. [2] If approved. POC = proof of concept; AEDs= Anti-Epileptic Drugs.

DRAVET SYNDROME

Rare Genetic Epilepsy Associated with Developmental Delay

Patient population

- ~10K patients diagnosed in the US[1,2]
- Homogeneous population with SCN1A mutation found in ~85% of patients[1]

Seizure type

- Predominant seizure type convulsive[3]

Disease burden

- Seizures leading to developmental impairment[3]
- ~1 in 5 die before adulthood, with 73% due to sudden unexpected death in epilepsy before 11 years of age[4]

“Our treatment goals continue to evolve as seizures persist”

Pediatric neurologist

1. Wu Y. Pediatrics 2015;136:1310–5., 2. DS Takeda Internal estimates/data on file Feb 2021., 3. Anwar. A. Cureus 2019;11:5006., 4. Cooper MS. Epilepsy Res 2016;128:43–7.

LENNOX-GASTAUT SYNDROME

Rare Heterogeneous Epilepsy Associated with Intellectual Disability

Patient population

- ~30-50K patients diagnosed in the US[1,2]
- Heterogeneous patient population[3]

Seizure type

- Associated with multiple seizure types including drop seizures[3]

Disease burden

- ~60% of patients unable to perform activities of daily living independently[3]
- Mortality 14-fold higher than in general population[4]

“As parents, we’re constantly in crisis mode”

Parent of LGS patient

1. Trevathan E. Epilepsia. 1997 Dec;38(12):1283-8., 2. LGS Takeda Internal estimates/data on file Feb 2021., 3. Kim H.J. Epilepsy Research 2015;110(10-19)., 4. Resnick T. J Child Neurol 2017;32:947–55.

CURRENT TREATMENTS LEAVE SUBSTANTIAL UNMET NEED

DS and LGS Treatment Challenges

- Persistent seizures in ~80% of patients[1-3]
- Additive drug side effects
- Drug-drug interactions
- Safety concerns / monitoring

DS and LGS Treatment Needs

- Efficacy on top of current standard of care
- Treatments with fewer side effects
- Less complicated to prescribe, given high poly-pharmacy rates
- Low-burden therapies for physicians, caregivers, and patients

Unmet needs highlight the importance of redefining treatment goals beyond seizure control

[1]Samanta D. Neuropediatrics. 2020 Apr;51(2):135-145.,
[2]Adam Strzelczyk. CNS Drugs (2021) 35:61–83,
[3]Takeda 2020 Global HCP market research

SOTICLESTAT WITH POTENTIAL FIRST-IN-CLASS MOA

Soticlestat inhibits cholesterol 24-hydroxylase (CH24H) enzyme[1,2]

↓

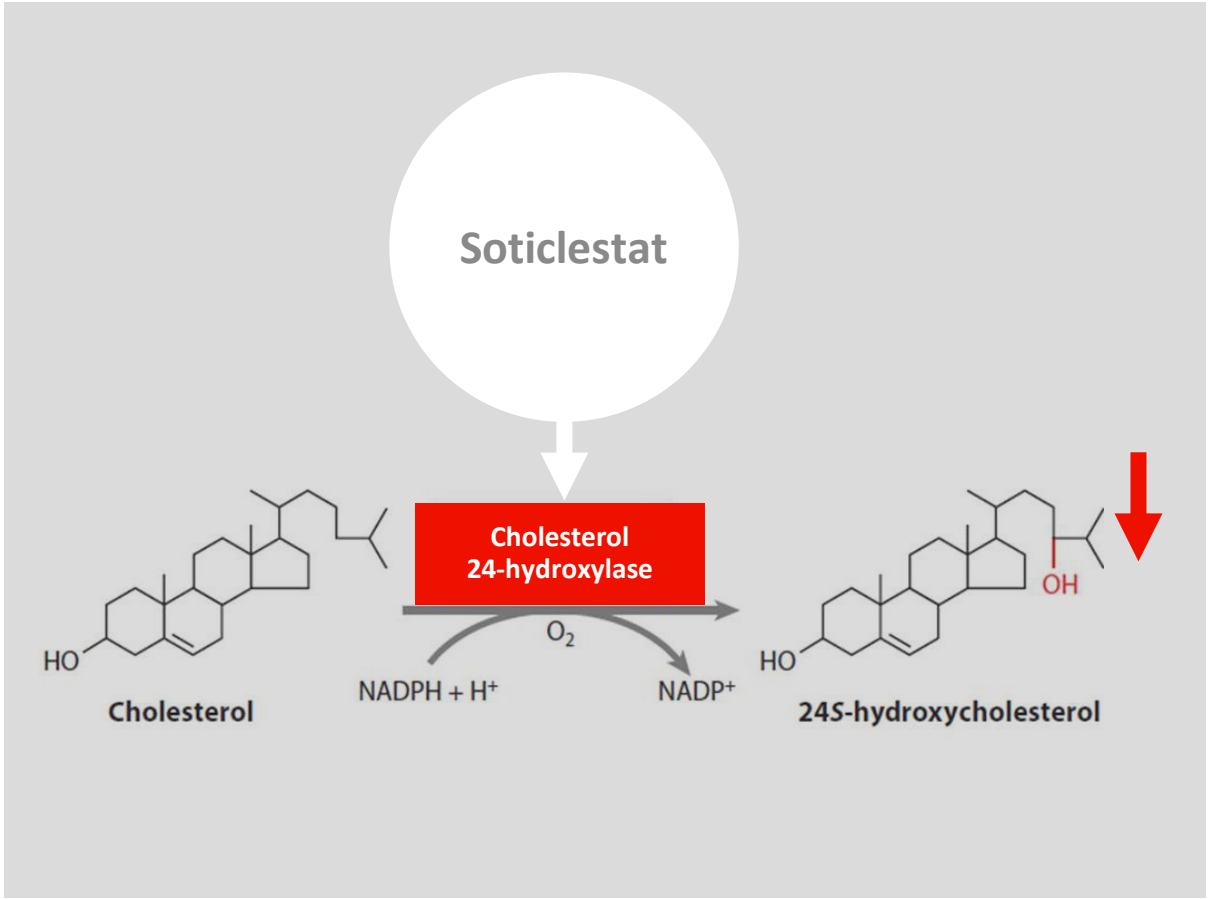
Dose-dependent reduction in 24HC levels[1,2]

↓

Reduced glutamatergic signaling & reduced inflammation[1,2]

↓

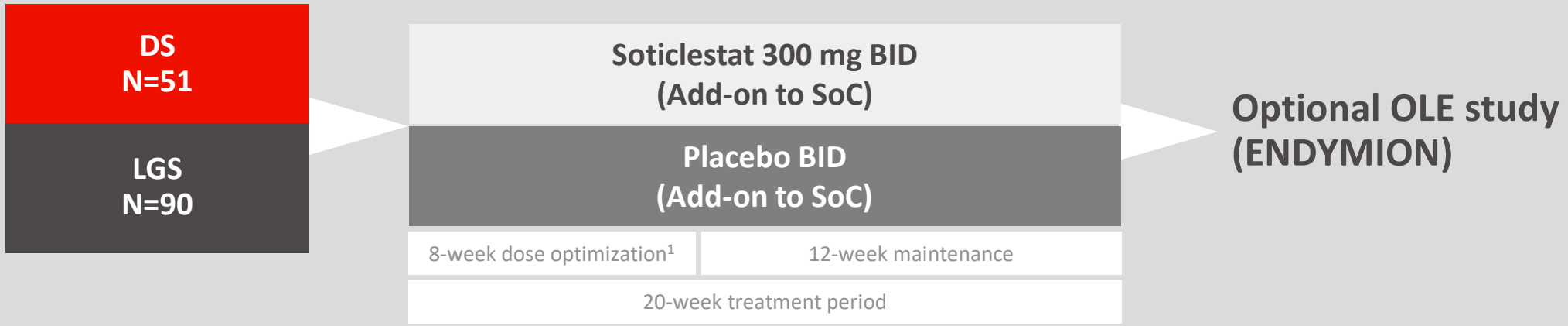
Potential to reduce seizure susceptibility and improve seizure control[1]



 [1]Salamone A, et al. ECE 2018., [2]Nishi T, et al. AAN 2018.

Annu. Rev. Biochem. 2009. 78:1017–40

ELEKTRA: PHASE 2 RANDOMIZED PBO-CONTROLLED STUDY OF SOTICLESTAT IN DS & LGS – ADJUNCTIVE TO SOC



Key Inclusion Criteria

- Aged ≥2 and ≤17 years
- Currently taking 1–4 AEDs
- ≥3 convulsive (DS); ≥ 4 Drop (LGS) seizures during 28-day Baseline

Endpoints: % change from baseline in

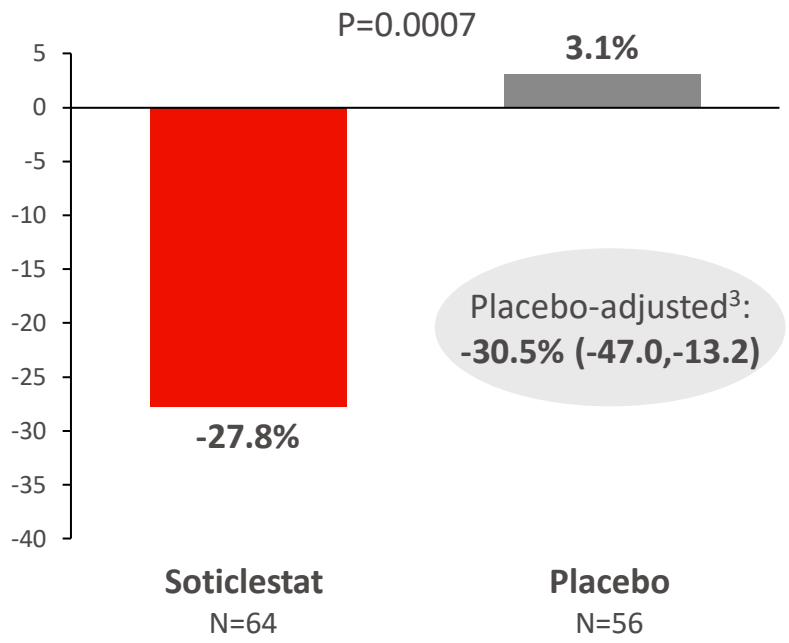
- Primary:
  - Seizure frequency for combined DS & LGS patients (maintenance period)
- Key secondaries:
  - Seizure frequency for combined DS & LGS patients (full treatment period)
  - Convulsive seizure frequency in DS patients (full treatment period)
  - Drop seizure frequency in LGS patients (full treatment period)

[1]100 mg BID, 200 mg BID, 300 mg BID (mg/kg dosing <60 kg) oral tablets; BID=twice daily; PBO=Placebo-controlled; SOC = Standard of Care

