Takeda R&D Day 2024

Focus on Late-stage Pipeline & Market Opportunity

Friday, December 13th, 2024

Tokyo

Better Health, Brighter Future

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Takeda's financial statements are prepared in accordance with International Financial Reporting Standards ("IFRS").

This presentation and materials distributed in connection with this presentation include certain financial measures not presented in accordance with IFRS, such as Core Revenue, Core Operating Profit, Core Net Profit, Core EPS, Constant Exchange Rate ("CER") change, Net Debt, EBITDA, Adjusted EBITDA, Free Cash Flow and Adjusted Free Cash Flow. Takeda's management evaluates results and makes operating and investment decisions using both IFRS and non-IFRS measures included in this presentation. These non-IFRS measures exclude certain income, cost and cash flow items which are included in, or are calculated differently from, the most closely comparable measures presented in accordance with IFRS. Takeda's non-IFRS measures are not prepared in accordance with IFRS and such non-IFRS measures should be considered a supplement to, and not a substitute for, measures prepared in accordance with IFRS (which we sometimes refer to as "reported" measures). Investors are encouraged to review the definitions and reconciliations of non-IFRS financial measures to their most directly comparable IFRS measures, which are in the financial appendix of Takeda's FY2024 Q2 quarterly earnings presentation.

Peak Revenue Potential and PTRS Estimates

References in this presentation to peak revenue ranges are estimates that have not been adjusted for probability of technical and regulatory success (PTRS) and should not be considered a forecast or target. These peak revenue ranges represent Takeda's assessments of various possible future commercial scenarios that may or may not occur. References in this presentation to PTRS are to internal estimates of Takeda regarding the likelihood of obtaining regulatory approval for a particular product in a particular indication. These estimates reflect the subjective judgment of responsible Takeda personnel and have been approved by Takeda's Portfolio Review Committee for use in internal planning.

Exchange Rates

In this presentation, certain amounts presented in Japanese yen have been translated to US dollars solely for the convenience of the reader at the exchange rates disclosed herein. The rate and methodologies used for these convenience translations differ from the currency exchange rates and translation methodologies under IFRS used for the preparation of Takeda's consolidated financial statements. These translations should not be construed as a representation that the relevant Japanese yen amounts could be converted into U.S. dollars at this or any other rate.

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Elritercept license agreement

Elritercept is included for reference only. Takeda entered into an exclusive license agreement with Keros for global rights, in all territories outside of mainland China, Hong Kong and Macau, to Elritercept. The closing of the transaction is subject to receipt of regulatory approval(s), expected in the first calendar quarter of 2025. Takeda does not currently have rights to Elritercept.

Today's Agenda

TIME (JST)	AGENDA
8:30-8:40	**A Global, Innovation-driven Biopharmaceutical Company** *Christophe Weber, President & CEO*
8:40-9:00	**R&D Strategy and Pipeline Highlights** *Andy Plump, President Research & Development*
9:00-9:50	**Neuroscience: Deep-dive on Orexin Franchise** *Sarah Sheikh, Head of Neuroscience Therapeutic Area Unit and Head of Global Development* *Ramona Sequeira, President of Global Portfolio Division*
9:50-10:00	*Break*
10:00-11:30	**Gastrointestinal and Inflammation (GI&I): Deep-dive on Zasocitinib, Rusfertide, Mezagitamab, Fazirsiran** *Chinwe Ukomadu, Head of GI&I Therapeutic Area Unit* *Ramona Sequeira, President of Global Portfolio Division*
11:30-12:00	Lunch
12:00-12:20	**Oncology: Deep-dive on Elritercept – newly announced BD deal** *P.K. Morrow, Head of Oncology Therapeutic Area Unit* *Teresa Bitetti, President of Global Oncology Business Unit*
12:20-13:15	**Q&A Session**
13:15-14:00	*Reception*

Better health for people, brighter future for the world

Our vision is to discover and deliver life-transforming treatments, guided by our commitment to:

PATIENT **PEOPLE** **PLANET**

…AND BY UNLEASHING THE POWER OF DATA AND DIGITAL

We are guided by our values of Takeda-ism which incorporate **Integrity**, **Fairness**, **Honesty**, and **Perseverance**, with Integrity at the core.
They are brought to life through actions based on **Patient-Trust-Reputation-Business**, in that order.

A global, innovation-driven biopharmaceutical company

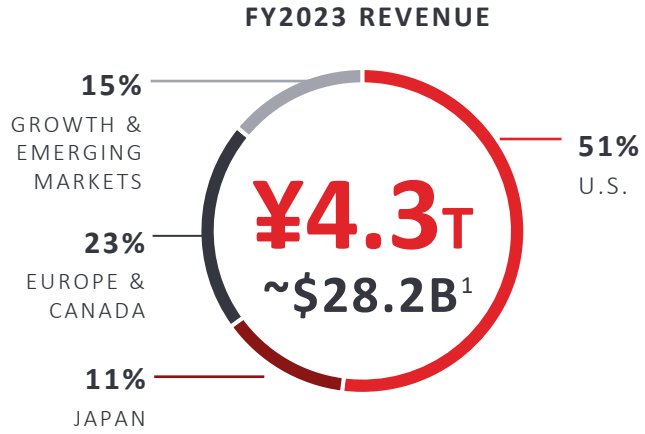
Global Footprint Aligned With Key Market Opportunities

GLOBAL HEADQUARTERS **TOKYO, JAPAN**

GLOBAL HUB **CAMBRIDGE, MA, USA**

PRESENCE IN APPROX **80** COUNTRIES & REGIONS

6 KEY BUSINESS AREAS REPRESENT ~94% OF REVENUE
GI, RARE DISEASES, PLASMA-DERIVED THERAPIES, ONCOLOGY, VACCINES, NEUROSCIENCE



R&D Engine Focused on Discovering & Developing Highly Innovative Medicines

3 CORE R&D THERAPEUTIC AREAS
GASTROINTESTINAL & INFLAMMATION, NEUROSCIENCE, ONCOLOGY

4 FOCUS MODALITIES
SMALL MOLECULES, BIOLOGICS, ANTIBODY DRUG CONJUGATES (ADCs), ALLOGENEIC CELL THERAPIES

2 RESEARCH SITES
SHONAN, JAPAN
CAMBRIDGE, MA, USA

¥770B ~$5.1B[2] ANNUAL R&D INVESTMENT (FY2024 FORECAST)

1. Convenience translation calculated with 1 USD = 151.22 JPY, the Noon Buying Rate certified by the Federal Reserve Bank of New York on March 29, 2024
2. Convenience translation calculated with FY2024 full year assumption rate of 1 USD = 150 JPY

Committed to growth & shareholder returns

Revenue Growth

- Growth & Launch Products represent ~50% of revenue with double-digit % growth[1]
- Limited generic exposure in biopharma portfolio (after U.S. VYVANSE) until early 2030s[2]
- Long-term stable growth outlook for PDT business with margin improvement

Pipeline Acceleration

- Accelerating late-stage assets with potential to generate significant value
- Three new molecular entities with Phase 3 data readouts expected by end of CY2025

Margin Improvement

- Targeting Core Operating Profit margin improvement to reach low-to-mid 30s%
- Unleashing the power of data, digital & technology to boost efficiencies across the entire value chain

Shareholder Returns

- Strong cashflow outlook underpins progressive dividend policy
- Investing in R&D and pursuing asset-specific business development to further enhance long-term corporate value

1. As of FY2024 H1, growth at Constant Exchange Rate (CER). For the definition please refer to the financial appendix of Takeda's FY2024 Q2 quarterly earnings presentation.
2. Major products expected to face generic/biosimilar competition between FY2024-2029 represent less than 10% of FY2023 revenue: Gattex U.S. (FY25), Iclusig U.S. (FY26) , Trintellix U.S. (FY26), Vectibix JP (FY26), Vyvanse EU (FY28), Livtencity U.S. (FY28), Ninlaro U.S. (FY29)

Our late-stage pipeline has significant revenue potential

Late-Stage Pipeline Peak Revenue Potential of $10 - 20B

★ Oveporexton (TAK-861)
Narcolepsy Type 1

$2 – 3B

Zasocitinib (TAK-279)
Psoriasis & Psoriatic Arthritis

$3 – 6B

Ulcerative Colitis & Crohn's Disease

Potential for significant upside

★ Rusfertide (TAK-121)
Polycythemia Vera

$1 – 2B

★ Fazirsiran (TAK-999)
Alpha-1 Antitrypsin Related Liver Disease

$1 – 3B

★ Mezagitamab (TAK-079)
Immune thrombocytopenia & Immunoglobulin A Nephropathy

$1 – 3B

★ Elritercept (TAK-226)
Myelodysplastic Syndromes

$2 – 3B

★ Orphan Drug Designation potential
(in any region / indication for a given asset)

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Late-stage programs have significant value potential; oveporexton, zasocitinib, rusfertide phase 3 data expected in 2025

Three Phase 3 Data Readouts Over the Next 12 Months

- Oveporexton in Narcolepsy Type 1
- Zasocitinib in Psoriasis
- Rusfertide in Polycythemia Vera[1]

>70% PTRS[2] to approval

Late-Stage Peak Revenue Potential

$10 - 20B

Target Filing Dates by Indication

FY25 / FY26

Oveporexton (TAK-861)
Narcolepsy Type 1

Zasocitinib (TAK-279)
Psoriasis

Rusfertide (TAK-121)
Polycythemia Vera

FY27 - FY29

Zasocitinib (TAK-279)
Psoriatic Arthritis

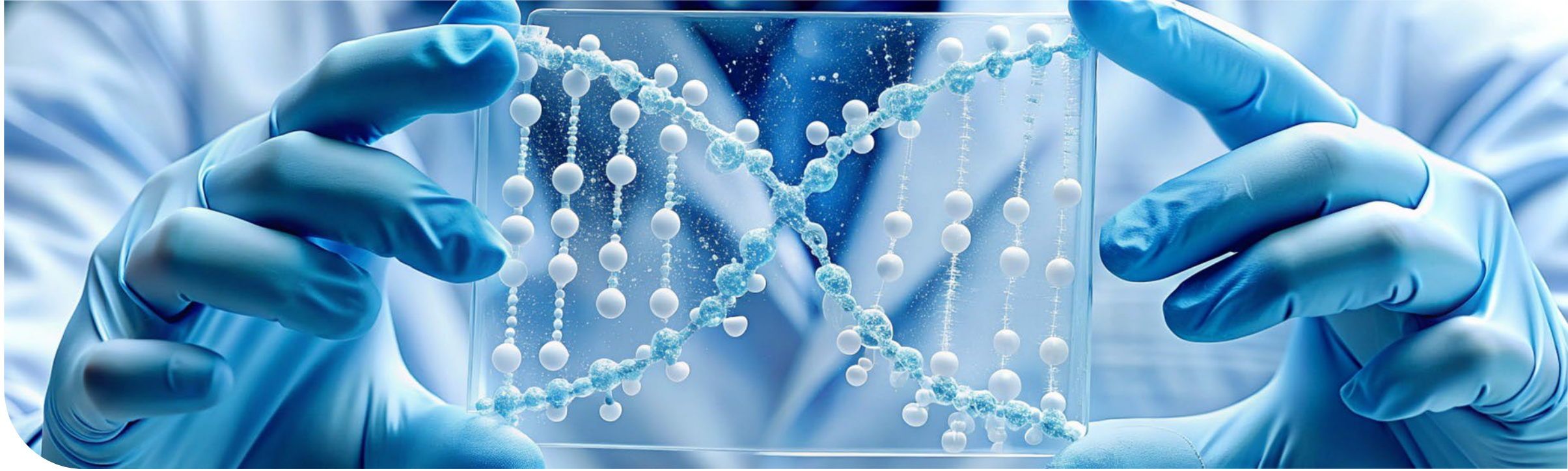
Mezagitamab (TAK-079)
IgA Nephropathy
Immune Thrombocytopenia

Fazirsiran (TAK-999)
AATD Liver Disease

Elritercept (TAK-226)
Myelodysplastic Syndromes

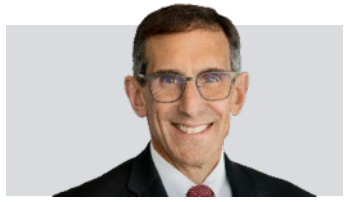
1. Our partner Protagonist Therapeutics is responsible for Phase 3 development of Rusfertide and has stated Phase 3 data may be available as soon as March 2025 which is our Q4 FY24
2. Please refer to the Important Notice at the start of this presentation for more information about PTRS and peak revenue estimates

Please refer to the Important Notice at the start of this presentation for more information about the Elritercept license agreement



R&D Strategy and Pipeline Highlights

Accelerating Our Late-Stage Pipeline to Transform Patients' Lives and Deliver Significant Value to Takeda

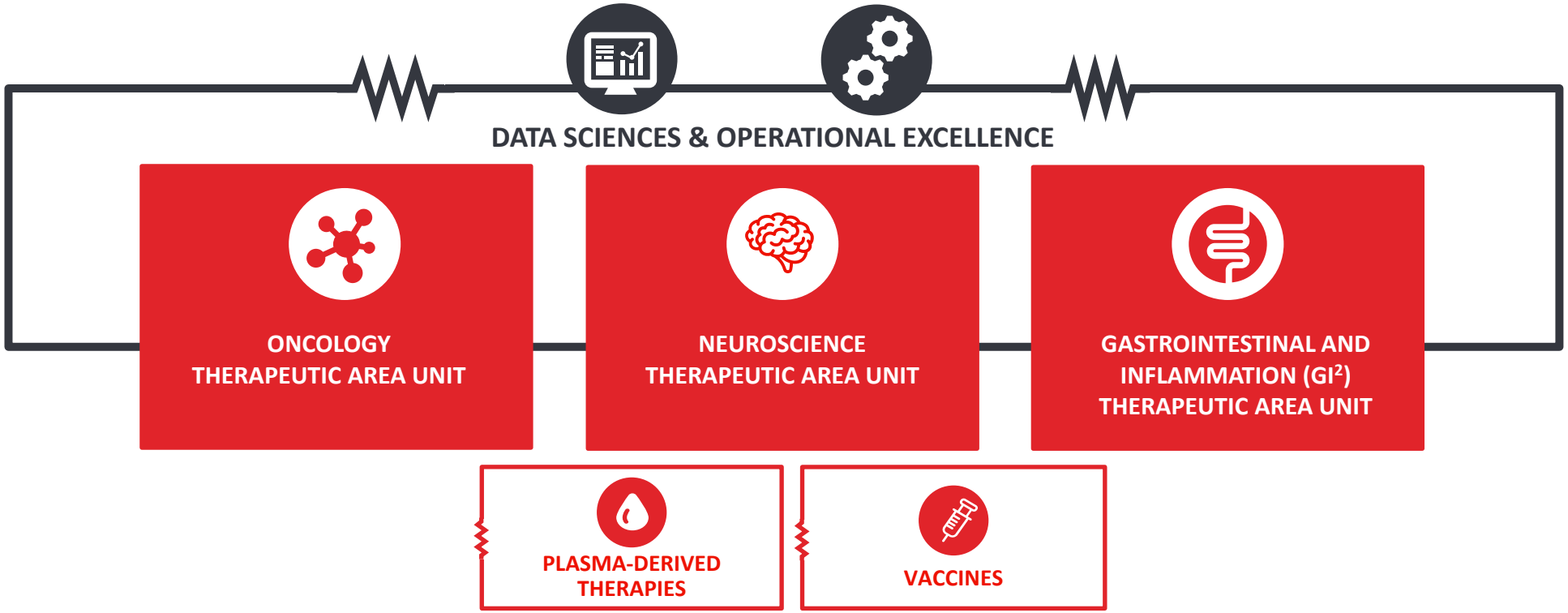


Andy Plump President, Research & Development

We discover, develop and deliver life-transforming medicines for rare and more prevalent diseases across our focused therapeutic areas