SOTICLESTAT MET PRIMARY ENDPOINT IN THE ELEKTRA STUDY[1]

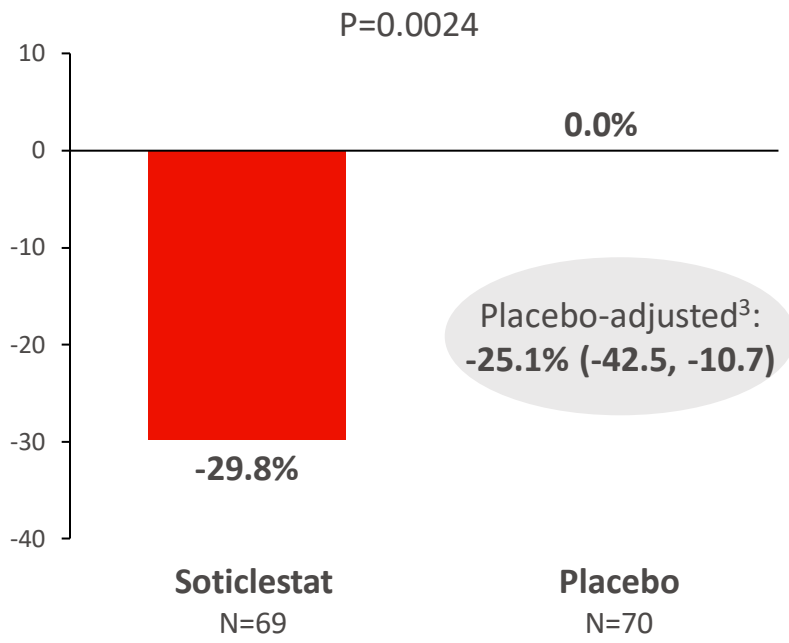
12-Week Maintenance Period (Primary) – Efficacy Set

Median change from Baseline in Seizure Frequency[2] (Convulsive and Drop)



20-Week Full Treatment Period – mITT

Median change from Baseline in Seizure Frequency[2] (Convulsive and Drop)



Combined DS & LGS populations achieved statistically significant placebo-adjusted seizure reductions

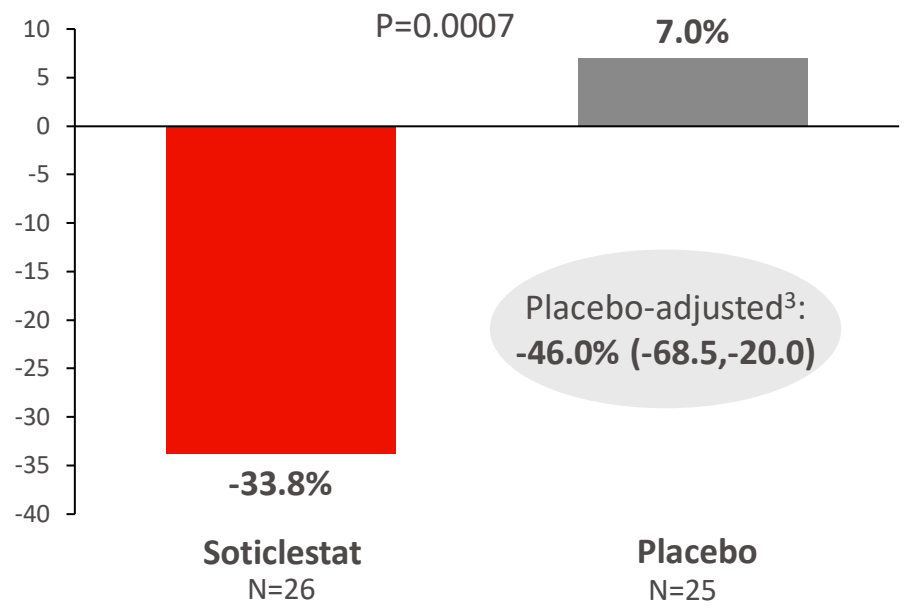
- **-30.5% over 12-week maintenance period**
- **-25.1% over 20-week full treatment period**

[1]Hahn et al. AES 2020; [2]Seizure frequency per 28 days; [3]Asymptotic 95% confidence interval and Hodges-Lehmann estimation of the median of differences in % change between the two arms from un-adjusted rank statistics. Modified intent-to-treat (mITT) = All randomized subjects who received at least ≥ 1 dose of study drug and were assessed for ≥1 day during treatment. The efficacy analysis set (ES) = All mITT subjects whose efficacy assessments were compliant with PA2 (8 weeks of dose optimization before entry into 12-weeks of maintenance).

ELEKTRA[1] - STATISTICALLY SIGNIFICANT SEIZURE REDUCTION IN DRAVET SYNDROME COHORT

Dravet Syndrome (Convulsive Seizures)

Median change from baseline in seizure frequency[2] during 20-week treatment period (mITT)



Dravet Syndrome

- Statistically significant placebo-adjusted median seizure reduction of 46%
- DS cohort was not powered for efficacy

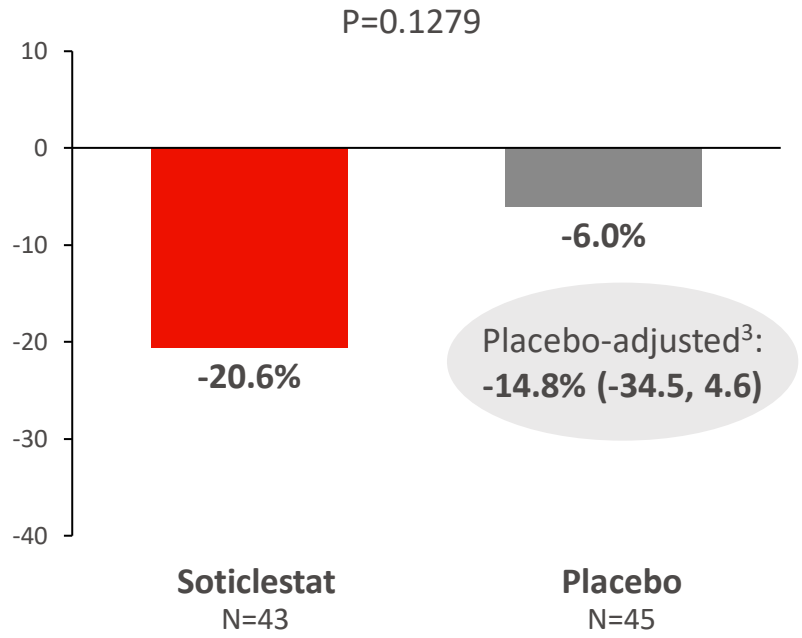
Statistically significant efficacy results in DS supportive of moving into Phase 3

[1]Hahn et al. AES 2020; [2]Seizure frequency per 28 days; [3]Asymptotic 95% confidence interval and Hodges-Lehmann estimation of the median of differences in % change between the two arms from un-adjusted rank statistics. The modified intent-to-treat (mITT) = All randomized subjects who received at ≥ 1 dose of study drug and were assessed for ≥1 day during treatment.

ELEKTRA[1] – NUMERICAL SEIZURE REDUCTION IN LGS COHORT

Lennox-Gastaut Syndrome (Drop Seizures)

Median change from baseline in seizure frequency[2] during 20-week treatment period (mITT)



Lennox-Gastaut Syndrome

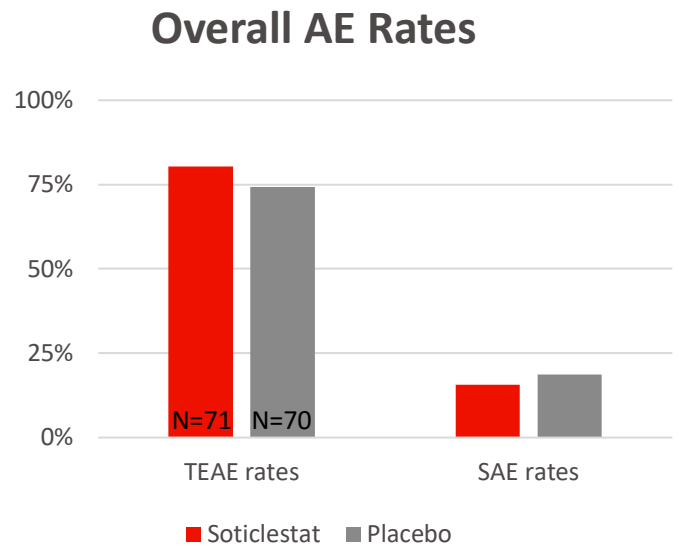
- Placebo-adjusted median seizure reduction of 14.8% did not reach statistical significance
- LGS cohort was not powered for efficacy
- Broad range of drop seizure frequency at baseline of 4 to >5,000 drop seizures/28 days
- Sensitivity analysis supportive of more stringent, countable drop seizure definition

Encouraging efficacy results in LGS support moving into Phase 3 with appropriate sample size and more stringent, countable drop seizure definition

[1]Hahn et al. AES 2020; [2]Seizure frequency per 28 days; [3]Asymptotic 95% confidence interval and Hodges-Lehmann estimation of the median of differences in % change between the two arms from un-adjusted rank statistics. The modified intent-to-treat (mITT) = All randomized subjects who received at ≥ 1 dose of study drug and were assessed for ≥1 day during treatment.

PROMISING EMERGING SAFETY AND TOLERABILITY PROFILE SUPPORTIVE OF MOVING INTO PHASE 3 DEVELOPMENT

ELEKTRA TEAEs

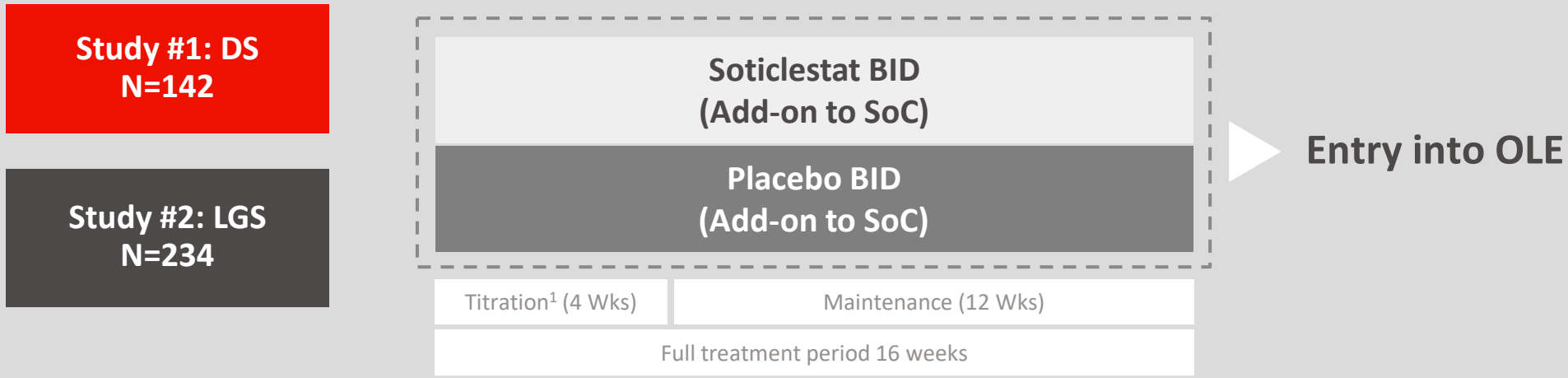


TEAEs >5% in soticlestat & >3% difference from placebo	Soticlestat (N=71)	Placebo (N=70)
Pyrexia	11 (15.5%)	8 (11.4%)
Somnolence	6 (8.5%)	3 (4.3%)
Lethargy	5 (7%)	0 (0%)
Constipation	4 (5.6%)	0 (0%)

- Safety profile consistent with previous findings; no new safety findings
- TEAEs and SAEs similar in frequency across soticlestat vs. placebo
- Main TEAEs for soticlestat over placebo are lethargy/somnolence and constipation

 TEAE = treatment emergent adverse events; SAE = serious adverse events

TWO GLOBAL PHASE 3 PBO-CONTROLLED STUDIES IN DS & LGS STARTING MID-2021



Trial Design

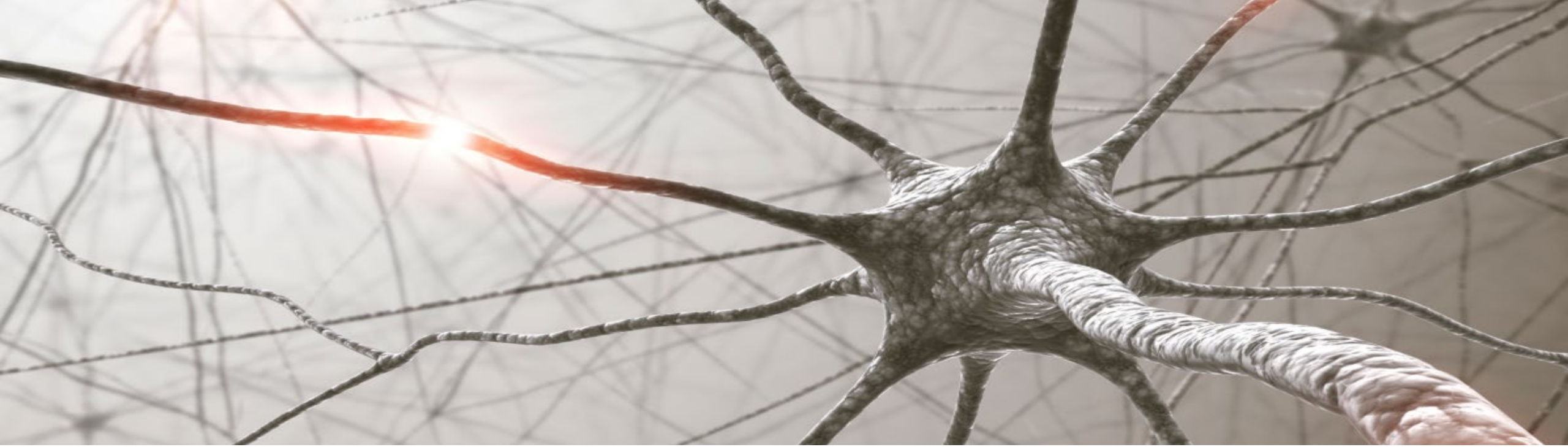
- Trial design based on feedback from FDA, EMA & PMDA
- Ages ≥2 years
- Adjunctive to AEDs
- Active seizures at baseline[2]

Outcome Measures

- Primary:
  - Frequency change in convulsive seizures (DS study) during full treatment period
  - Frequency change in MMD seizures (LGS study) during full treatment period

WHAT'S AHEAD:
Two pivotal studies in LGS and DS starting mid-2021 and possible regulatory filings in FY23

[1]100 mg BID, 200 mg BID, 300 mg BID (mg/kg dosing <45 kg) oral tablets. [2]DS: ≥4 convulsive seizures at baseline. LGS: ≥8 Major Motor Drop (MMD) seizures at baseline. For LGS, countable drop seizures reliably recognized by the caregivers and consistently implemented by the investigators.
AED=Anti Epileptic Drugs; BID=Twice daily' PBO=Placebo-controlled.; MMD major motor drops



Soticlestat – Market Opportunity

SOTICLESTAT HAS THE POTENTIAL TO EXTEND TREATMENT GOALS BEYOND SEIZURE REDUCTION

DS and LGS Treatment Challenges	Potential Soticlestat Benefits Based on Data to Date
Persistent seizures in ~80% of patients [1-3]	Novel MoA with demonstrated seizure reduction[4]
Additive drug side effects	Low rates of adverse events[4]
Drug-drug interactions	Do not anticipate clinically relevant drug-drug interactions
Safety concerns / monitoring	Less potential for safety or monitoring requirements

[1]Samanta D. Neuropediatrics. 2020 Apr;51(2):135-145; [2]Adam Strzelczyk. CNS Drugs (2021) 35:61–83; [3]Takeda 2020 Global HCP market research; [4]Hahn et al. AES 2020

SOTICLESTAT HAS THE POTENTIAL TO HELP THE MAJORITY OF DS AND LGS PATIENTS

Market Opportunity

~10K diagnosed DS Patients (US)[1-2] & ~30-50K diagnosed LGS Patients (US)[3-4]

Significant potential to improve diagnosis rates, esp. ex-US

~80% patients not controlled with current treatments, seeking new options[5-7]

Because of soticlestat's profile it has the potential to be used early line and for patients not well controlled on other AEDs

[1]Wu Y. Pediatrics 2015;136:1310–5., [2]DS Takeda Internal estimates/data on file Feb 2021. [3]Trevathan E. Epilepsia. 1997 Dec;38(12):1283-8., [4]LGS Takeda Internal estimates/data on file Feb 2021.
[5]Samanta D. Neuropediatrics. 2020 Apr;51(2):135-145., [6]Adam Strzelczyk. CNS Drugs (2021) 35:61–83, [7]Takeda 2020 Global HCP market research

TAKEDA ASPIRES TO RAISE DS AND LGS TREATMENT EXPECTATIONS FOR PATIENTS, CAREGIVERS, AND PHYSICIANS

Soticlestat

Potential First-In-Class Seizure Reduction Treatment

First approval anticipated FY2023

Re-define treatment goals

Prepare for global launch

Establish soticlestat as therapy of choice

KEY TAKEAWAYS FOR SOTICLESTAT IN DRAVET SYNDROME AND LENNOX-GASTAUT SYNDROME

1

Potential first-in-class therapy

- Novel mechanism of action that may reduce seizure susceptibility and improve seizure control

2

Promising option for patients and caregivers

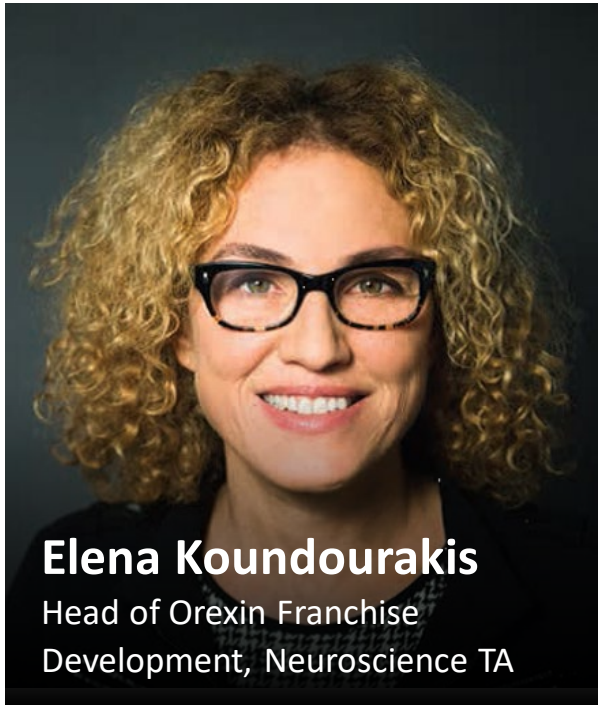
- Demonstrated efficacy in double-blind, placebo-controlled, POC study (ELEKTRA)[1]
- Promising emerging safety and tolerability profile
- Complementary approach to other AEDs with different mechanisms

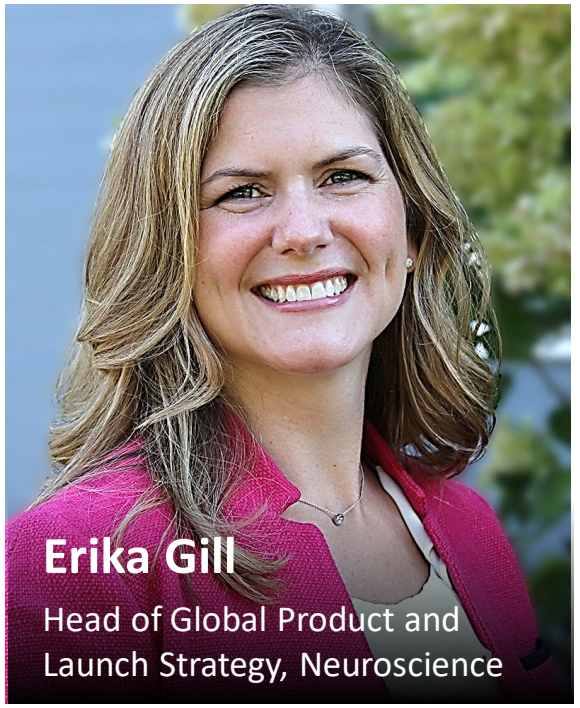
3

Takeda leveraging capabilities to develop & commercialize globally[2]

- Global capabilities and local footprint will enable worldwide development program
- Regulatory approval in US, Europe, Japan, China, and other global markets expected to start in FY2023

 [1] Hahn et al. AES 2020. [2] If approved. POC = proof of concept; AEDs= Anti-Epileptic Drugs.