R&D STRATEGY

INNOVATIVE BIOPHARMA



PARTNERSHIPS

Our scale, focus, and capabilities have advanced significantly since FY2015

FY2015

Regional Development and Launch Capability

10 Therapeutic Areas, Small Molecule Focus

R&D Investment **346** bn JPY

Small Late-Stage Pipeline

FY2024

Global Development, Global Launch Capability

3 Therapeutic Areas, **4** Key Modalities

R&D Investment **770** bn JPY[1]

Robust, High Value Late-Stage Pipeline

R&D Transformation

Shire Integration

Enhance R&D Productivity
Invest Data Sciences + AI

1. Projected R&D Investment as of Q2 FY24 earnings, October 31, 2024.

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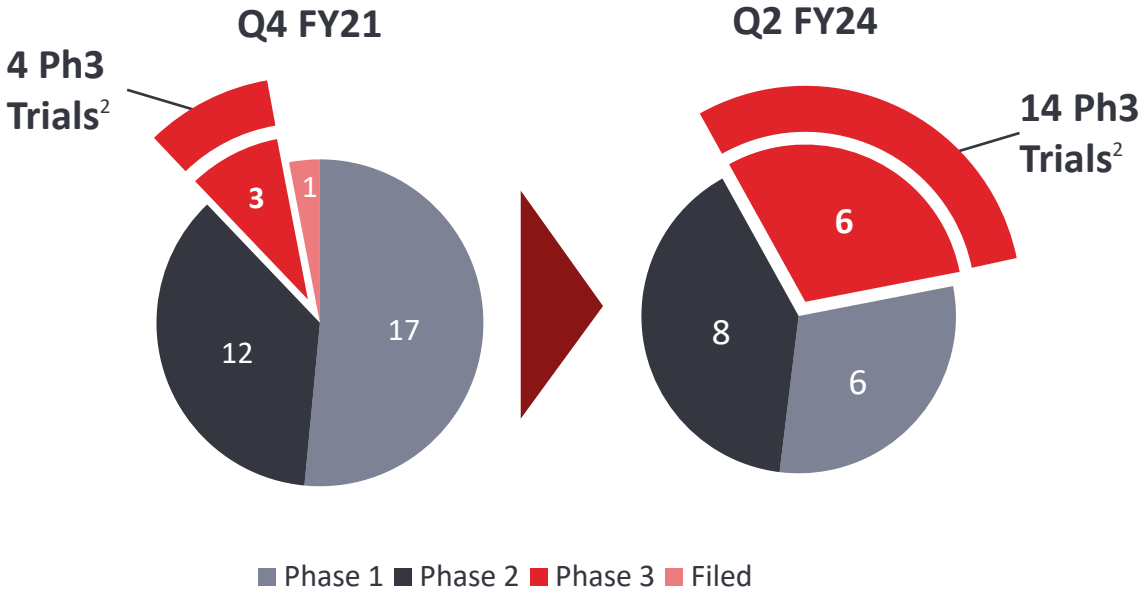
We have built strong global development, regulatory and launch expertise

	FY2021	FY2022	FY2023
FIRST NME APPROVALS	LIVTENCITY® (maribavir) tablets 200mg	Qdenga® Dengue Tetravalent Vaccine (Live, Attenuated)	ADZYNMA ADAMTS13, recombinant-krhn Eohilia™ (budesonide oral suspension) 2mg Fruzaqla® (fruquintinib) capsules 5 mg • 1 mg
KEY LCM APPROVALS			Entyvio® vedolizumab — U.S. SC in UC and Crohn's[2] HyQvia Inmunoglobulina Humana Normal al 10% con Hialuronidasa Humana Recombinante — CIDP maintenance
MAJOR MARKET APPROVALS[1]	15	7	25

1. Major Markets: US, EU, Japan or China
2. U.S. approval for Entyvio SC was in September 2023 for UC and April 2024 for Crohn's

Rigorous prioritization to deliver our high value late-stage pipeline

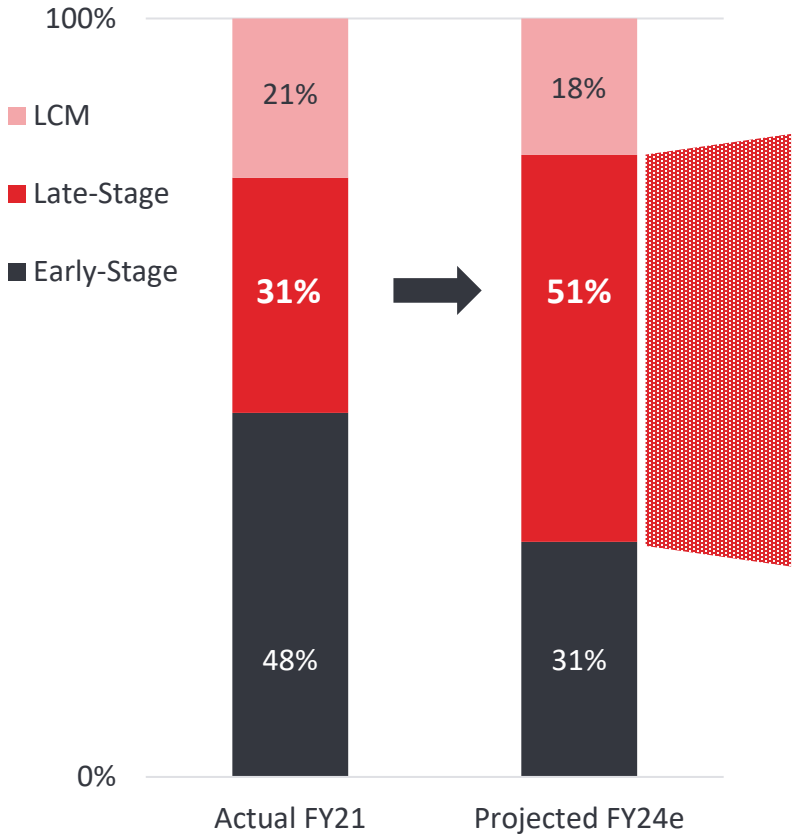
GLOBAL NMEs[1]



Program Selection Criteria

1. Unmet medical need
2. Scientific validity
3. Accelerated development path
4. Commercial opportunity

% OF EXTERNAL SPEND[3]



Investing in Robust Late-Stage Pipeline FY25+

$4.7	**$5.1**
Total R&D Spend[4] (Bn USD)	

1. Lead indication only, no regional assets/expansions
2. Phase 3 trials ongoing or planned that support the development of the NMEs
3. External spend refers to direct pipeline spend in R&D Business Unit. Early-stage refers to pre-proof of concept; late stage refers to post-proof of concept.
4. Total R&D Spend refers to all R&D related expenses as per Takeda's consolidated statement of profit and loss. Calculated with actual FY2021 average exchange rate of 1 USD = 112 JPY and FY2024 full year assumption rate of 1 USD = 150 JPY respectively.

Future Fit development model: delivering improved speed, quality and efficiencies across the pipeline

Execute Clinical Trials with top tier industry performance

Research	Development				
Preclinical	Ph 1	Ph 2	Ph 3	Filing	Launch

Study level: 3 core elements that can be optimized

FF

Study & Planning

Study planning, site selection, and site activation improved performance

Recruitment & Conduct

Recruitment enhanced by leveraging advanced analytics

Closeout & Reporting

Document generation powered by AI and automation for regulatory submission

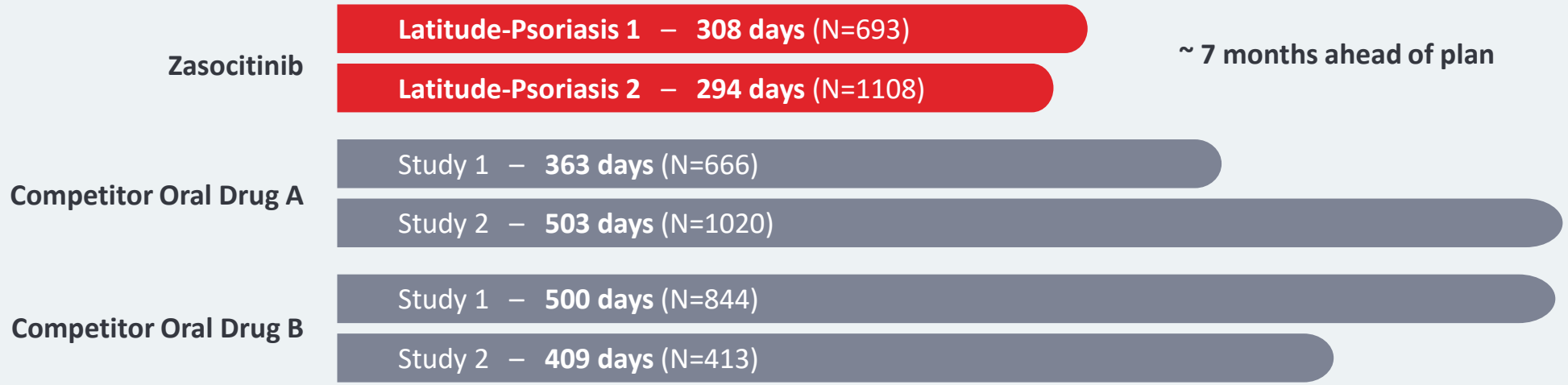
People & Process

COMPASS

Clinical trial management and analytics

Future Fit and prioritization has led to significant acceleration for zasocitinib and oveporexton

Psoriasis: Time to recruit pivotal trials



Neuroscience: Development timelines

1. Industry average neurology development for FIH to Filing ~11 years. Source: Neurology Industry Source: IQVIA Pipeline Intelligence, Dec 2023; Citeline Trialtrove, IQVIA Institute, Jan 2024
2. Average Sleep Medication development for FIH to Filing ~8 years. Source: FDA website and desk research.
3. FIH: First in human

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Right modalities and resourcing from project inception; Research engine to fuel our sustainable pipeline

Sustainable acceleration of First-in-Human, and BLA/NDA First Filing

Preclinical stage: 3 core elements for optimization

Accelerate Delivery to Clinic (Fast to First-in-Human)

Fast pivot to develop TAK-360 leveraging AI and cryogenic electron microscopy

Shonan iPark, Japan

Driving Efficiency with Real-Time Decision Support

Quality targets, right modalities, and resourcing from project inception

Apply Digital Accelerators

Building unified digital infrastructure and the Lab of the Future at 585 Kendall with augmented ways of working

585 Kendall, Cambridge

Our sustainable pipeline provides opportunities across all our therapeutic areas

	EARLY-STAGE PROGRAMS / SELECT LCMs			
GASTROINTESTINAL AND INFLAMMATION	**TAK-227** Celiac Disease	**TAK-101** Celiac Disease	**TAK-007** Autoimmune Disease[1]	
	zamaglutenase Celiac Disease	**TAK-004** Nausea & Vomiting	**ADZYNMA®** ★ iTTP	
NEUROSCIENCE	**TAK-360** NT2 / IH	**danavorexton**[2] Respiratory	**TAK-341** ★ MSA	**TAK-594** ★ Frontotemporal Dementia
ONCOLOGY	**TAK-186** EGFR Solid Tumor	**dazostinag** Solid Tumors	**TAK-012** Acute Myeloid Leukemia[1]	
	TAK-280 B7-H3 Solid Tumor	**TAK-500** Solid Tumors		
PLASMA-DERIVED THERAPIES	**TAK-881** PID	**HYQVIA®** PID, SID, CIDP, MMN (JP)		
SELECT OPTIONS[5]	**ACI-24.060**[3] Alzheimer's Disease		**olverembatinib**[4] **HQP1351** CP-CML	

Potential first-in-class anti-Abeta active immunotherapy
Designed to induce antibody response against toxic forms of Abeta driving plaque formation in Alzheimer's disease

Potential best-in-class TKI to elevate treatment of CML
Oral, third-generation BCR-ABL TKI for patients with chronic-phase CML resistant to and/or intolerant of first-and second-generation

★ Orphan Drug Designation potential (in any region / indication for a given asset)

NME | LCM

1. TAK-007 Phase 1 trial in autoimmune disease is planned
2. Danavorexton (TAK-925) trials in respiratory conditions under development
3. ACI-24.060 is included for reference only. AC Immune retains ownership of this asset and is solely responsible for its clinical development prior to Takeda's potential exercise of its option to exclusively license certain rights, which is subject to customary conditions including regulatory approval. Currently in Phase 2.
4. Olverembatinib/HQP1351 is included for reference only. Ascentage Pharma retains ownership of this asset and is solely responsible for its clinical development prior to Takeda's potential exercise of its option to exclusively license certain rights, which is subject to customary conditions including regulatory approval. Currently in Phase 3.
5. Select options: Other selected assets that Takeda holds contractual rights to potentially clinically develop and/or commercialize in the future.