Orexin Franchise Strategy Update

First potential medicine to treat the underlying disease in patients with Narcolepsy Type 1

KEY TAKEAWAYS FOR OREXIN FRANCHISE

1

On track for First Approval of an Oral Orexin Agonist in Narcolepsy Type 1 (NT1)

- **TAK-994**: Progressed to Ph2b (TAK-994-1501)
- Approval in FY2024 dependent upon clinical data

2

Narcolepsy Type 2 (NT2) & Idiopathic Hypersomnia (IH) to follow

- **TAK-994:** Achieved ePOC in Sleep Deprived Healthy Volunteers (TAK 994-1503)
- NT2 cohort in TAK-994-1501

3

Potential Additional Indications and Assets to be developed in parallel

- **TAK-925 IV**: 5 ePOC established across multiple disease settings
- **TAK-861:** Longer Oral Agonist enters clinic in FY2021

ePOC: early proof of concept

NARCOLEPSY TYPE 1 (NT1), NARCOLEPSY TYPE 2 (NT2) AND IDIOPATHIC HYPERSOMNIA (IH) ARE ALL CENTRAL DISORDERS OF HYPERSOMNOLENCE WITH SIGNIFICANT UNMET NEED

- Orexin deficiency is the cause of NT1; unknown pathophysiology for NT2/IH
- Common challenge: misdiagnosis and undertreatment
- Different disorders with overlapping clinical features especially Excessive Daytime Sleepiness (EDS)

	NT1	NT2	IH
Excessive Daytime Sleepiness	✓	✓	✓
Sleep Paralysis	✓	✓	sometimes
Hallucinations	✓	✓	sometimes
Cataplexy	✓	✗	✗
Disrupted Nighttime Sleep	✓	occasionally	✗
Sleep Inertia	occasionally	sometimes	✓

✓ >50% | sometimes 20-50% | occasionally <20%

Based on Article Reviewed: 1. Sturzenegger C et al. J Sleep Res 2004;13:395–406; 2. Roth T et al. J Clin Sleep Med 2013;9:955–65; 3. Scammell T. Ann Neurol 2003;53:154–66; 4. Black J et al. Sleep Med 2016;24:57–62; 5. Maski K et al. Sleep 2020;43:zsaa066; 6. Trotti LM. Sleep Med Rev 2017;35:76–84; 7. Maski K et al. J Clin Sleep Med 2017;13:419–25; 8. Evangelista E et al. Sleep 2020;zsaa264 9. Trotti et al LM. Sleep Med 2020: 75:343-349

WHAT IS IT LIKE FOR PEOPLE TO LIVE WITH NT1?

Extreme
SLEEPINESS

FEAR of
cataplectic attacks

DISRUPTION
of daily life

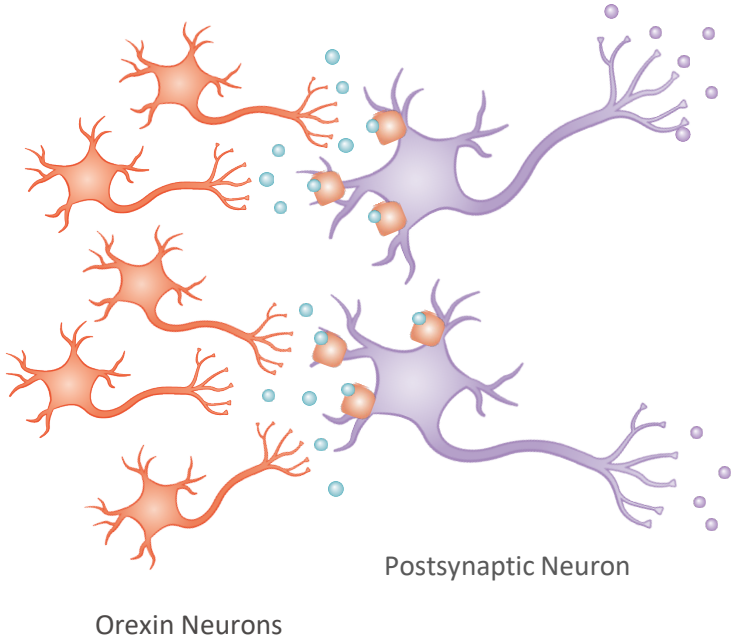
MISUNDERSTOOD
by HCPs and family

"We take current meds to survive.
We want new medications to help us live"

Narcolepsy Patient Advisor (Takeda Sponsored Patient Advisory Board)

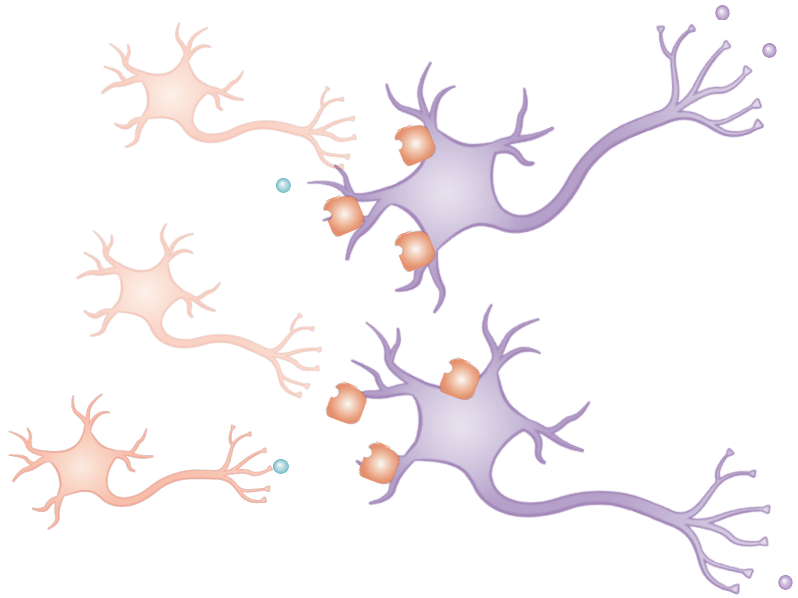
NARCOLEPSY TYPE I IS CAUSED BY SEVERE LOSS OF OREXIN PRODUCING NEURONS IN THE BRAIN

Healthy Individual



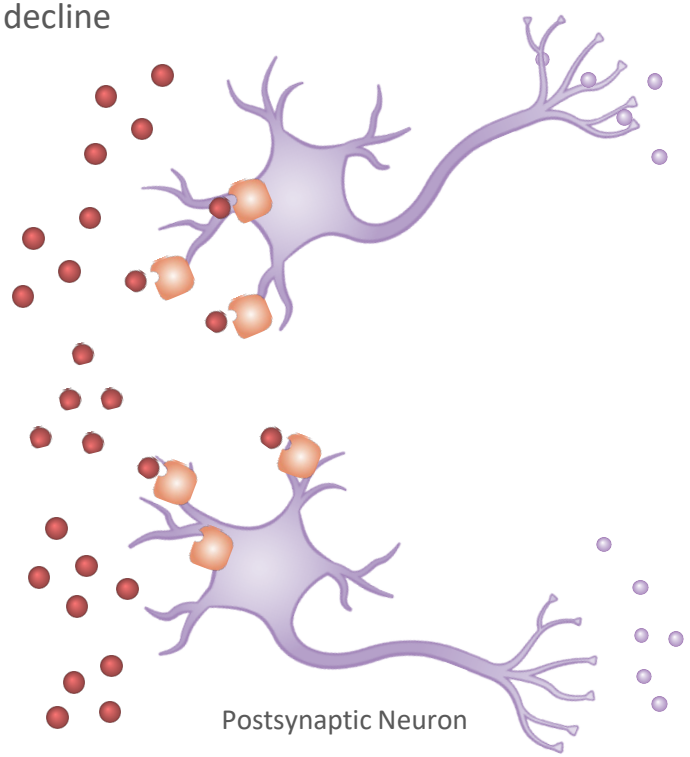
Individual with Narcolepsy type 1

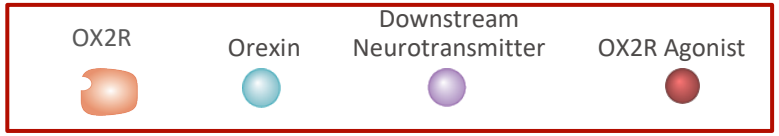
Reduced availability of orexin as orexin neurons are lost reducing downstream neurotransmitter activity.



Highly Specific OX2R Agonist

May **restore downstream neurotransmitter activity** lost when endogenous orexin levels decline





1. Mahoney CE, et al. *Nat Rev Neurosci.* 2019;20(2):83-93. | 2. Chastain EM, et al. *Biochim Biophys Acta.* 2011;1812:265–274. | 3. Nishino S. *Sleep Med*. 2007;8(4):373-399. | 4. Saper CB, et al. *Trends Neurosci*. 2001;24(12):726-731. | 5. Yoshida Y, et al. *Eur J Neurosci*. 2001;14(7):1075-1081.

TAKEDA SCIENTISTS IN JAPAN DISCOVERED OREXIN AGONISTS WITH APPROPRIATE PHYSIOCHEMICAL PROPERTIES AND GOOD BRAIN PENETRATION

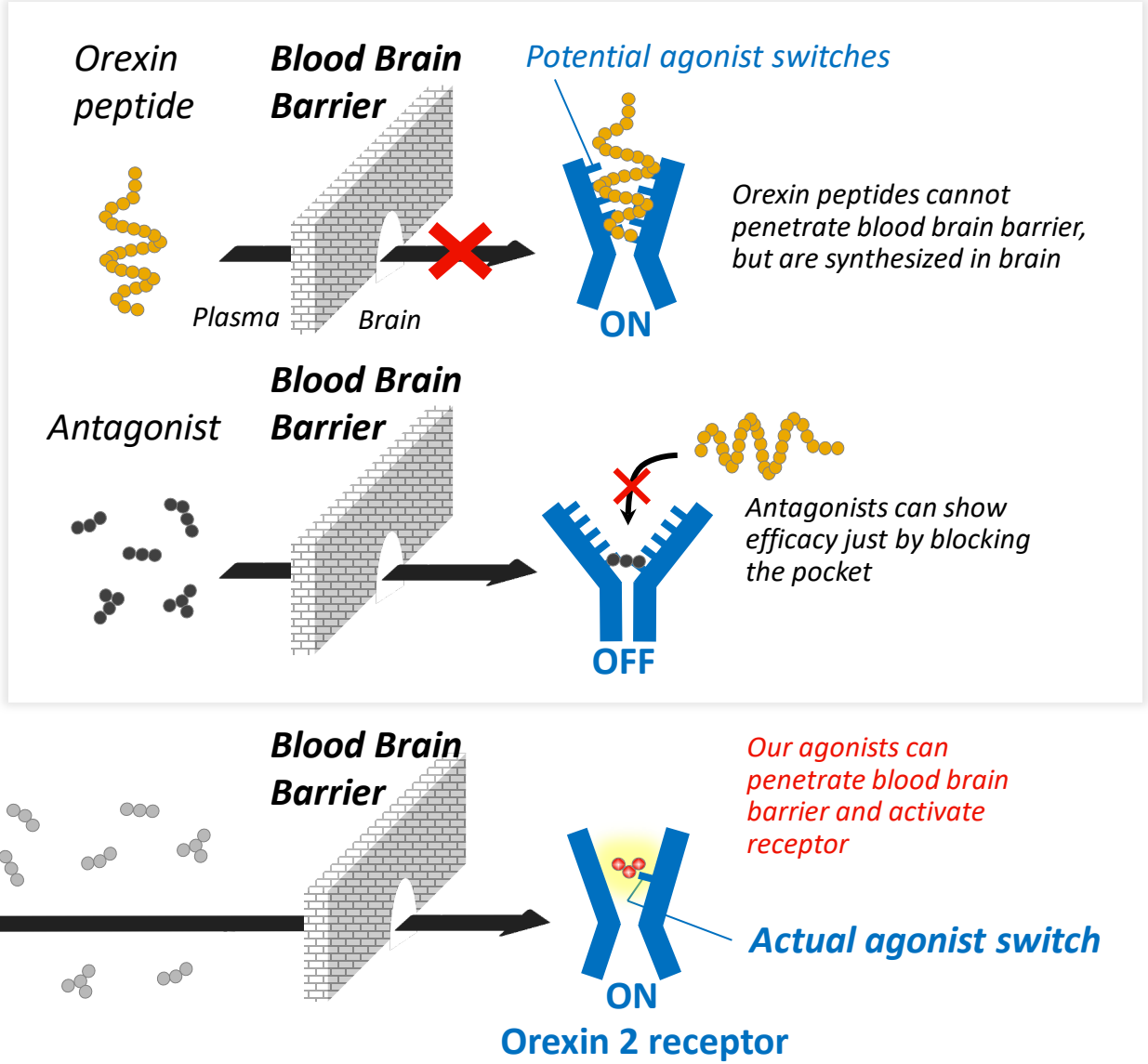
Difficulties in discovery of OX2R agonists

Large molecule for receptor activation ⟷ **Small molecule for brain penetration**

Additional challenges:
- Safety profiles
- Ideal PK profiles, etc.

Takeda:
- ✓ **has significant experience in GPCR drug discovery, especially in medicinal chemistry field.**
- ✓ **has drug discovery capability in sleep/wake field and developed Ramelteon.**

Succeeded in discovery of blood brain barrier penetrable OX2R agonists

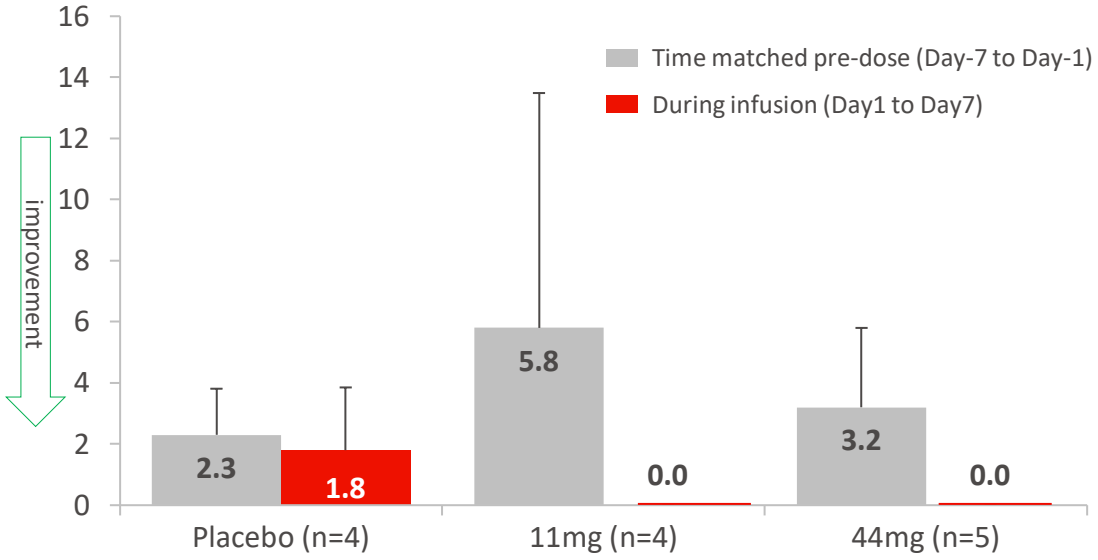


* G-Protein coupled receptors (GPCR). *Nature Cell Biology*, 2000, 2(10), 703-708., *Nature*, 2001, 411(6837), 613-617., *Nature*, 2003, 422(6928), 173-176., *Nature*, 2014, 513(7516), 124-127., etc.

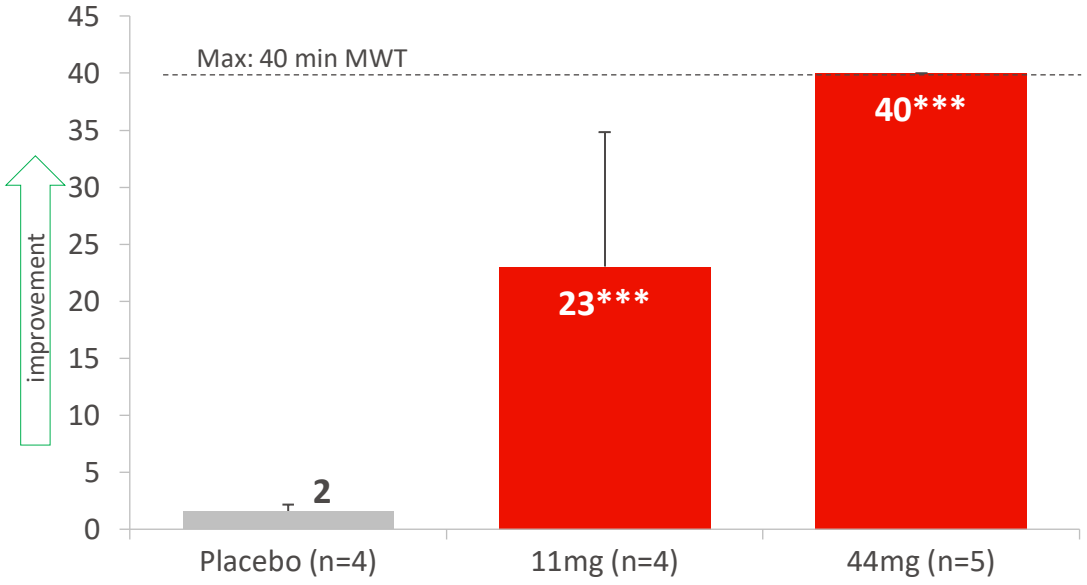
TAK-925 OREXIN IV FORMULATION IMPROVED MAINTENANCE OF WAKEFULNESS AND REDUCED CATAPLEXY IN NT1

POC NT1: 7-day Repeated Dosing Study[2]

TAK-925 average number of cataplexy attacks during 7 day period (mean, SD)[1]



TAK-925 IV Day 7 average sleep latency in Maintenance of Wakefulness Test (MWT) of NT1 patients (mean, SD)[1]



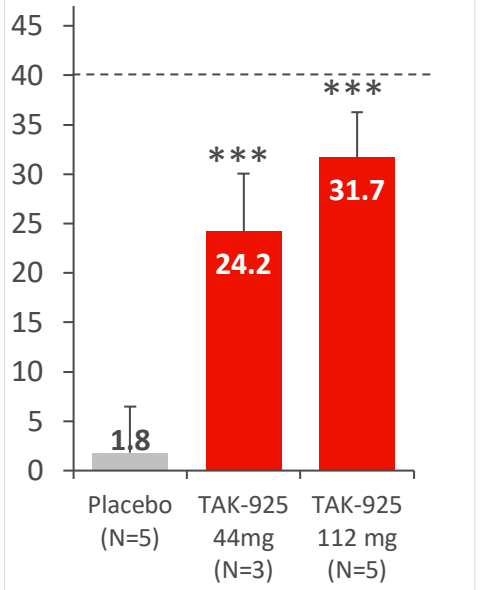
- No serious AEs were reported and no subjects were discontinued from the study due to an AEs.
- Four participants who received TAK-925 44 mg experienced drug-related TEAEs: pollakiuria (n = 4), salivary hypersecretion (n = 1) and hyperhidrosis (n = 1)

1. Observed mean and standard deviation shown. No statistical comparison to placebo was done for cataplexy. ***: p-value <0.001 comparing to placebo for MWT
2. Tanaka S.. European Sleep Research Society 2020 Virtual Congress, September 22-24, 2020

TAK-925 OREXIN IV FORMULATION SUPPORTS POTENTIAL FOR BROADER ROLE OF AN OREXIN AGONIST

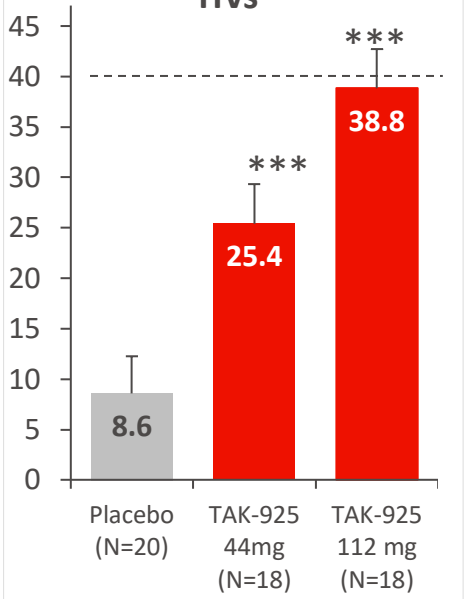
TAK-925-1003[1]

Narcolepsy Type 2[1]



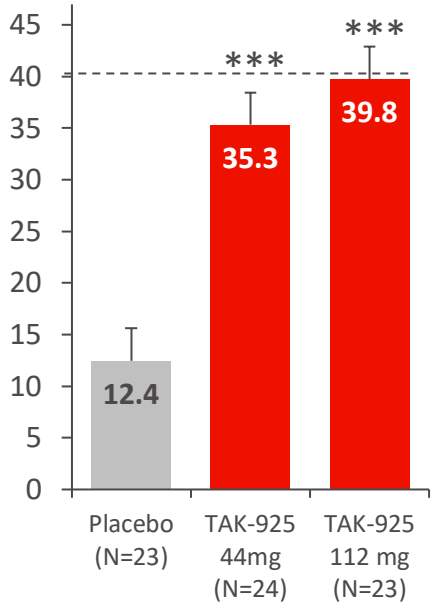
TAK-925-1002[2]

Acute sleep phase delay paradigm in HVs



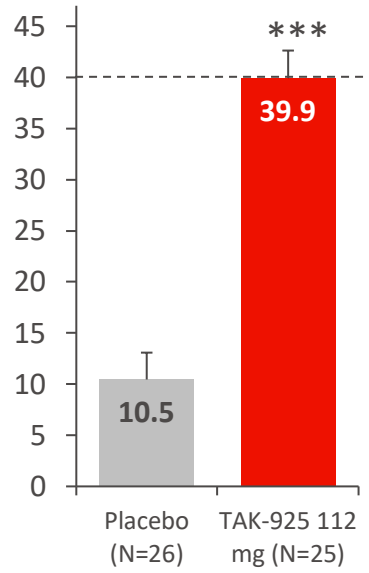
TAK-925-2001[3]