Partnering to expand our pipeline and maximize R&D investment

Acquisitions

Zasocitinib[1]

GammaDelta

Takeda Development

Late-stage/Commercialization

FRUZAQLA

Rusfertide

Partner Development/Takeda Commercialization

In-licensing

Elritercept

Takeda Development

Fazirsiran

Shared Development

Options[2]

Olverembatinib

ACI-24.060

Partner Development with Opt-in Rights

1. Takeda acquired zasocitinib from Nimbus Therapeutics
2. Options: Other selected assets that Takeda holds contractual rights to potentially clinically develop and/or commercialize in the future

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Neuroscience: Deep-dive on Orexin Franchise

Sarah Sheikh
Head of Neuroscience Therapeutic Area Unit & Global Development

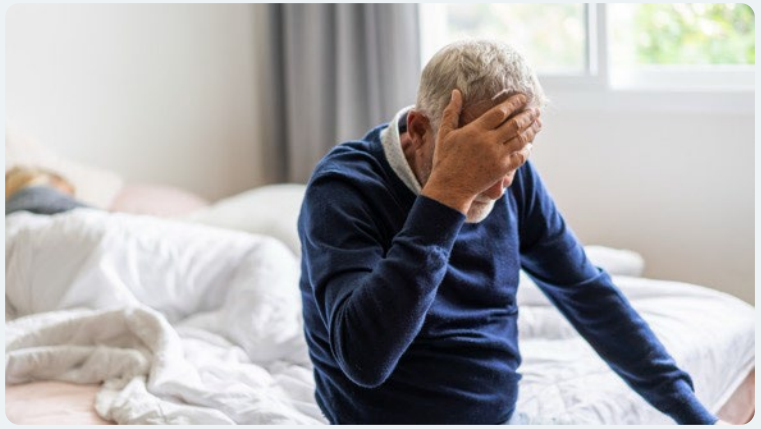
Ramona Sequeira
President, Global Portfolio Division

Better Health, Brighter Future

Recent scientific advancements & regulatory momentum heralds a new era in Neuroscience

High Unmet Need

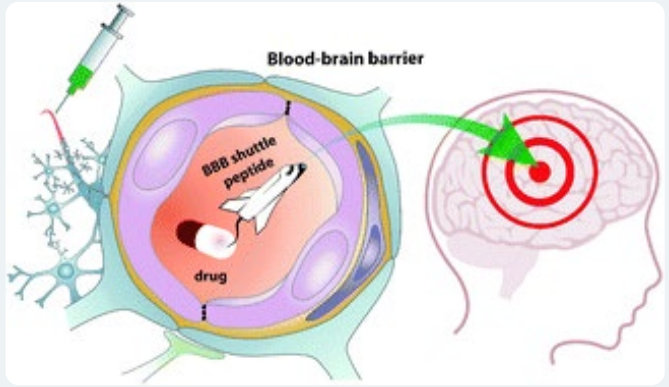
Estimated to be **9 million deaths** per year due to neurological conditions[1]



- **1 in 3 people** will develop a neurological disorder in their lifetime
- Neurological disorders impose **$1.1 trillion** in direct global healthcare costs annually

Growing Scientific Understanding

- **Enhanced understanding** of underlying pathophysiology
- Identification & validation of **previously undruggable targets**
- Discovery of **novel biomarkers to de-risk**
- **Enhanced Drug Delivery tools**



BBB Shuttle Technology

Innovative Regulatory Approaches

Evidenced by Numerous **Recent FDA Approvals**

- **32** new neurological indications approved from 2018-2023
- Advancement in supportive reimbursement framework

1. Lancet Neuro, 2019 May;18(5):459–480 WHO https://www.who.int/news/item/14-03-2024-over-1-in-3-people-affected-by-neurological-conditions--the-leading-cause-of-illness-and-disability-worldwide 2) Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016 3) Estimating the Economic Impact of Direct Health Expenditure on Brain Disorders, Globally and in the United States 4) https://www.ncbi.nlm.nih.gov/books/NBK53103/ 5) Thomas et al, 2024, A Comprehensive Review of Novel FDA-approved Neurological Indications from 2018–2023 6) https://pmc.ncbi.nlm.nih.gov/articles/PMC9945815/

Our vision is to be a leader and partner in neuroscience by discovering and delivering life-changing medicines for people and society

Strategically focused on three core areas

OREXIN	NEURODEGENERATION	RARE NEUROLOGY
Transform care for rare sleep disorders and orexin-related conditions	Address the leading driver of health burdens in an aging society	**Address the devastating diseases** with significant unmet need
Leverage Takeda's pioneering science to fully harness orexin biology	Utilize validated targets & next-gen modalities to alleviate societal burden	Develop potential **disease modifying medicines**

Leading Orexin Franchise

Takeda pioneering the field of orexin therapeutics – franchise leading with oveporexton, a potential first-in-class treatment for NT1

Oveporexton (TAK-861): *First & Fast[3] in NT1*

- **The most advanced orexin agonist – Addressing orexin deficiency as the underlying pathophysiology in NT1**[1]
- **Target Ph3 readout in CY2025**
- Ph2 and Long-term Extension (LTE) data support potential **transformative profile**
- Significantly accelerated Phase 3 program
- **Breakthrough therapy designation** received in U.S., China

TAK-360 and beyond: *Additional assets/indications*

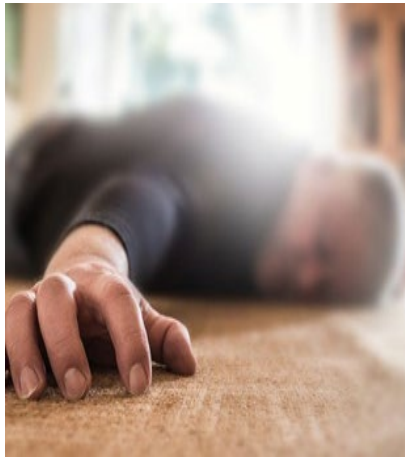
- **TAK-360: Accelerated development in NT2 & IH**
  - New chemistry and profile
  - Fast track designation received in U.S.
  - Target Ph2 start FY2024 in NT2/IH
- **Exploration of indications** pertinent to orexin biology: sleep-wake, respiration and metabolism
- **Tailored assets/profiles (e.g., TAK-925**[2] **and others)** to deliver optimal exposure for additional indications

1. Dauvilliers, Y., N Engl J Med, 2023; 389, 309-321;
2. Suzuki M et al., British Journal of Anaesthesia, 2024; IARS Conference, Denver, 2023; HV: Healthy Volunteer
3. Referring to the accelerated development timeline

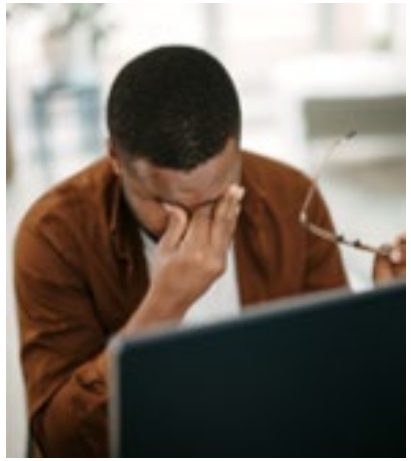
NT1 patients face daytime and nighttime debilitating symptoms impacting daily function

Daytime Symptoms

Excessive Daytime Sleepiness (EDS)

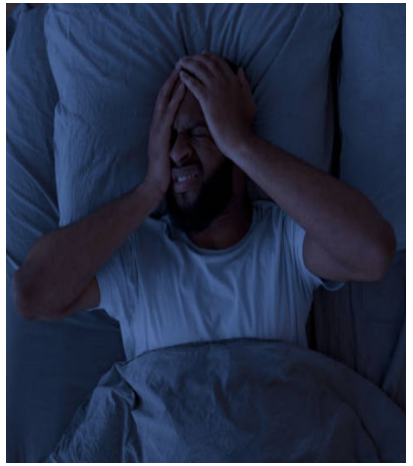


Cataplexy



Cognitive Symptoms

Nighttime Symptoms



Disrupted Nighttime Sleep, Disturbing Dreams[1]

Hallucinations, Sleep Paralysis

These symptoms may have significant impact on daily functions

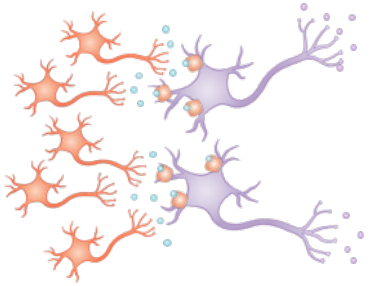
Reduced **Work productivity**	Reduced **School Performance**	Challenged **Social Interactions**	Reduced **Personal Responsibilities**	Limited **Recreational Activities**

1 Sateia MJ. Chest 2014;146:1387–94

NT1 pathophysiology is caused by loss of orexin neurons

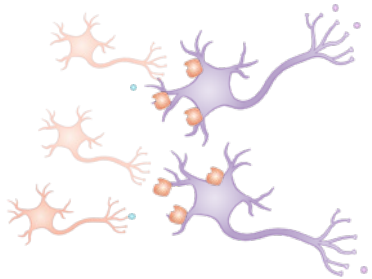
01 Healthy Individual

Healthy orexin neurons with normal postsynaptic downstream neurotransmitter activity



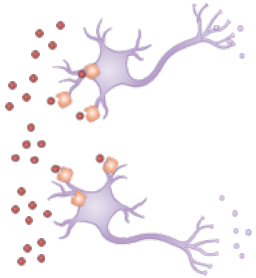
02 Individual with Narcolepsy type 1

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



03 Highly Specific OX2R Agonist

Orexin 2 receptor (OX2R) agonist may **restore downstream neurotransmitter activity** lost when endogenous orexin levels decline



OX2R

Orexin

Downstream Neurotransmitter

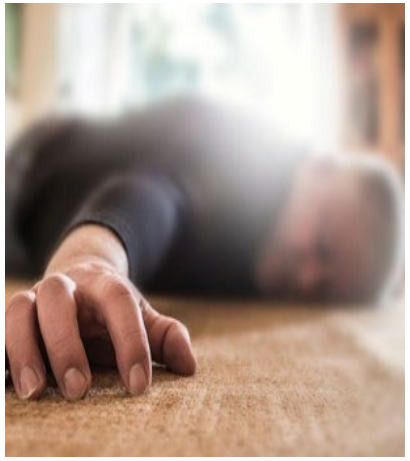
OX2R Agonist

Mahoney CE, et al. *Nat Rev Neurosci.* 2019;20(2):83-93; Chastain EM, et al. *Biochim Biophys Acta.* 2011;1812:265–274; Nishino S. *Sleep Med.* 2007;8(4):373-399; Saper CB, et al. *Trends Neurosci.* 2001;24(12):726-731; Yoshida Y, et al. *Eur J Neurosci.* 2001;14(7):1075-1081; Dauvilliers, Y., N Engl J Med, 2023; 389, 309-321

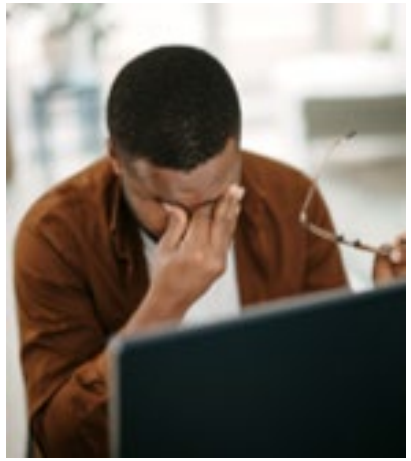
Comprehensive approach to evaluate full spectrum of NT1 symptoms with established and novel endpoints defining a new treatment class

Daytime Symptoms

Excessive Daytime Sleepiness (EDS)

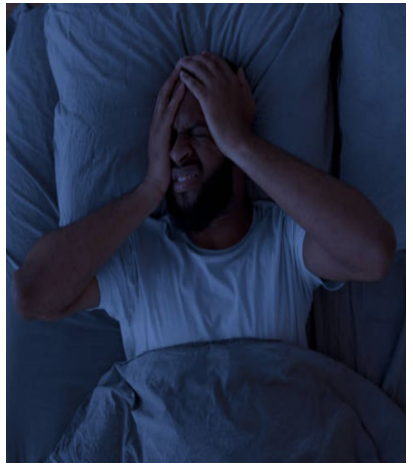


Cataplexy



Cognitive Symptoms

Nighttime Symptoms



Disrupted Nighttime Sleep, Disturbing Dreams[1]

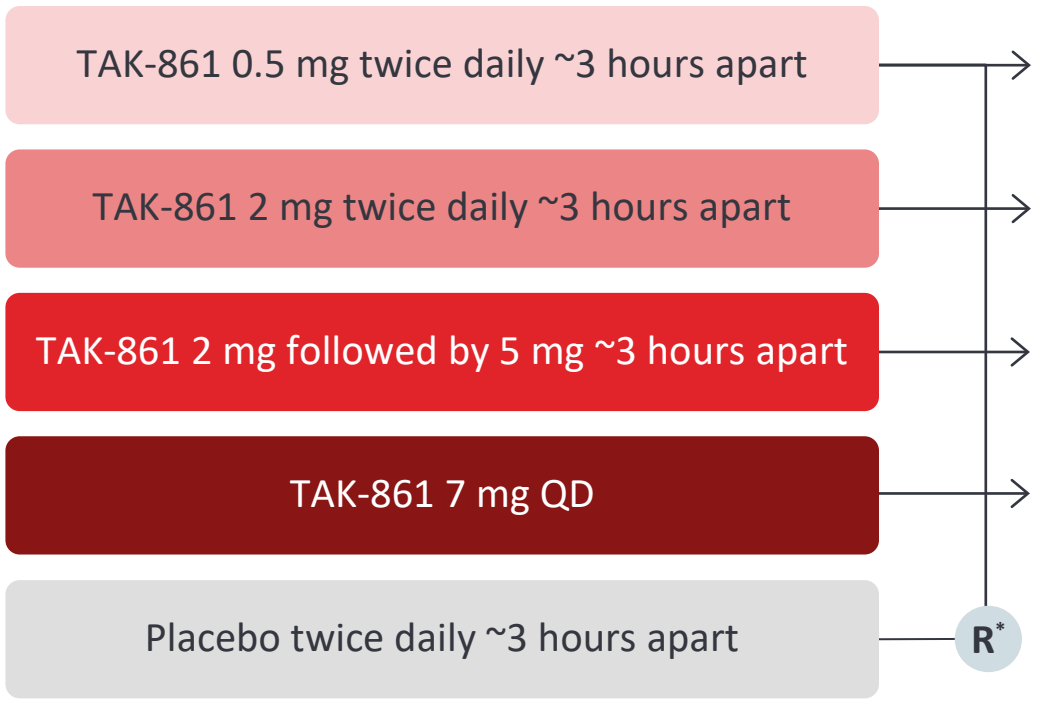
Hallucinations, Sleep Paralysis

MWT, ESS	**WCR**	**PVT**	**Sleep Diary, PSG**

NSS-CT, FINI, CGI-C, PGI-C

ESS: Epworth Sleepiness Scale; **MWT:** Maintenance of Wakefulness Test; **NSS-CT:** Narcolepsy severity scale; **PVT:** Psychomotor Vigilance Task; **WCR:** Weekly cataplexy rate; **FINI:** Functional Impacts of Narcolepsy Instrument; **CGI-C**: **Clinical** Global Impression of Change; **PGI-C**: Patient Clinical Global Impression of Change; **PSG:** polysomnography