Residual EDS in OSA



TAK-925-2002[4]

Idiopathic hypersomnia



Efficacy Endpoint: mean Sleep onset latency (min) and 95% CI

Safety profile: No Serious Adverse Events or TAEs leading to D/C or deaths. Increases of urinary events and BP/HR have been observed

1. Tanaka S., European Sleep Research Society 2020 Virtual Congress, September 22-24, 2020
2. Evans R., WORLD SLEEP, Vancouver, Canada, September 20-25, 2019
3. Rubens R. data to be Presented at American Academy of Neurology (AAN) Annual Meeting April 17-22, 2021
4. Takeda data on file; TAK-925-2002

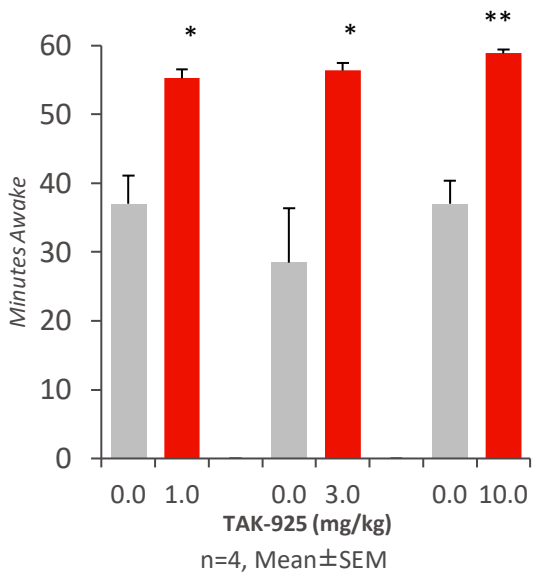
MWT sleep latency: LS mean (95% CI) sleep onset latency in minutes except for NT2 which is change from baseline at Day 1

***: p-value <0.0001

PRECLINICAL DATA SHOWS TAK-994 HAS THE POTENTIAL FOR SIMILAR EFFICACY AS TAK-925

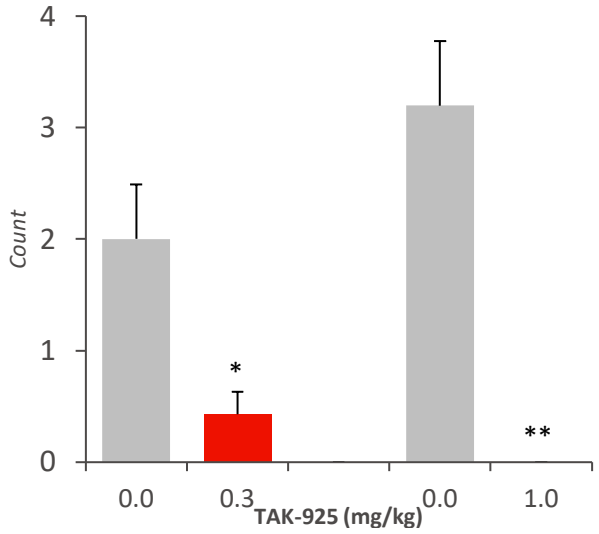
TAK-925[1]

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



n=4, Mean±SEM

Cataplexy-like episodes in NT1 mouse model for three hours

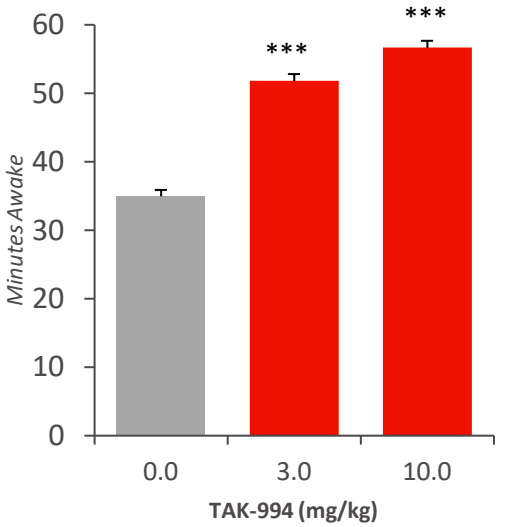


n=7 (0.3 mg/kg); n=5 (1.0 mg/kg), Mean±SEM

*$P \leq 0.05$, **$P \leq 0.01$, compared with control (0.0 mg/kg) (two-tailed paired t-test with closed testing procedure from the high dose side)

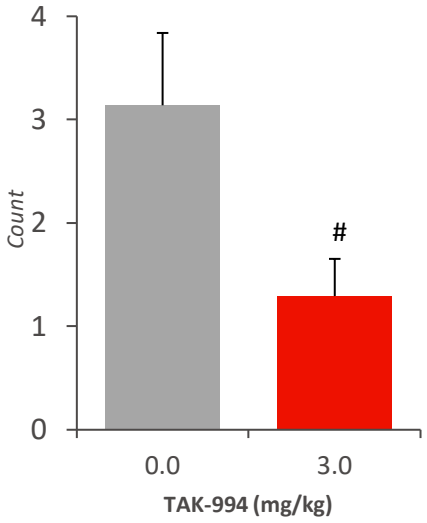
TAK-994[2]

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



n=7, Mean±SEM

Cataplexy-like episodes in NT1 mouse model for three hours



n=7, Mean±SEM

***p≤ 0.001, compared with control (0.0 mg/kg) (two-tailed Williams test).
p≤ 0.05, compared with control (0.0 mg/kg) (two-tailed paired t-test).

1. Suzuki M., *Presented at SLEEP 2018, Baltimore, USA, June 2-6, 2018*
2. Kimura H., *Presented at WORLD SLEEP, Vancouver, Canada, September 20-25, 2019*

FIRST ORAL OREXIN AGONIST TAK-994 IS PROGRESSING IN CLINICAL TRIALS IN NT1 AND NT2

A double-blind, ph2 study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of TAK-994 in patients with narcolepsy type 1 or narcolepsy type 2

Part A (NT1 Multiple Rising Dose)

4 weeks treatment

Randomized 2:1 TAK-994 vs placebo

Part B (NT1 Pivotal)

8 weeks treatment

Randomized 1:1:1:1 TAK-994 (low, medium, high dose) vs placebo

Part C (NT1 China)

Part D (NT2 Multiple Rising Dose)

Safety extension

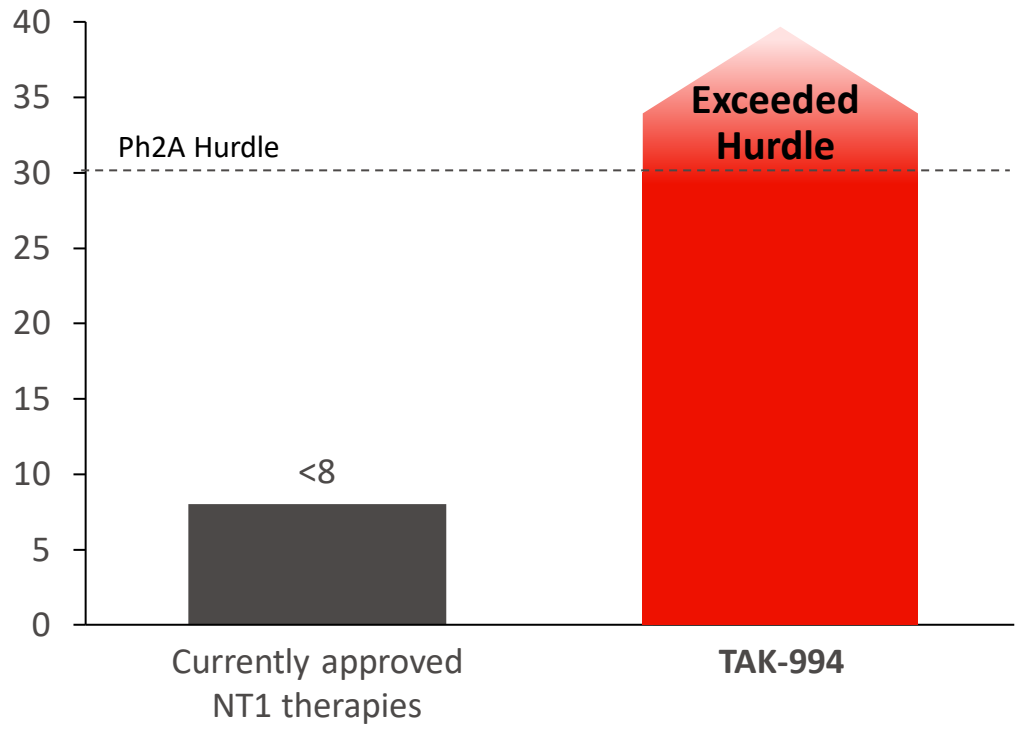
SPARKLE
OREXIN INNOVATION

Key Efficacy Endpoints: *Sleep Latency in MWT, Epworth Sleepiness Scale & Weekly Cataplexy Rate*

Safety and Tolerability

TAK-994 ORAL AGONIST MET ePOC CRITERIA AND HAS THE POTENTIAL TO TRANSFORM THE TREATMENT FOR PATIENTS WITH NT1

Comparison of sleep latency in the Maintenance of Wakefulness Test (MWT) *Placebo adjusted (minutes)*



TAK-994-1501: Criteria For Progression To Part B

MWT-placebo adjusted, minimum 30min improvement over baseline AND one or both below are met:

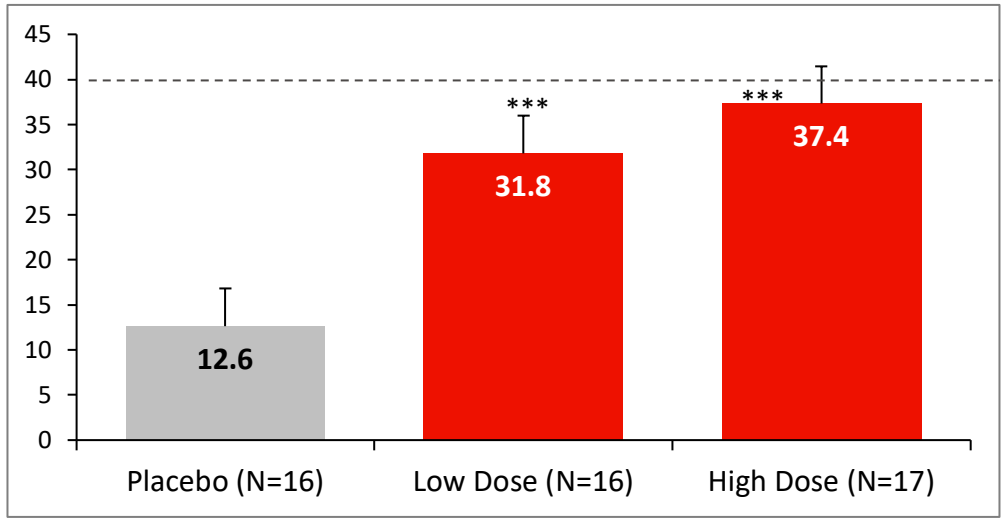
- ESS -placebo adjusted, minimum 4pts reduction over baseline; OR
- WCR-placebo adjusted, minimum 40% reduction in Weekly Cataplexy Rate from baseline

Safety evaluation

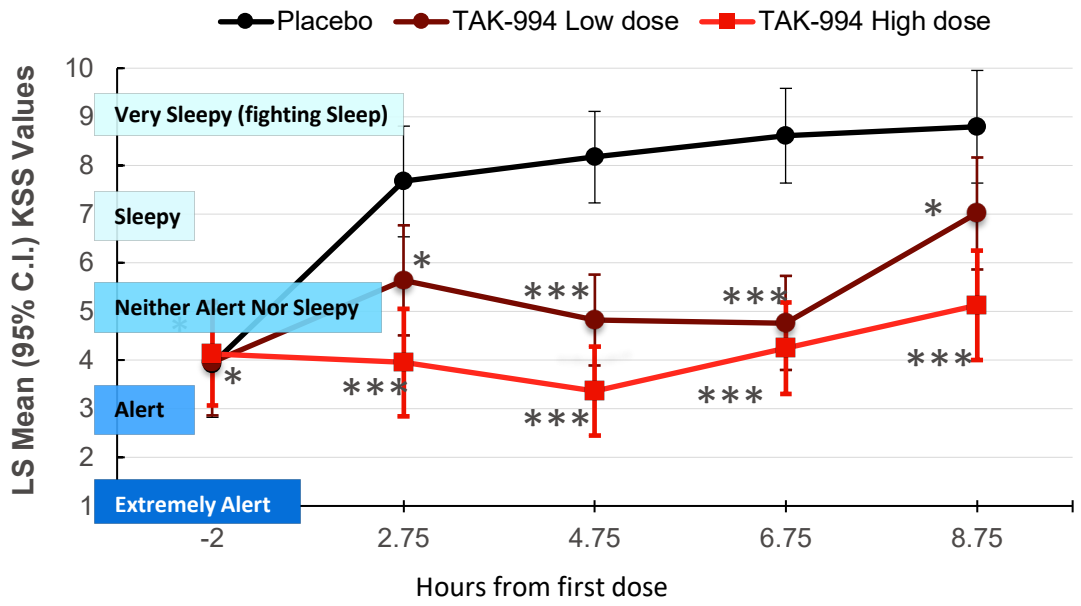
FIRST ORAL OREXIN AGONIST TAK-994 ACHIEVED POC IN SLEEP DEPRIVED HEALTHY VOLUNTEERS WITH NORMAL OREXIN LEVELS (TAK-994-1503)*

Two doses of TAK-994 demonstrated statistically significant improvements in the objective (MWT) and subjective (KSS) measures of wakefulness.

Mean sleep latency from 4 Maintenance of Wakefulness (MWT) trials *min (95% CI)*



Pre- and Post-Dose KSS LS Means by Time



Differences from placebo: * p-value <0.05 *** p-value <0.0001

- TAK-994 was well tolerated with no serious adverse events (AEs), no discontinuations due to AEs, and no clinically significant laboratory values. All TAK-994 TEAEs were mild in intensity.
- Safety and efficacy findings consistent with previous studies with TAK-925 IV

 *'Takeda data on file; TAK-994-1503

OREXIN FRANCHISE NEXT STEPS AND KEY MILESTONES





Narcolepsy Type 1	Narcolepsy Type 2	Pivotal Studies	NT1 Approval	Potential Additional Indications
Ongoing Global Ph2 study in NT1 and NT2 with TAK-994 Data will inform Pivotal Studies Design		Scope to be determined based upon HA and HTA feedback	Global launches	Multiple assets
FY2021		FY2021-FY2023	FY2024	FY2025+

TAKEDA IS PIONEERING THE FIELD OF OREXIN THERAPEUTICS WITH A PIONEERING MULTI-ASSET FRANCHISE LED BY THE ORAL OREXIN AGONIST, TAK-994

Narcolepsy Type 1 first

- Bring **TAK-994** quickly to patients with highest unmet linked to Orexin deficiency
- Launch with **EDS** and **cataplexy** data **globally**
- **Distinct biological effect** of orexin agonism on NT1 vs NT2 and IH

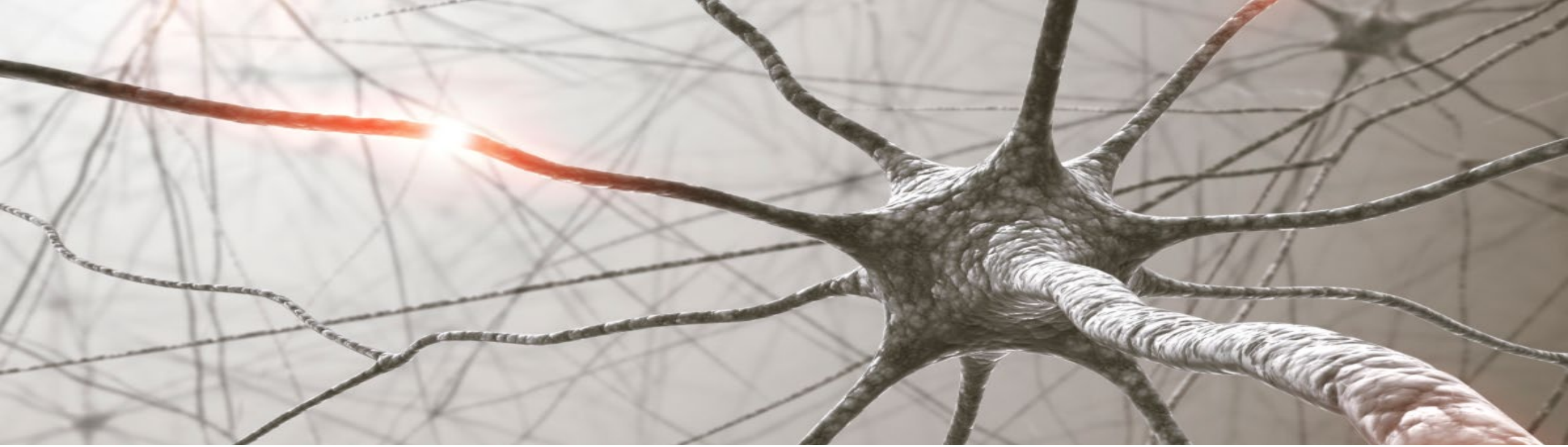
Narcolepsy Type 2 & Idiopathic Hypersomnia to follow

Follow NT1 with TAK-994 in **NT2 and IH**

- **Potentially, a different dosing** compared to NT1
- Having dedicated trials simplifies the development plan and associated operations

Other indications and assets to be evaluated and potentially developed in parallel

- Evaluate additional indications for **TAK-994**
- Assess potential indications **for TAK-861**
- Evaluate **TAK-925 (IV)** in **hospital settings**



Oral Orexin Agonist TAK-994 – Market Opportunity

KEY TAKEAWAYS FOR ORAL OREXIN AGONIST TAK-994 NARCOLEPSY TYPE 1 (NT1)

1

NT1 is caused by an orexin deficiency, which disrupts sleep awake cycles

- NT1 is rare, underdiagnosed and undertreated
- NT1 is chronic and severe

2

Current NT1 treatments do not address underlying orexin deficiency

- Treatment escalation and polypharmacy are common
- Despite treatment, NT1 is not controlled

3

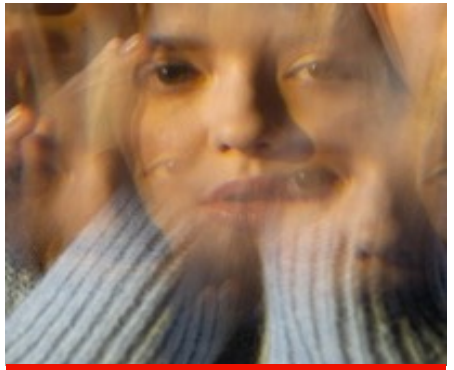
If approved, TAK-994 will be the first to treat orexin deficiency

- Anticipated first approval FY2024
- Label expansions planned, and data dependent, as part of the Orexin Franchise strategy

NT1 IS CHRONIC AND SEVERE CHARACTERIZED BY A PENTAD OF SYMPTOMS

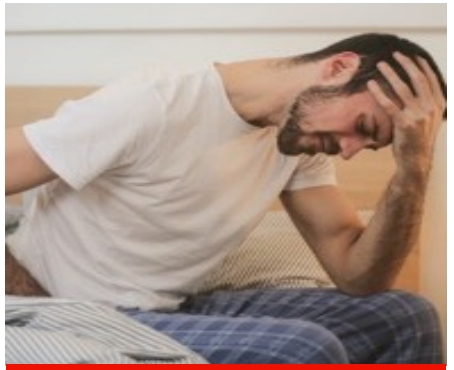
Excessive Daytime Sleepiness (EDS)

Cataplexy



Hallucinations

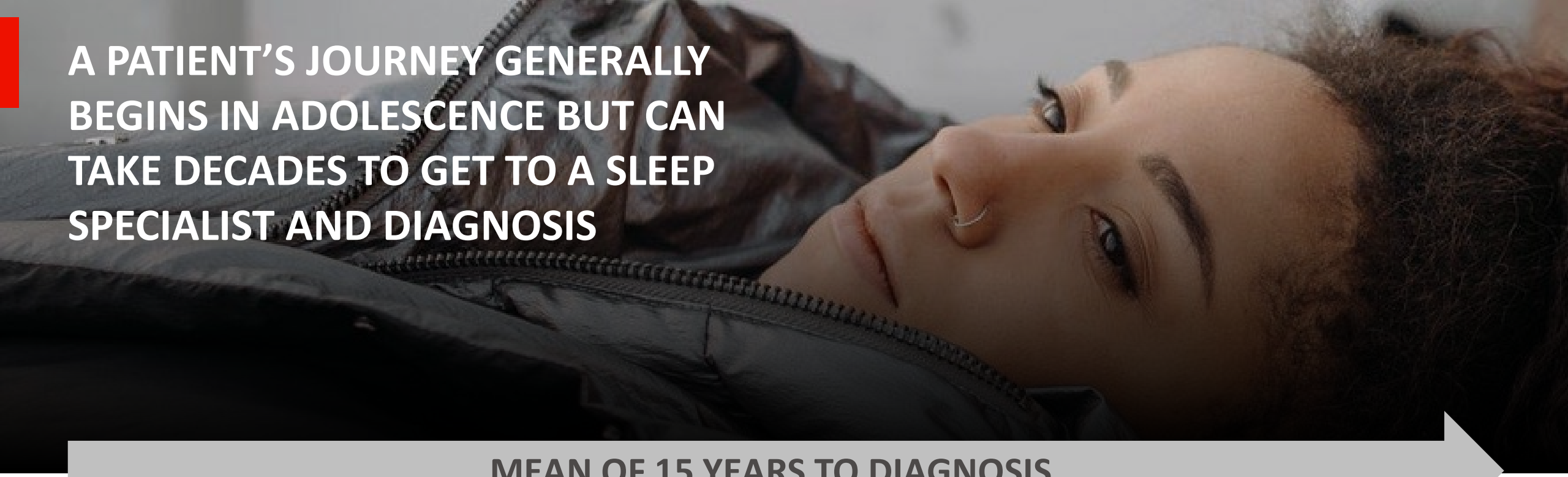
Sleep Paralysis



Disrupted Nighttime Sleep[1]