The extensive oveporexton (TAK-861) phase 2 program laid solid foundation for phase 3 program



Long Term Extension (LTE)

Key Efficacy Measures

- MWT
- ESS
- WCR
- NSS-CT

Safety

- TEAEs

95% of participants that completed the placebo-controlled study enrolled in the LTE

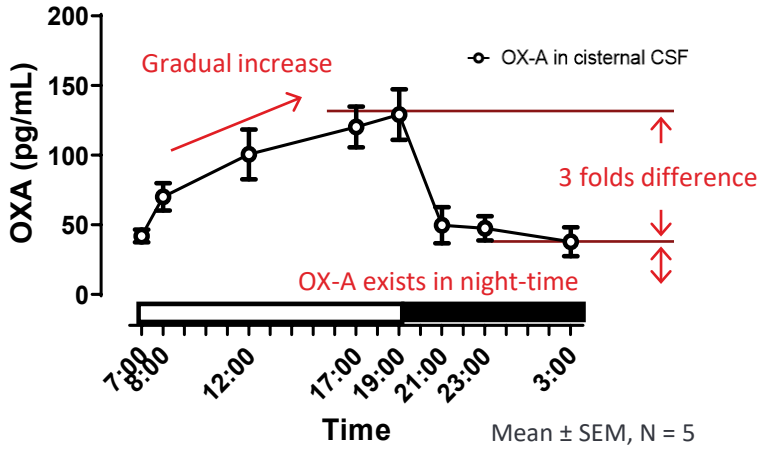
*Randomized to active arms

Optimized dosing regimen critical to deliver transformative efficacy while minimizing adverse events

TAK-861 BID profile mimics natural diurnal orexin tone

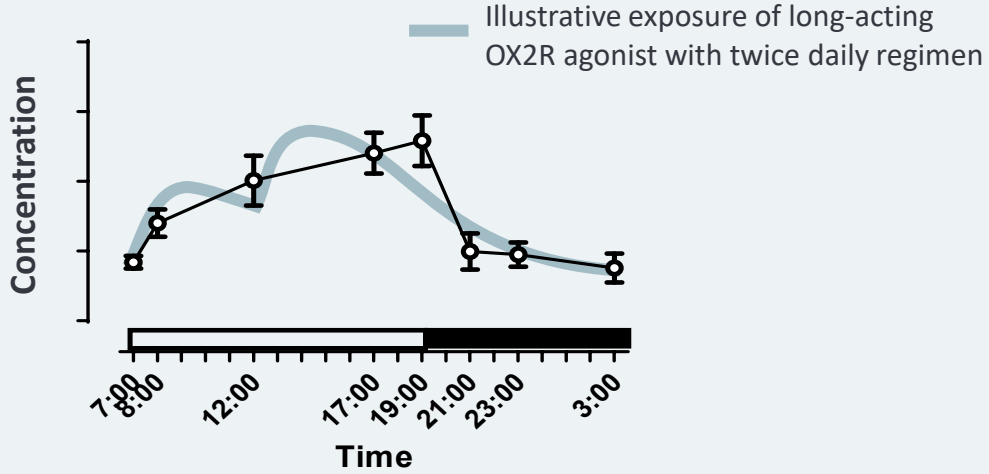
Diurnal fluctuation of orexin levels in monkey CSF

Takeda's novel method enabling accurate measurement of OX-A[1]



- OX-A gradually increases in day-time but still present during night-time
- Reliable model to predict human PK based on Takeda OX2R experience

Long-acting orexin 2 receptor (OX2R) agonist

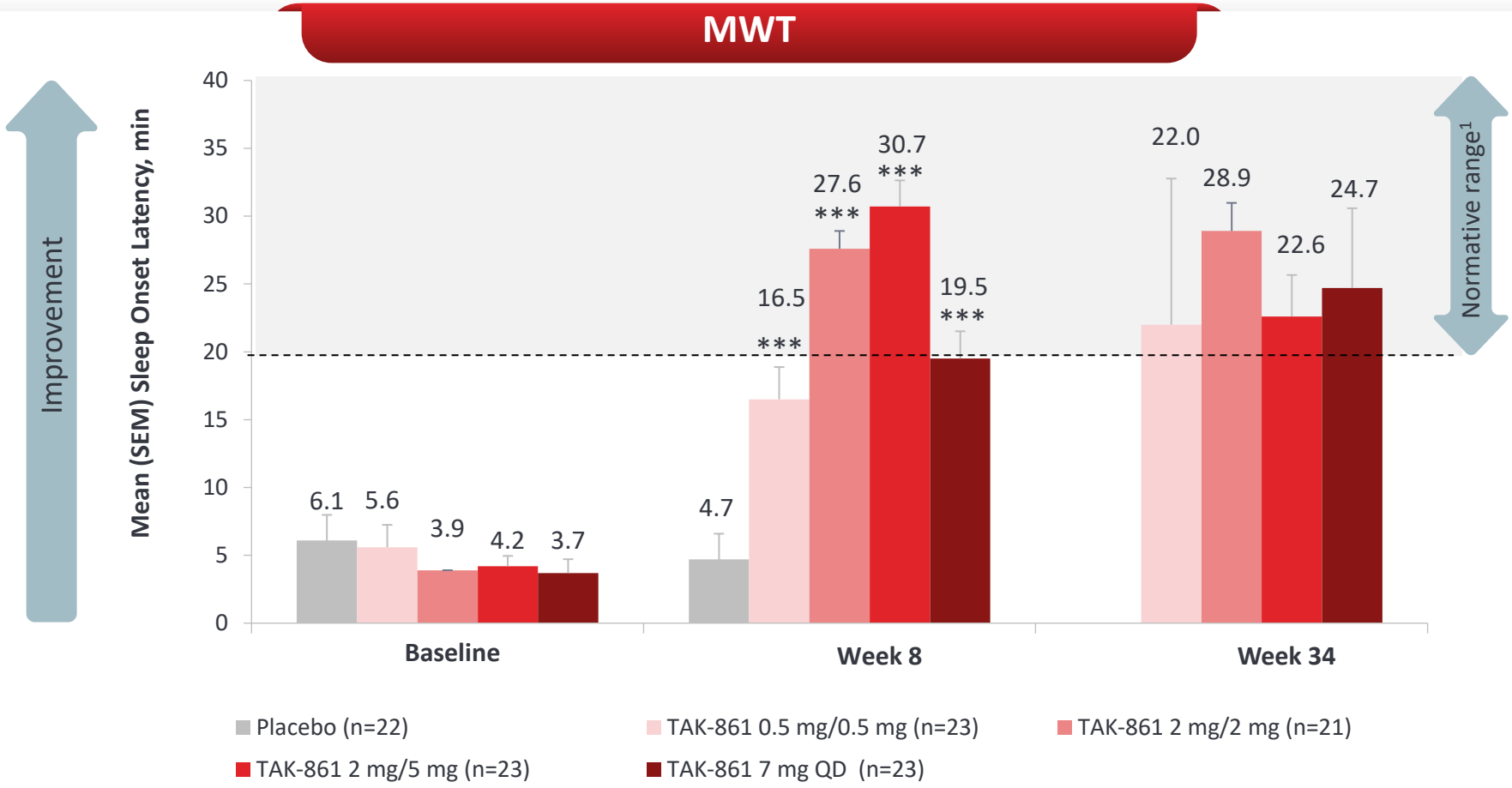


- Long-acting OX2R agonist with BID dosing mimics diurnal orexin fluctuation
- Long half-life maintains sufficient exposure during the day
- Exposure levels are reduced at night, mimicking the orexin tone

1. Narita et al., ACS Chem Neurosci, 2023

Oveporexton (TAK-861) demonstrated normalization of wakefulness (MWT) at 8 weeks and maintained over an additional 6 months

The Maintenance of Wakefulness Test (MWT): daytime polysomnographic procedure which quantifies wake tendency by measuring ability to remain awake during soporific circumstances (sleepiness condition such as dark quiet room)



Excessive Daytime Sleepiness (EDS)

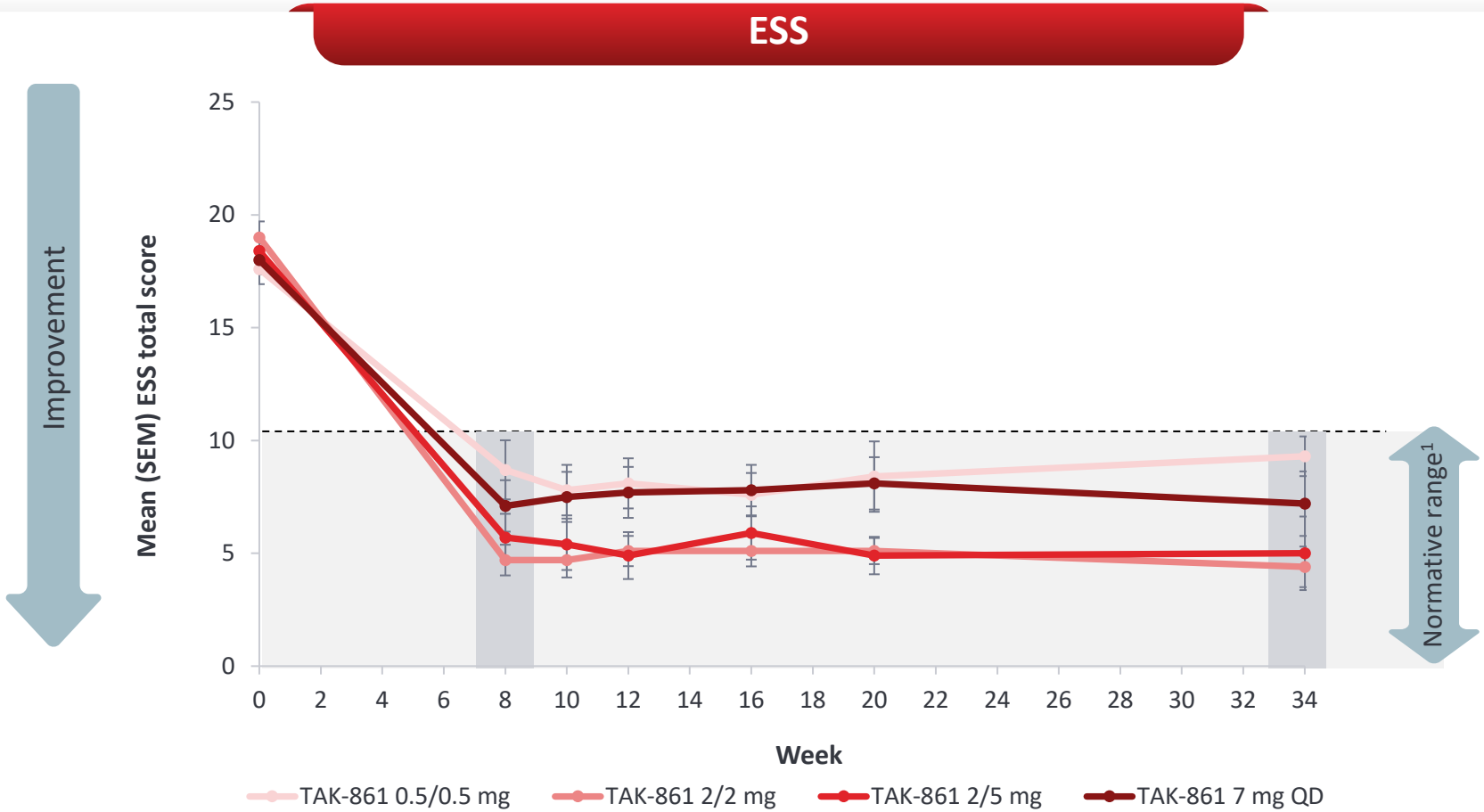
- Oveporexton **normalized** sleep latency on MWT
- **Sustained improvements in wakefulness in NT1 patients** over an additional 6 months of treatment

***p≤0.001, all doses statistically significant compared to placebo at week 8 time point.

1. Doghramji K, et al. ,*Electroencephalogr Clin Neurophysiol* 1997; 103: 554-62.

Oveporexton (TAK-861) demonstrated normalization of wakefulness (ESS) at 8 weeks and maintained over an additional 6 months

The Epworth Sleepiness Scale (ESS): short self-assessment to identify how likely to fall asleep during daytime, measured by eight questions. Total score range 0-24 (each question 0-3). Scores <10 reflect normal levels of daytime sleepiness, and scores over 10 reflect excessive daytime sleepiness



Excessive Daytime Sleepiness (EDS)