 1 Sateia MJ. Chest 2014;146:1387–94

A PATIENT'S JOURNEY GENERALLY BEGINS IN ADOLESCENCE BUT CAN TAKE DECADES TO GET TO A SLEEP SPECIALIST AND DIAGNOSIS



MEAN OF 15 YEARS TO DIAGNOSIS

- **SYMPTOM ONSET**
- **PRE-DIAGNOSIS**
- **DIAGNOSIS**
- **TREATMENT**

CURRENT NT1 TREATMENTS DO NOT ADDRESS UNDERLYING OREXIN DEFICIENCY

Treatment escalation and polypharmacy are common

50% Newly diagnosed patients progress to second line within 1 year[1]

65% Of second line patients receive more than one medication (polypharmacy)[2]

Despite treatment, NT1 is not controlled

75% Experience daily EDS despite treatment[3]

50% Experience 1-2 episodes of Cataplexy per day despite treatment[3]

We're not curing these patients. They improve, but they aren't normal. We need to get them to normal. ~ **Prescriber**

1. Takeda commissioned market research and claims analysis
2. Takeda commissioned market research and claims analysis
3. Maski K, et al. J Clin Sleep Med 2017;13;419–25

≈90% of patients believe there is a need for more treatment options[1,2]

>90% physicians want new treatment with new MOA[1,2]

TAKEDA BELIEVES PATIENTS AND PHYSICIANS MAKE SIGNIFICANT TRADE-OFFS WITH CURRENT THERAPIES

"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."

Patient with NT1

1.Thorpy, Hopper, Patroneva, Burden of Narcolepsy: A Survey of Patients and Physicians, Neurology Apr 2019, 92 (15 Supplement) P3.6-036
2. Narcolepsy Network, 2018 Know Narcolepsy Survey. Available at: https://narcolepsynetwork.org/surveyresults/, Last Accessed: March 15, 2021

NT1 RARE, UNDERDIAGNOSED AND UNDERTREATED

Adult NT1 Prevalence	
US	135K[1]
EU	66K[2,3]
JAPAN	64K[4]
CHINA	395K[5]

30-50% — Estimated diagnostic rate in developed countries (only 6% in China with largest prevalence)[6]

15 years — Mean diagnostic delay[7]

75% — Treatment Rate[8]

Opportunity to increase diagnosis and treatment rates with an innovative therapy

1. Silber MH et al. Sleep 2002;25:197–202; Longstreth WT Jr. et al. Sleep Med 2009;10:422–6; Scheer D et al. Sleep 2019;42.
2. Heier , M., et al., Prevalence of narcolepsy with cataplexy in Norway. Acta Neurologica Scandinavica , 2009. 120(4): p. 276 280
3. Hublin , C., et al, The prevalence of narcolepsy: an epidemiological study of the Finnish Twin Cohort. Annals of neurology, 1994. 35(6): p. 709 716
4. Internal analysis of JMDC claims database
5. Wing YK et al. Ann Neurol 2002;51:578–84; Han F et al. Sleep 2001;24:321–4
6. Silber et al. 2002 and Scheer et al. 2019
7. Thorpy MJ, et al. Sleep Med 2014;15:502–7
8. Takeda commissioned market research and claims analysis

TAK-994
Oral Orexin Agonist

First to target underlying cause of NT1

First approval expected FY2024 (if successful)

TAKEDA HAS THE POTENTIAL TO TRANSFORM TREATMENT WITH ORAL OREXIN AGONIST TAK-994

Increase Recognition and Diagnosis Rates	**Prepare for NT1 launch and label expansions**	**Establish TAK-994 as a breakthrough treatment**

KEY TAKEAWAYS FOR ORAL OREXIN AGONIST TAK-994 NARCOLEPSY TYPE 1 (NT1)

1

NT1 is caused by an orexin deficiency, which disrupts sleep awake cycles

- NT1 is rare, underdiagnosed and undertreated
- NT1 is chronic and severe

2

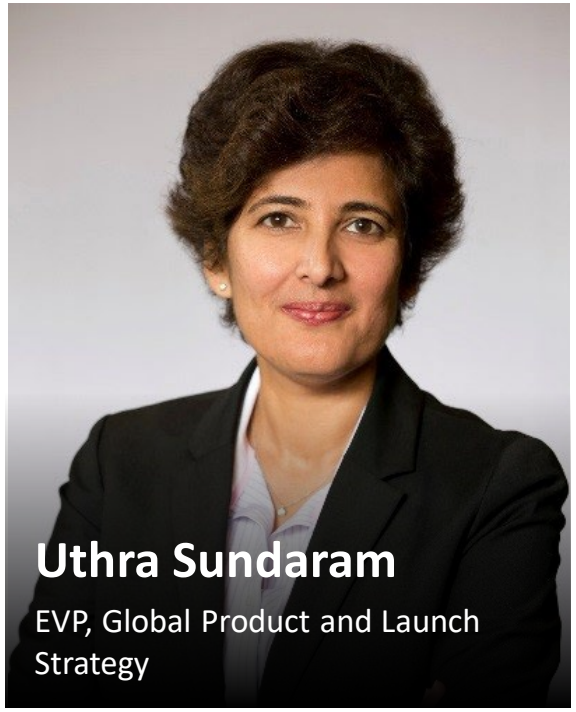
Current NT1 treatments do not address underlying orexin deficiency

- Treatment escalation and polypharmacy are common
- Despite treatment, NT1 is not controlled

3

If approved, TAK-994 will be the first to treat orexin deficiency

- Anticipated first approval FY2024
- Label expansions planned, and data dependent, as part of the Orexin Franchise strategy



Uthra Sundaram

EVP, Global Product and Launch Strategy

DELIVERING AN INNOVATIVE PIPELINE TO OUR PATIENTS

SPOTLIGHT ON SELECT WAVE 1 PROGRAMS

STRONG R&D AND COMMERCIAL PARTNERSHIP DRIVES OVERALL SUCCESS

Transforming **Partnership**

Transforming **Science**

Transforming **Lives**

BRINGING OUR **PIPELINE TO LIFE**

Global Capabilities to Deliver Life Transforming Treatments

LAUNCH EXCELLENCE

- Patient Journey & Diagnosis
- Data, Insights & Analytics
- Patient Services
- Value Based Partnerships
- Digital
- Evidence Generation

WAVE 1 PIPELINE ASSETS HAVE SIGNIFICANT MARKET POTENTIAL

	PRODUCT	INDICATION	FULL MARKET OPPORTUNITY[2]	TAKEDA'S PEAK REVENUE POTENTIAL[5]
ONCOLOGY	mobocertinib (TAK-788)	Exon 20 non-small cell lung cancer 1L Exon 20 non-small cell lung cancer 2L		$300 – 600MN
	pevonedistat (TAK-924)	Higher risk-Myelodysplastic syndromes Unfit Acute myeloid leukemia		$400 – 800MN
	TAK-007	3L+ Diffuse Large B-Cell Lymphoma 3L+ Chronic Lymphocytic Leukemia 3L+ Follicular Lymphoma		$700 – 1,500MN
RARE GENETIC & HEMATOLOGY	TAK-609	Hunter CNS (intrathecal)[1]		<$100MN
	maribavir (TAK-620)	CMV infection in transplant patients (R/R & 1L)		$700 – 800MN
	TAK-611	Metachromatic leukodystrophy (intrathecal)		$300 – 450MN
	TAK-755	cTTP / iTTP, Sickle cell disease		$1,000 – 1,500MN

	PRODUCT	INDICATION	FULL MARKET OPPORTUNITY[2]	TAKEDA'S PEAK REVENUE POTENTIAL[5]
NEUROSCIENCE	Orexin programs[3]	Narcolepsy type 1 (NT1) Narcolepsy type 2 (NT2) Idiopathic hypersomnia		$3,000 – 4,000MN (NT1) $1,000 – 2,000MN (NT2 + IH)
	soticlestat (TAK-935)	Dravet syndrome, Lennox-Gastaut syndrome		$400-500MN
GASTROENTEROLOGY (GI)	Eohilia[4] (TAK-721)	Eosinophilic Esophagitis		$300 – 500MN
VACCINES	TAK-003	Prevention of dengue		$700 – 1,600MN

KEY	≤ $0.5BN	$0.5BN - $1.0BN	$1.0BN - $3.0BN	≥ $3.0BN
				

1. *MPSII market in total (somatic + CNS)*
2. *Market potential indicates Takeda's best estimate about addressable market size, based on available data and estimates.*
3. *Other rare indications than NT1, NT2 and IH are not included in the calculation.*
4. *Eohilia is the proposed brand name for TAK-721. TAK-721 is an investigational treatment and has not been approved for use by the FDA or other regulatory authorities. In active discussions with the FDA. Projected approval subject to outcome of discussions*
5. *Includes incremental revenue not adjusted for Probability of Technical Success (PTS) and is not a "forecast" or "target" figure. PTS applies to the probability that a given clinical trial/study will be successful based on pre-defined endpoints, feasibility and other factors and regulatory bodies will grant approval. Actual future net sales achieved by our commercialized products and pipelines will be different, perhaps materially so, as there is a range of possible outcomes from clinical development, driven by a number of variables, including safety, efficacy and product labelling. If a product is approved, the effect of commercial factors including the patient population, the competitive environment, pricing and reimbursement is also uncertain*

UPCOMING INVESTOR EVENTS

4Q20 EARNINGS CALL	**MAY 11, 2021**
ONCOLOGY STRATEGIC UPDATE CALL	**JUNE 2021** (DATE TO BE CONFIRMED)
PEVONEDISTAT DEEP DIVE CALL	**2021 – DATA DRIVEN** (DATE TO BE CONFIRMED)

QA Session