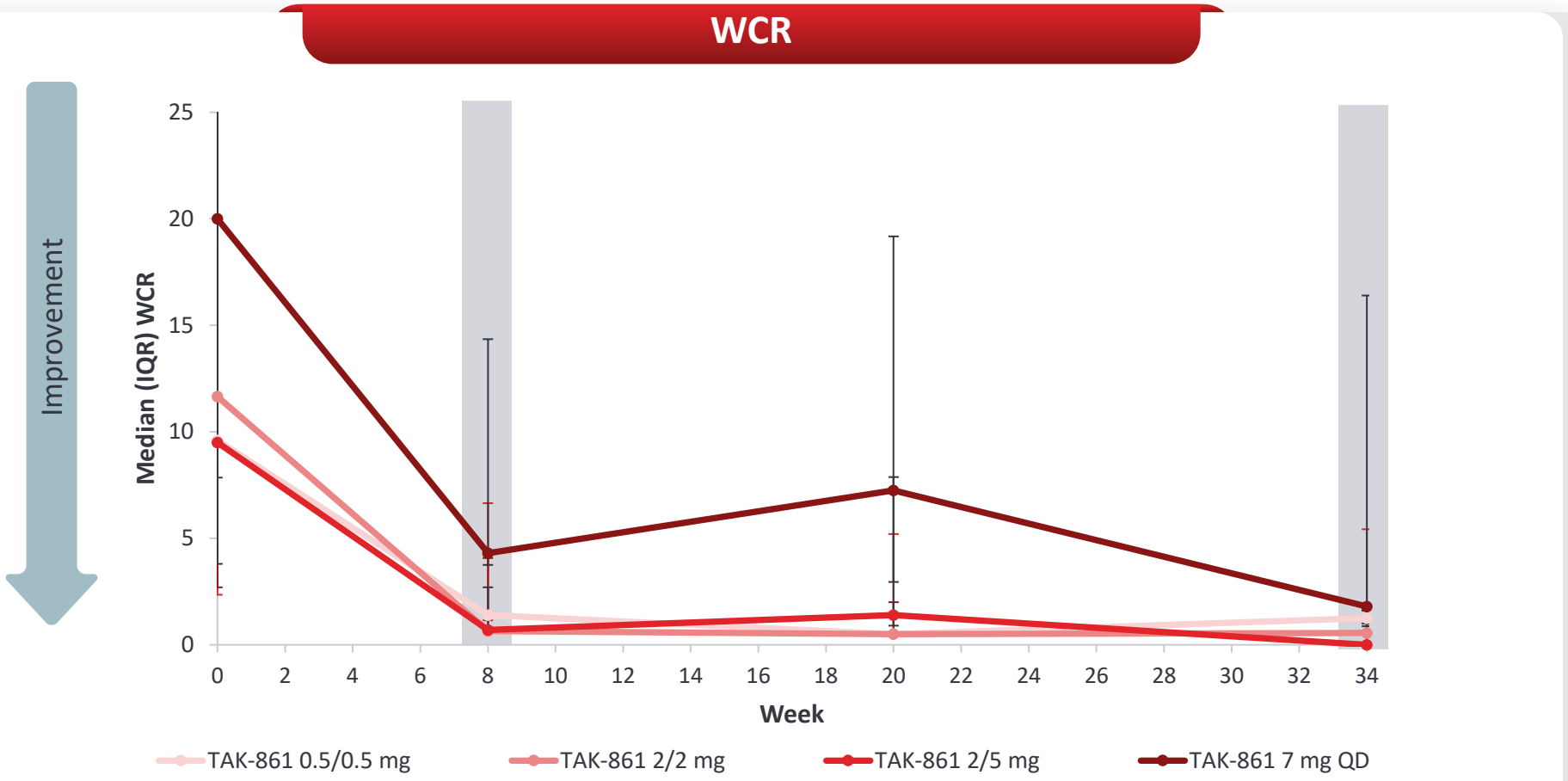
- Most participants (>90%) **achieved** ESS scores comparable to healthy individuals (≤10) with oveporexton
- Oveporexton demonstrated **statistically significant** and **clinically meaningful** improvement in subjective wakefulness (ESS)
- All improvements **sustained** over an additional 6 months of treatment

All doses statistically significant (p≤0.001) compared to placebo at week 8 time point.

1. Johns MW, *Sleep* 1991; 14: 540-5.

Oveporexton (TAK-861) demonstrated sustained reduction in cataplexy events over an additional 6 months

Weekly Cataplexy Rate (WCR): average number of cataplexy events per week



Cataplexy

- Oveporexton showed **statistically significant and clinically meaningful reduction** in cataplexy events compared to placebo
- **Reduction in WCR is sustained** over an additional 6 months of treatment

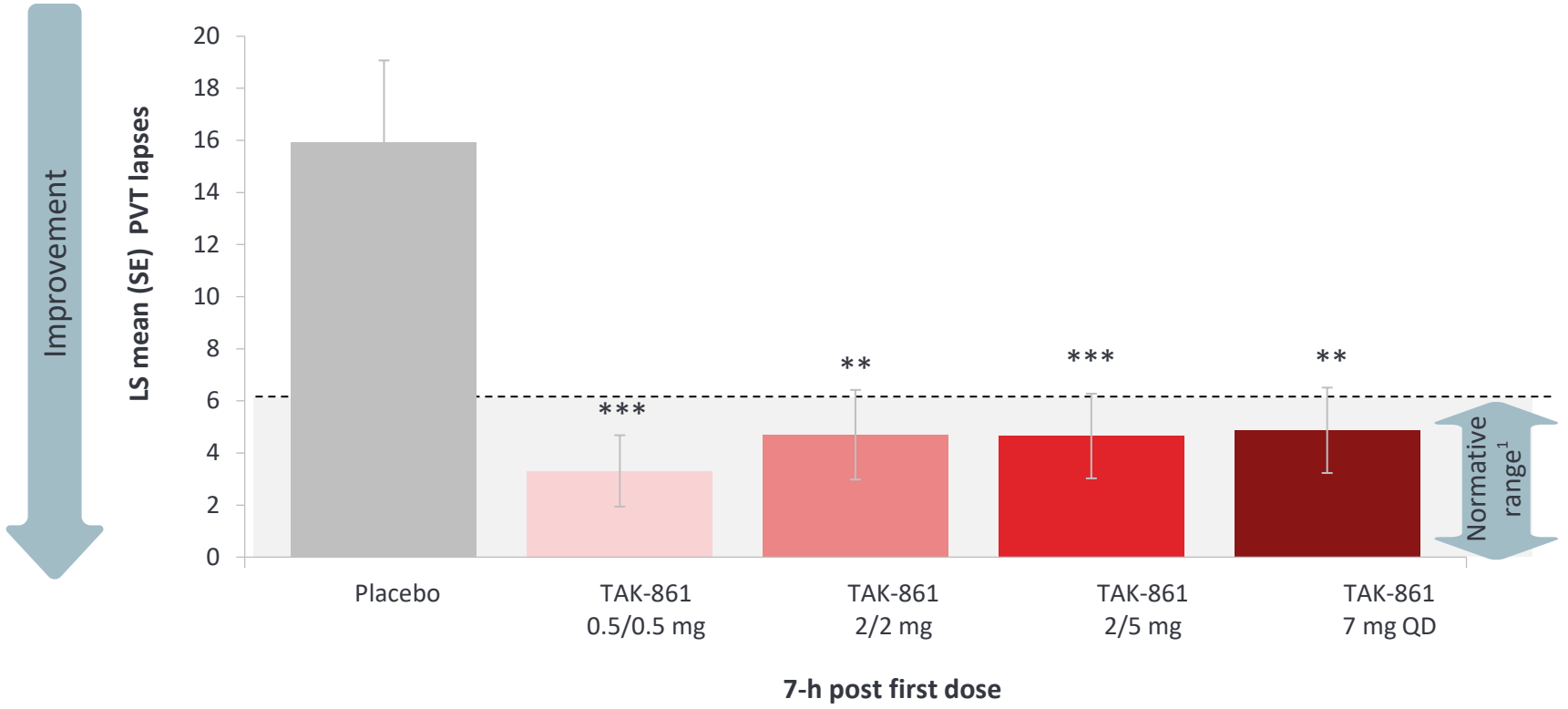
p ≤ 0.01 and p≤0.001, for 2/2 mg and 2/5 mg respectively compared to placebo at week 8 time point.

IQR: Interquartile Range

Oveporexton (TAK-861) improved cognitive symptoms in NT1 patients, offering a unique advantage over standard of care

Psychomotor Vigilance Test (PVT): simple 10 min reaction performance task to measure sustained attention (test counts # of lapses in attention)

Number of PVT lapses at week 8



Linear mixed effects model with square root transformation, presented on the original scale. *p<0.05; **p<0.01; ***p≤0.001.

Cognitive Symptoms

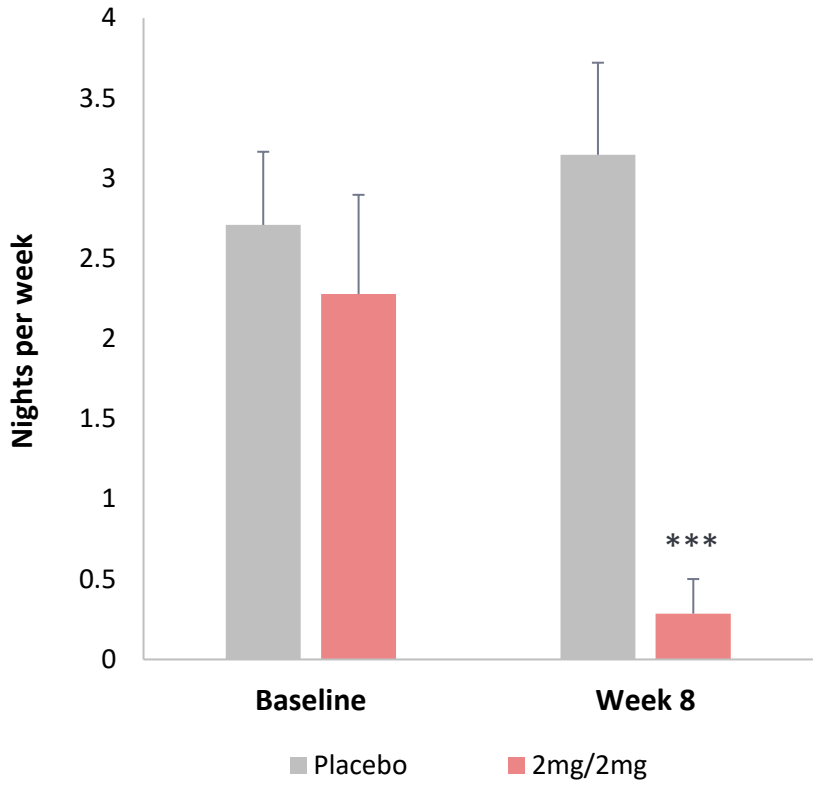
- Oveporexton resulted in statistically significant and clinically meaningful improvements in sustained attention (PVT) in participants with NT1
- Cognitive improvements are correlated with patient related outcomes such as subjective functioning and impression of change (FINI, CGI-C and other)

1. Cogstate, internal data; Data on File FINI: Functional Impacts of Narcolepsy Instrument, CGI-C: Clinical Global Impression of Change.

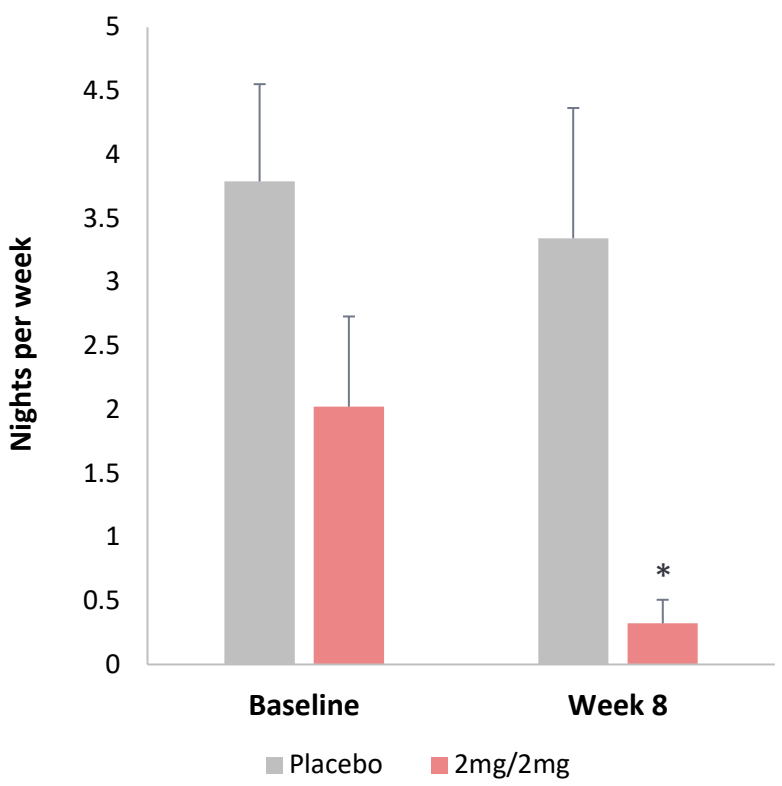
NT1 patients reported substantial improvements in nighttime symptoms with oveporexton (TAK-861)

Sleep diary: daily recording of last night's sleep quality and disturbances (difficulty falling or staying asleep, nightmares as well as sleep paralysis and hallucinations)

Nights Per Week With Disturbing Dreams



Nights Per Week With Hallucinations



Nighttime Symptoms

- Patients treated with oveporexton showed **substantial reductions** in the **frequency of disturbing dreams, nighttime hallucinations** and **sleep paralysis**
- Subjective measures are supported by objective assessments such as nocturnal polysomnography

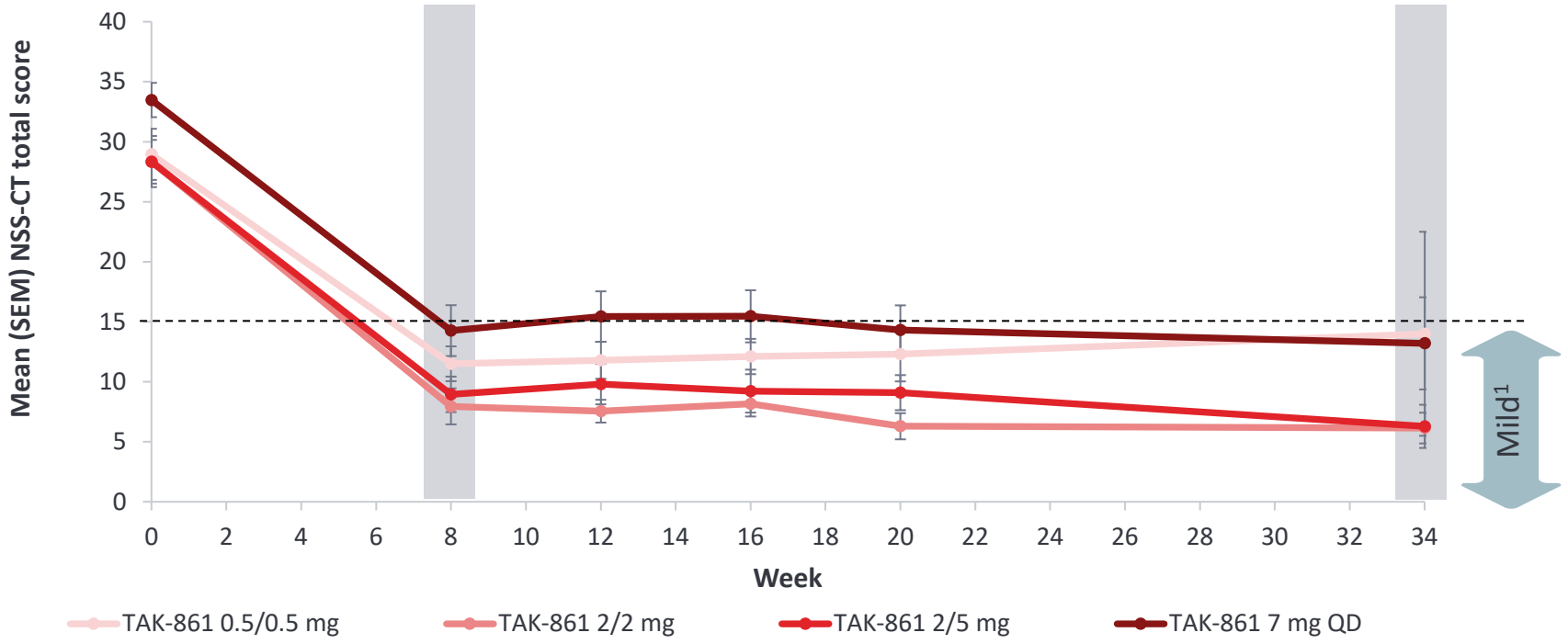
Figure shows the subset of patients who experienced the symptom at baseline. *p<0.05; ***p<0.001

Patient reported symptoms demonstrated sustained improvements in Narcolepsy Severity Score (NSS-CT) in participants with NT1

NSS: validated, self-administered, 15-item scale evaluating severity, frequency and impact of 5 narcolepsy symptoms (sleepiness, cataplexy, sleep paralysis, hallucinations and disrupted nocturnal sleep)[1,2].

NSS-CT total score

Excessive Daytime Sleepiness (EDS) | Cognitive Symptoms



All doses statistically significant (p≤0.001) compared to placebo at week 8 time point.

- Oveporexton showed clinically meaningful and statistically significant changes in NSS-CT compared with placebo
- Most treated NT1 participants reported 'mild' on the symptoms score – lowest symptom score on NSS-CT

NSS-CT, Narcolepsy Severity Scale for Clinical Trials; QD, once daily; 1. Dauvilliers Y, et al. *Sleep* 2020;43(6):1-11. 2. | Dauvilliers Y, et al. *Neurology* 2017;88(14):1358-1365.

Oveporexton (TAK-861) was well tolerated by participants with NT1 over an additional 6 months of treatment

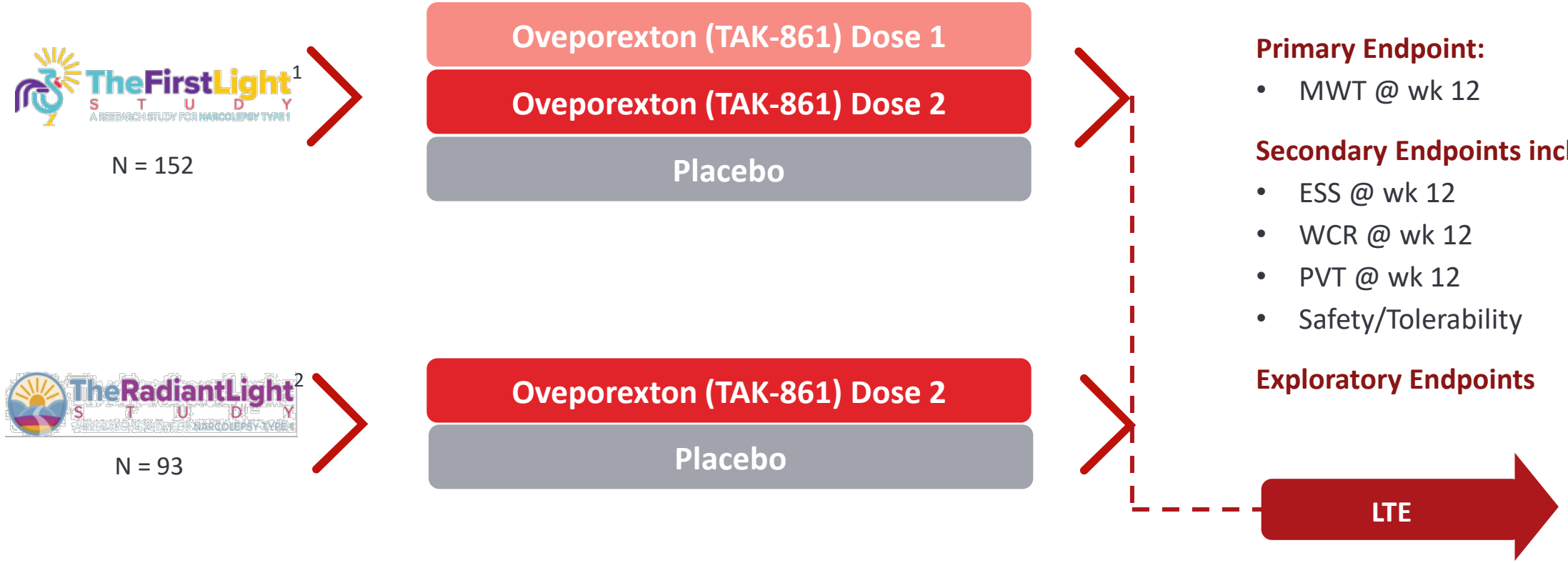
Oveporexton was **well tolerated by NT1 participants** with **no serious treatment-related TEAEs or discontinuations** due to TEAEs in the Ph2b trial and LTE.

The most common TEAEs observed were insomnia, urinary urgency and salivary hypersecretion. **Most AEs mild to moderate**, occurring within 1-2 weeks of treatment and transient.

No cases of hepatotoxicity or visual disturbances reported in Ph2b or in the ongoing LTE.

~90% of patients continuing in LTE - will provide long term data for benefit-risk.

Oveporexton (TAK-861) Ph3 NT1 studies on track to readout in CY2025



Primary Endpoint:

- MWT @ wk 12

Secondary Endpoints including:

- ESS @ wk 12
- WCR @ wk 12
- PVT @ wk 12
- Safety/Tolerability

Exploratory Endpoints

Ph2 completed Q4 FY2023

Ph3 start Q2 FY2024

Ph3 readout CY2025

Potentially transformative profile at launch

1. Clinicaltrial.gov-TAK-861-3001
2. Clinicaltrial.gov-TAK-861-3002

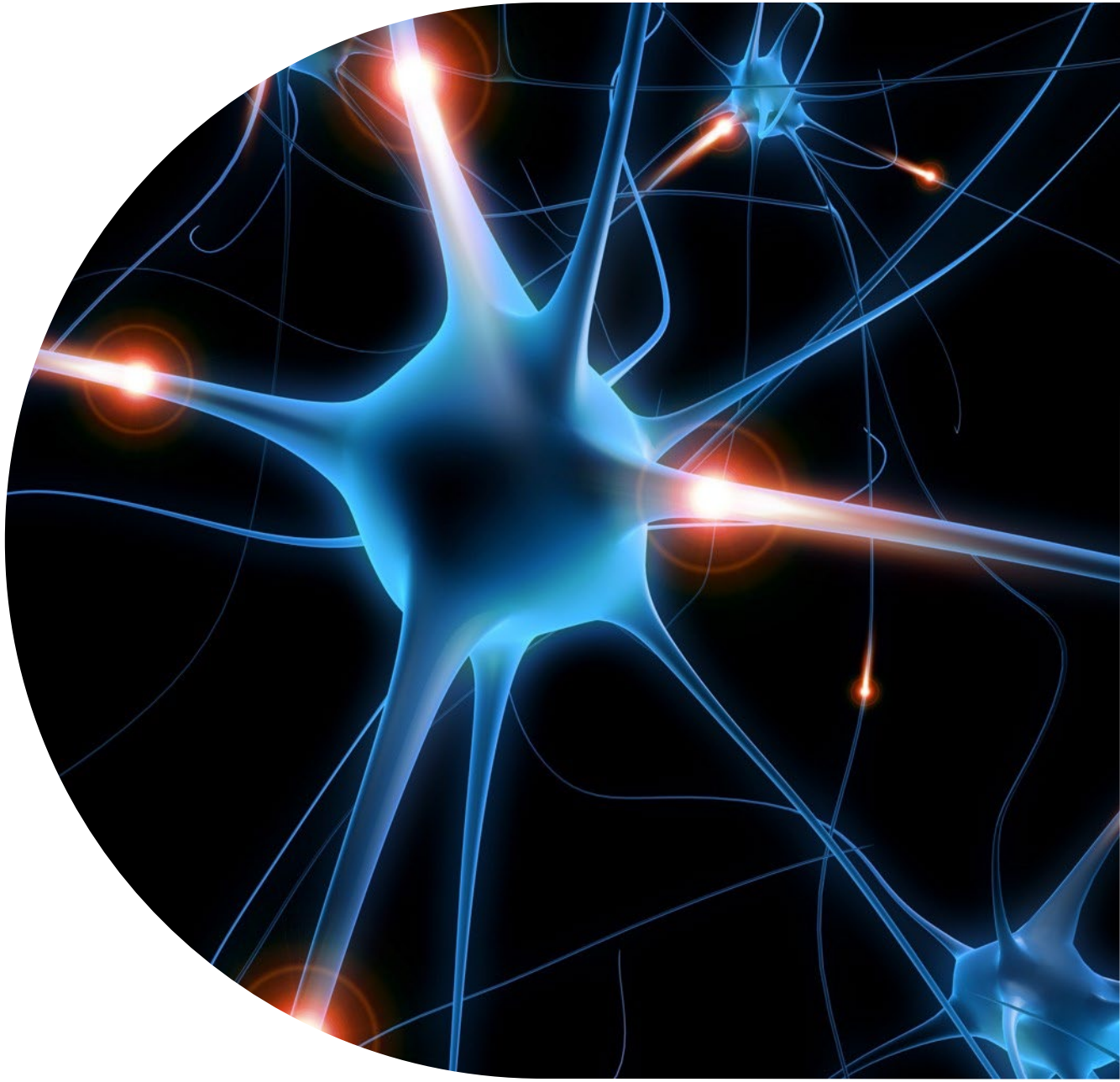
Oveporexton (TAK-861) with potential best-in-class, transformative profile addressing NT1 symptoms holistically

- **Positioned to be first orexin agonist with potentially transformative profile**:
- Statistically significant and clinically meaningful improvements in daytime and nighttime NT1 symptoms after 8 weeks of administration **returning patients to normative range**
  - **Sustained improvements** over an additional 6 months of treatment period
  - **Optimized BID profile** providing flexibility and optimal balance in efficacy and safety
- **Functional improvements** and quality of life **support the potential for a new standard of care for patients living with NT1**

- Oveporexton was **well tolerated by NT1 participants** with **no serious treatment-related TEAEs or discontinuations** due to TEAEs in the Ph2b trial and LTE
- **No cases of hepatotoxicity or visual disturbances** reported in Ph2b or in the ongoing LTE

TAK-360 and beyond

Additional assets/indications



Better Health, Brighter Future

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 cause of NT1; unknown pathophysiology for NT2/IH

Common challenge: misdiagnosis and undertreatment

Different disorders with overlapping clinical features especially EDS

	NT1	NT2	IH
Excessive Daytime Sleepiness	✓	✓	✓
Cognitive Symptoms	✓	✓	✓
Cataplexy	✓	✗	✗
Hallucinations	✓	✓	Sometimes
Sleep Paralysis	✓	✓	Sometimes
Disrupted Nighttime Sleep	✓	Occasionally	✗
Sleep Inertia	Occasionally	Sometimes	✓

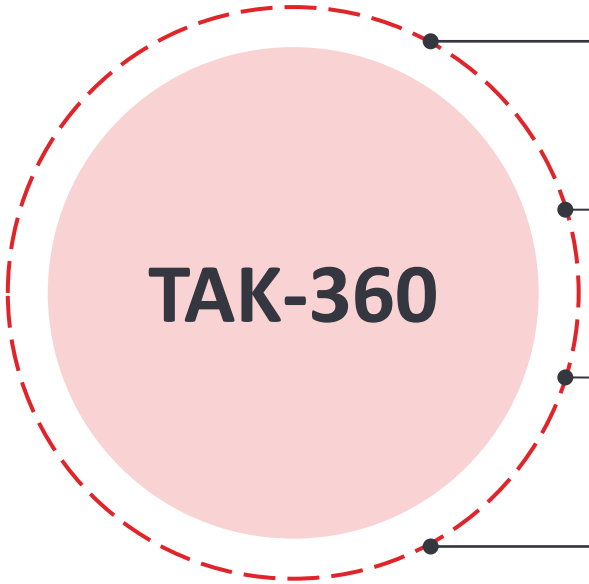
✓	Sometimes	Occasionally
>50%	20–50%	<20%

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

TAK-360: next-generation orexin agonist for NT2 and IH and potentially other indications in patients with normal orexin levels

Higher doses (>3X) of an OX2R agonist necessary for orexin normal populations

Best in class development guided by models using extensive OX2R agonism data across multiple assets



01 Distinct structure -- target profile supported by pre-clinical data

02 Potent - greater flexibility in dosing orexin normal population

03 Target engagement supported by exploratory digital biomarkers

04 PK profile suitable for NT2/IH, demonstrating good oral bioavailability

Ph1 started FY2024

Ph2 NT2/IH target start FY2024

Proof of concept FY2025

Takeda pioneering the field of orexin therapeutics – franchise leading with oveporexton, a potential first-in-class treatment for NT1

Oveporexton (TAK-861): *First & Fast[3] in NT1*

- **The most advanced orexin agonist – Addressing orexin deficiency as the underlying pathophysiology in NT1**[1]
- **Target Ph3 readout in CY2025**
- Ph2 and Long-term Extension (LTE) data support potential **transformative profile**
- Significantly accelerated Phase 3 program
- **Breakthrough therapy designation** received in U.S., China

TAK-360 and beyond: *Additional assets/indications*

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  - New chemistry and profile
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  - Target Ph2 start FY2024 in NT2/IH
- **Exploration of indications** pertinent to orexin biology: sleep-wake, respiration and metabolism
- **Tailored assets/profiles (e.g., TAK-925**[2] **and others)** to deliver optimal exposure for additional indications

1. Dauvilliers, Y., N Engl J Med, 2023; 389, 309-321;
2. Suzuki M et al., British Journal of Anaesthesia, 2024; IARS Conference, Denver, 2023; HV: Healthy Volunteer
3. Referring to the accelerated development timeline

Orexin Franchise
Market Opportunity

Unlocking the full value of orexin and potentially transforming patient care in sleep and beyond

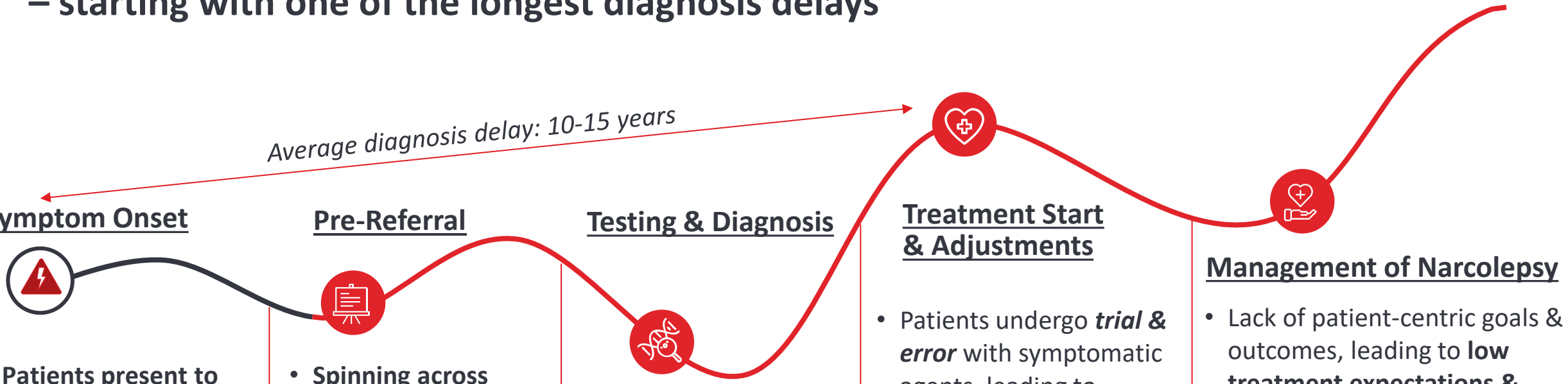
Narcolepsy is a life-altering condition with a significant burden – expanding far beyond symptoms

EDS or cataplexy are just the tip of the iceberg

True burden of narcolepsy is often unrecognized and underappreciated - leaving patients vulnerable to isolation and stigma

Impact of narcolepsy extends to many aspects of patient life, making daily activities: working, caring for a family or exercising often impossible

Patients with narcolepsy face significant challenges at each step of their journey – starting with one of the longest diagnosis delays



Symptom Onset

- **Patients present to primary care physicians** who often fail to recognize a sleep disorder
- **Dismissal** due to unspecific symptoms (excessive daytime sleepiness), **lexicon disconnect** and **low awareness**

Pre-Referral

- **Spinning across specialties** with misdiagnosis of depression, ADHD, anxiety with increasing stigma & isolation
- **Symptom overlap** with comorbidities and treatment of mood disorders masks narcolepsy

Testing & Diagnosis

- **Significant wait times** for sleep testing due to existing **infrastructure & technology constraints**
- **40% of patients** who reach a sleep specialist and undergo correct testing are **still misdiagnosed**

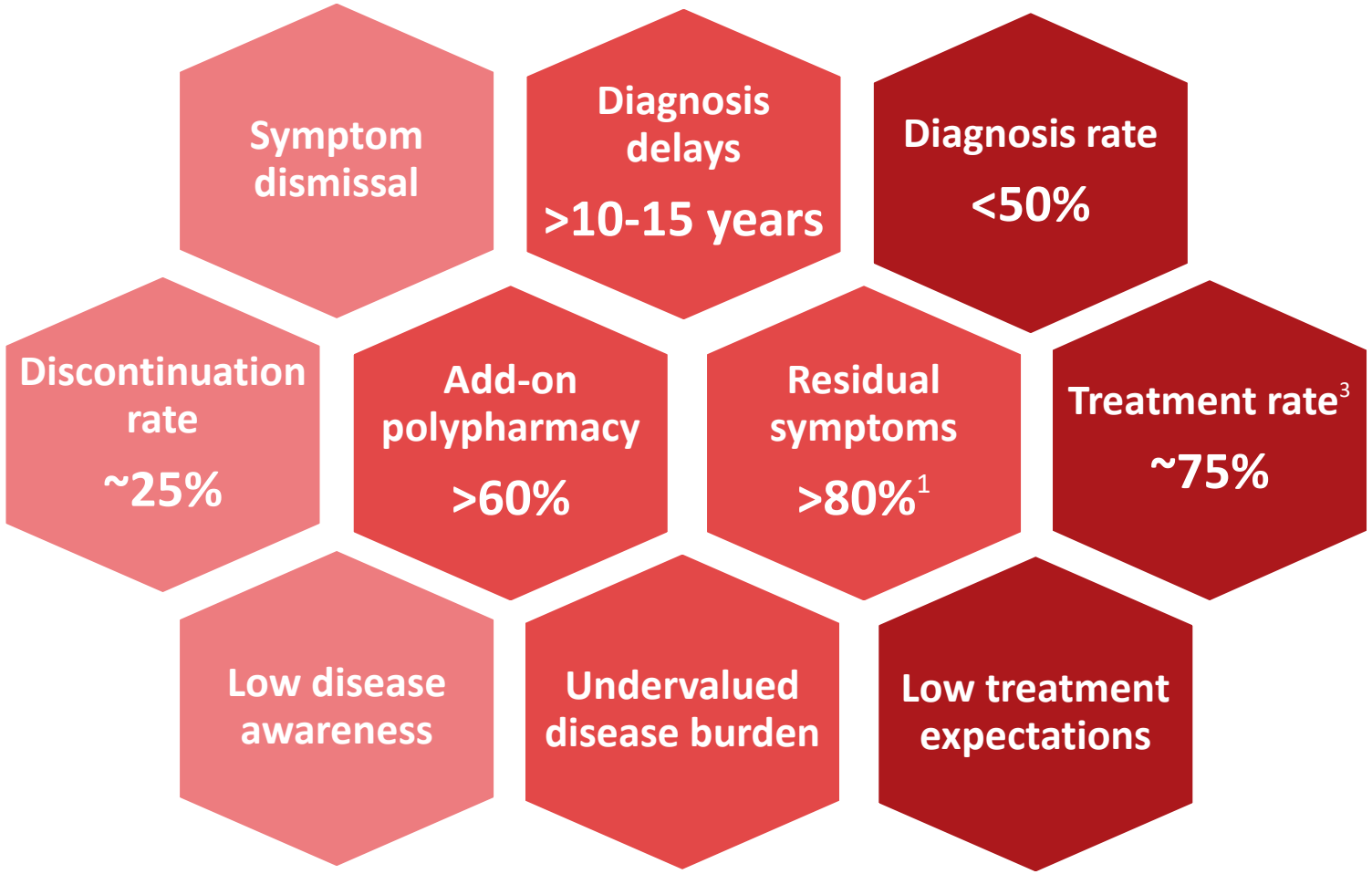
Treatment Start & Adjustments

- Patients undergo ***trial & error*** with symptomatic agents, leading to **polypharmacy & increasing burden**
- **Suboptimal treatment experience** leads to discontinuation & treatment burn-outs

Management of Narcolepsy

- Lack of patient-centric goals & outcomes, leading to **low treatment expectations & lifestyle limitations**
- Limited capacity for treatment follow-ups and monitoring, **with increasing patient burden & quality of life impact over time**

Significant unmet needs remain today - with no treatment options addressing the underlying cause and holistic burden of NT1



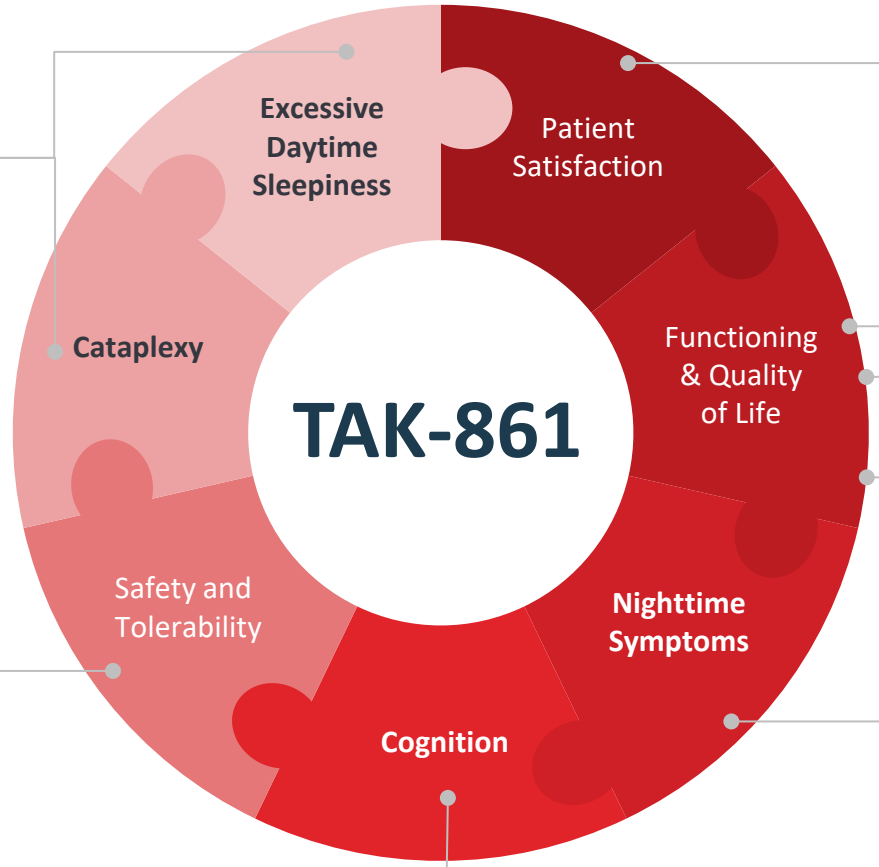
Published population-based prevalence estimates that NT1 affects ~95,000 - 120,000 people in U.S.[2]

1. *Burden of Illness Study Among Patients with Central Disorders of Hypersomnolence in Six European Countries, Y. Dauvilliers et al, EAN, 2024*
2. Silber MH, et al. *Sleep*. 2002;25(2):197-202
3. Treatment rate of diagnosed patients

Oveporexton (TAK-861) has the potential to address the overall disease burden important to patients with NT1

Potential first-in-class orexin agonist addressing broader disease burden and functional impacts

- **Sustained normalization of core symptoms** and significant reduction of cataplexy - enabling **potential disease control**



- **High treatment satisfaction**
- **Functional improvements** in activities of daily living, most meaningful to patients
- **Reduction of symptoms severity**
- Improvements in health-related **Quality of Life**
- Substantial improvement in **nighttime symptoms**
- **Generally safe and well tolerated** over long periods of time
- **Improvement on multiple cognitive symptoms** - attention, memory and executive functioning

Potentially transformative profile as the first treatment addressing orexin deficiency, the cause of NT1, and eliminating the need for polypharmacy

Takeda is advancing multiple industry-leading solutions to support a holistic transformation of narcolepsy patient care

Takeda Orexin Franchise Focus

Uncovering the True Burden of Narcolepsy

Evidence generation & real-world data

- Largest real-world studies on disease burden
- Pioneering data on broader impacts
- Elevating treatment expectations

"Being half-awake is not fully living"

Advancing & Accelerating Diagnosis

Industry-leading digital initiatives

- Novel biomarkers
- Wearable & home test solutions
- AI algorithms of high accuracy

"Living for years without answers with no diagnosis or misdiagnosis"

Redefine Treatment Outcomes

Capturing patient-centric outcomes of daily living

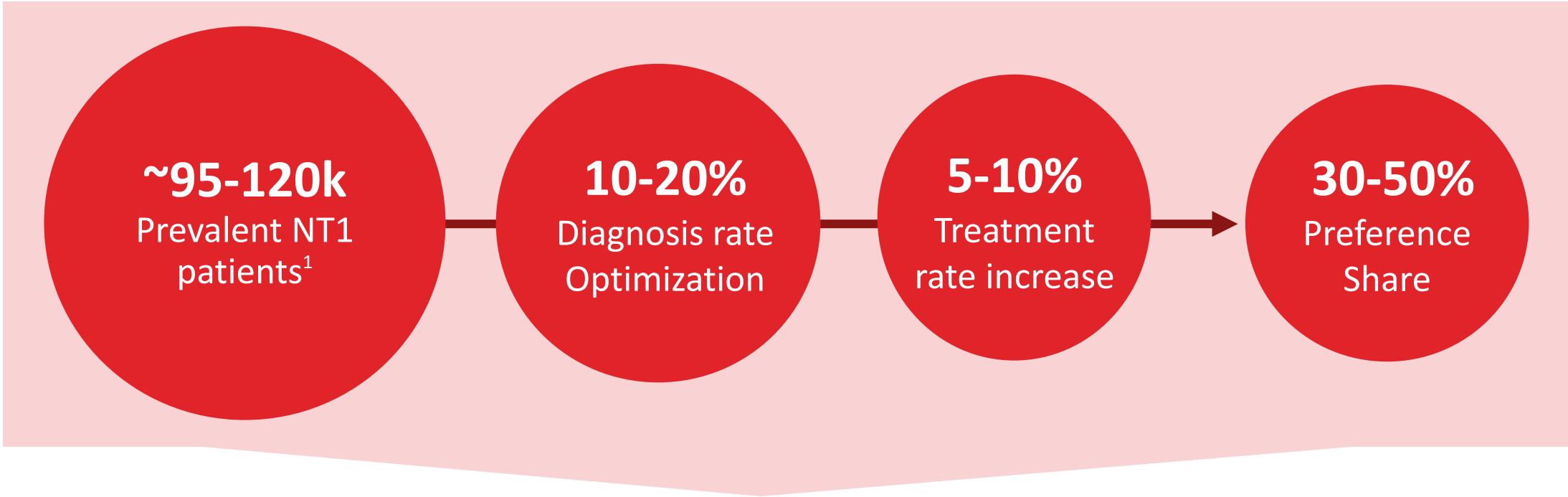
- Bridging symptoms with patient impacts
- First disease-specific PRO[1] measure
- Real-world monitoring of outcomes

"I want to have better medications, so that I am not just surviving"

Voice of the Patient

1. PRO: patient reported outcomes

Oveporexton – On track to be the first orexin agonist with potential to transform NT1 treatment paradigm, starting in the U.S.



Uncover the true burden of narcolepsy

Improve rate, speed and accuracy, of NT1 diagnosis utilizing digital tools

Redefine treatment outcomes with new MOA

Deliver transformative efficacy by addressing orexin deficiency

Oveporexton's (TAK-861) peak revenue potential : $2-3B

Source: 1. Silber MH, et al. Sleep. 2002;25(2):197-202. Scheer D, et al. Sleep. 2019 Jul 8;42(7):zsz091. Abioye, et al Sleep Medicine Volume 100, Supplement 1, December 2022, Page S154.
Takeda claims analysis; Takeda physician research; company filings.
Please refer to the Important Notice at the start of this presentation for more information about peak revenue estimates.

Tailored portfolio of potentially transformative treatments to unlock full value of orexin

Oveporexton:

$2-3B

NT1 PEAK REVENUE POTENTIAL

TAK-360: Accelerated Development

Tailored to address unique unmet needs in NT2 & IH

Additional Opportunities:

Sleep-Wake

Respiratory conditions

Metabolic disorders

Strong foundation of Takeda capabilities in maximizing global launches and advancing patient care ecosystems – powered by our established leadership in orexin science & development

Please refer to the Important Notice at the start of this presentation for more information about peak revenue estimates.

Takeda is unlocking the full value of orexin with a multi-asset, multi-indication franchise – Leading with oveporexton (TAK-861), peak revenue potential $2-3B

Oveporexton is on track to become the **1st and potentially best-in-class, transformative treatment** indicated for NT1

Unprecedented Ph2 and LTE data demonstrated oveporexton **normalized symptoms** across all aspects of the disease

Continue **expanding the franchise** by exploring indications relevant to orexin biology **leading with TAK-360 in NT2/IH**

Takeda is **uniquely positioned** to **holistically transform the treatment landscape** of NT1 and **advance diagnosis through digital innovation and data generation**

Global peak revenue potential: $2-3B

Please refer to the Important Notice at the start of this presentation for more information about peak revenue estimates.

Today's Agenda

TIME (JST)	AGENDA
8:30-8:40	**A Global, Innovation-driven Biopharmaceutical Company** *Christophe Weber, President & CEO*
8:40-9:00	**R&D Strategy and Pipeline Highlights** *Andy Plump, President Research & Development*
9:00-9:50	**Neuroscience: Deep-dive on Orexin Franchise** *Sarah Sheikh, Head of Neuroscience Therapeutic Area Unit and Head of Global Development* *Ramona Sequeira, President of Global Portfolio Division*
9:50-10:00	*Break*
10:00-11:30	**Gastrointestinal and Inflammation (GI&I): Deep-dive on Zasocitinib, Rusfertide, Mezagitamab, Fazirsiran** *Chinwe Ukomadu, Head of GI&I Therapeutic Area Unit* *Ramona Sequeira, President of Global Portfolio Division*
11:30-12:00	Lunch
12:00-12:20	**Oncology: Deep-dive on Elritercept – newly announced BD deal** *P.K. Morrow, Head of Oncology Therapeutic Area Unit* *Teresa Bitetti, President of Global Oncology Business Unit*
12:20-13:15	**Q&A Session**
13:15-14:00	*Reception*

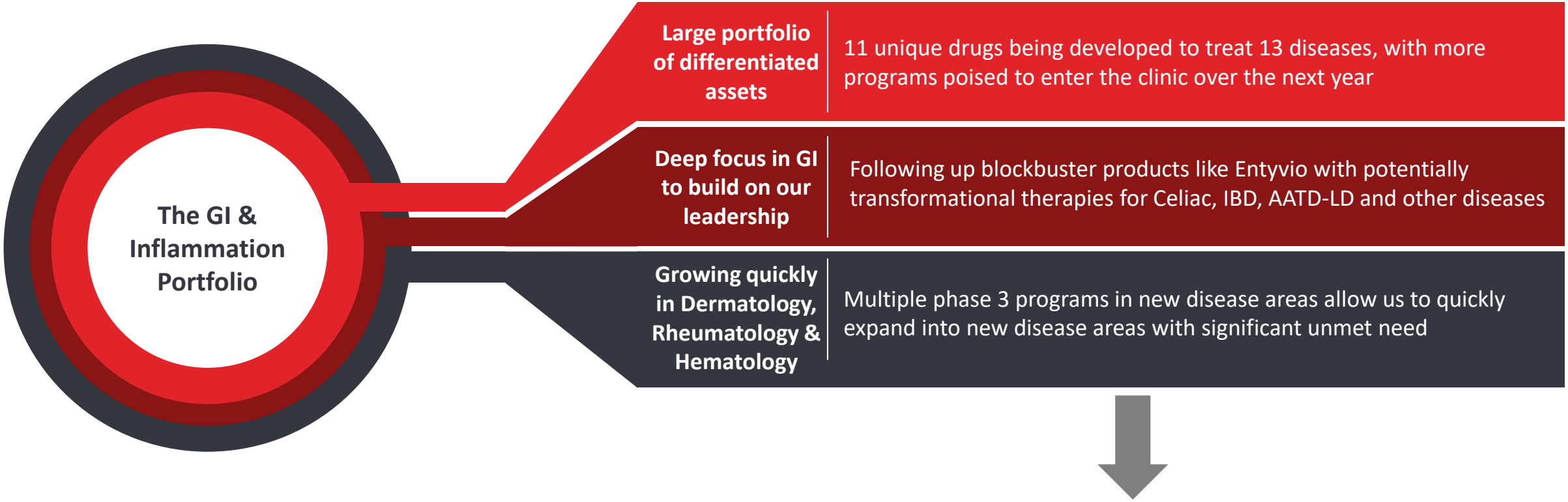
Gastrointestinal & Inflammation (GI&I): Deep-dive on Zasocitinib, Rusfertide, Mezagitamab, and Fazirsiran

Chinwe Ukomadu
Head of GI&I Therapeutic, Area Unit

Ramona Sequeira
President, Global Portfolio Division

Better Health, Brighter Future

The GI & Inflammation portfolio is designed to deliver high-value therapies in the next 5 years and over the long-term to ensure strong & sustainable growth



Our strategy rapidly expands Takeda into new inflammatory disease areas with high unmet need *in the near-term* while strengthening our leadership in GI *over the long-term*

Late-stage programs have significant value potential; oveporexton, zasocitinib, rusfertide phase 3 data expected in 2025

Three Phase 3 Data Readouts Over the Next 12 Months

- Oveporexton in Narcolepsy Type 1
- Zasocitinib in Psoriasis
- Rusfertide in Polycythemia Vera[1]

>70% PTRS[2] to approval

Late-Stage Peak Revenue Potential

$10 - 20B

Target Filing Dates by Indication

FY25 / FY26

Oveporexton
Narcolepsy Type 1

Zasocitinib
Psoriasis

Rusfertide
Polycythemia Vera

FY27 - FY29

Zasocitinib
Psoriatic Arthritis

Mezagitamab
IgA Nephropathy
Immune Thrombocytopenia

Fazirsiran
AATD Liver Disease

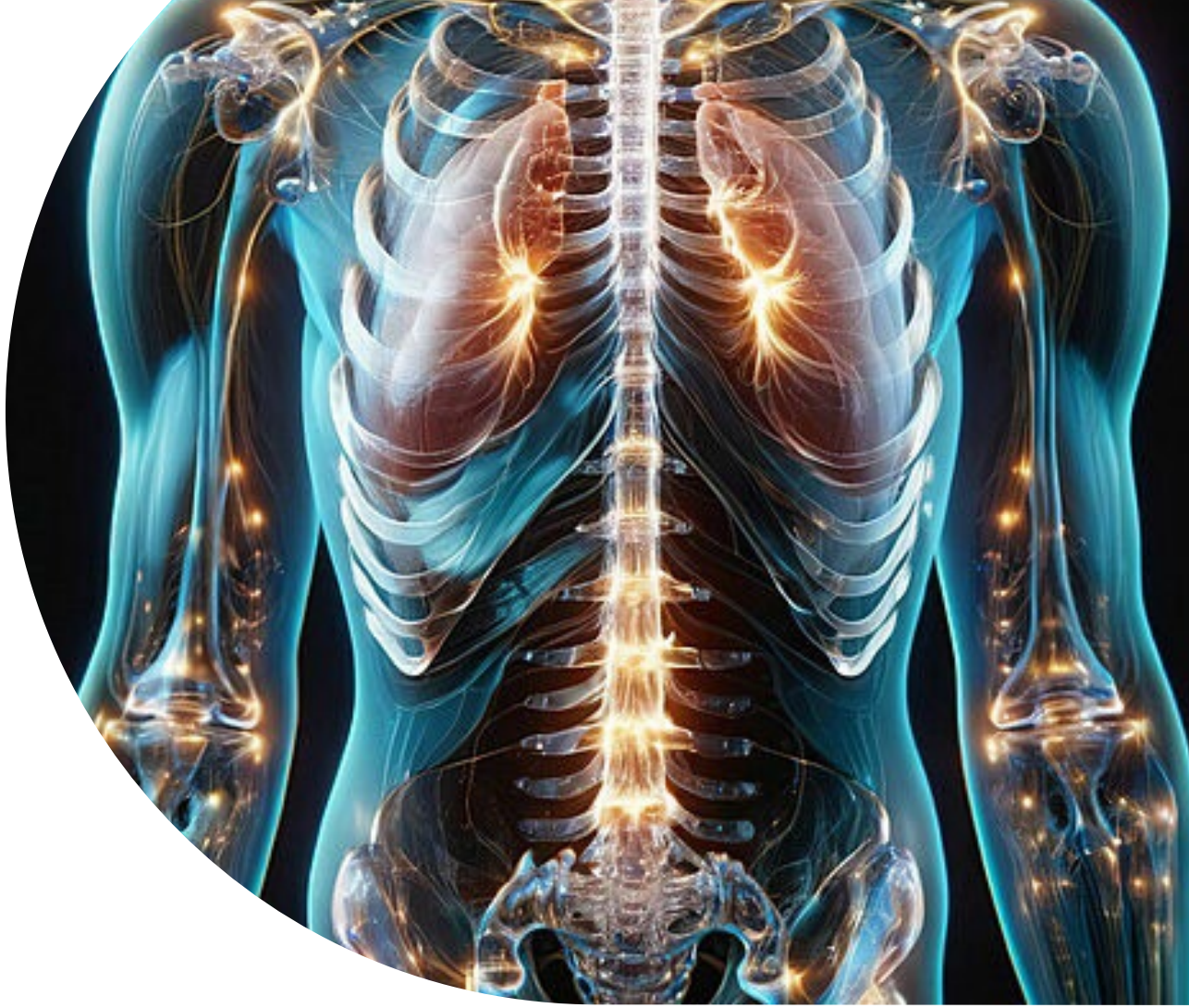
Elritercept
Myelodysplastic Syndromes

1. Our partner Protagonist Therapeutics is responsible for Phase 3 development of Rusfertide and has stated Phase 3 data may be available as soon as March 2025 which is our Q4 FY24
2. Please refer to the Important Notice at the start of this presentation for more information about PTRS and peak revenue estimates

Please refer to the Important Notice at the start of this presentation for more information about the Elritercept license agreement

Zasocitinib (TAK-279)

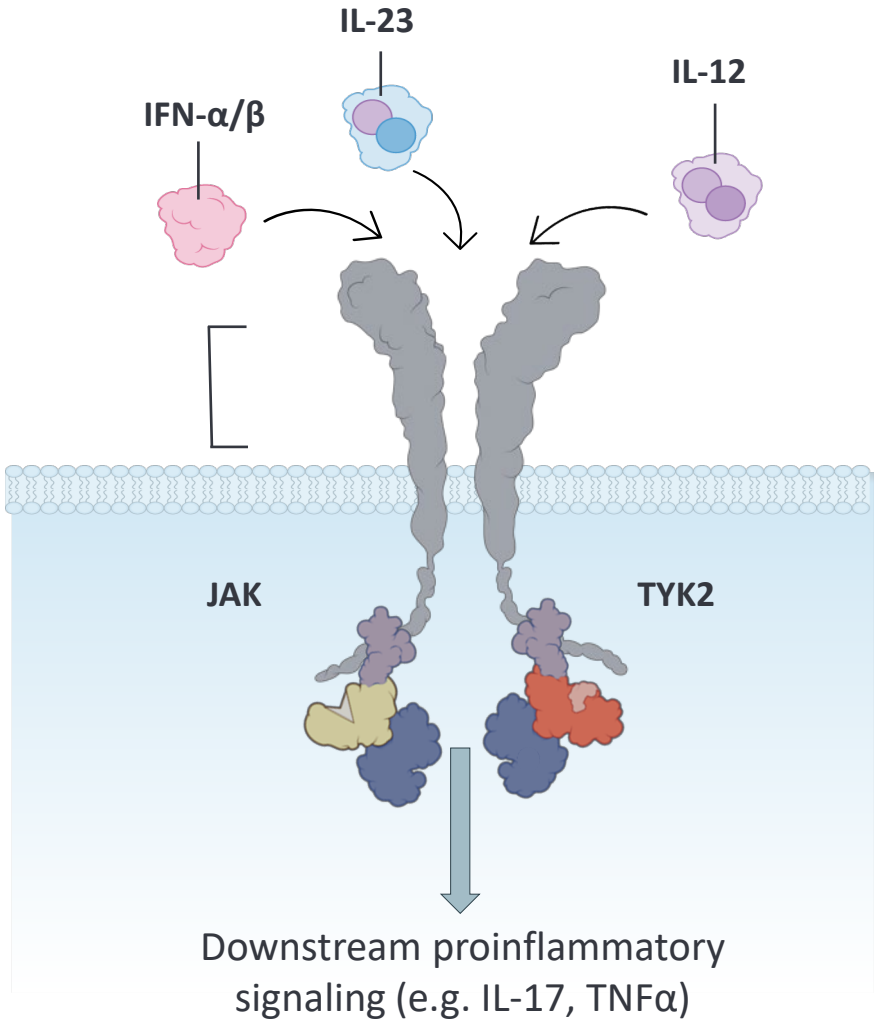
Next-generation TYK2 Inhibitor, potential to be the 1st choice advanced therapy



Better Health, Brighter Future

TYK2 is the fundamental regulator of immune signaling pathways including IL-23 and IFN α/β which play a critical role in inflammatory diseases

- IL-23 & INF α/β signaling plays a role in several inflammatory diseases such as,
  - PsO, PsA, UC, Crohn's and others
- TYK2 regulates the signaling of these pathways
- **The burden of disease is lessened by reducing the signaling of these pathways in patients with inflammatory diseases**



Adapted from Shang et al, 2022 and Muramoto et al, 2022.

IFN, interferon; IL, interleukin; JAK, Janus kinase; TNF, tumor necrosis factor; TYK2, tyrosine kinase 2. 1. Shang L, et al. J Inflamm Res. 2022;15:5373-5385. . 2. Manetti R, et al. J Exp Med. 1993;177:1199-1204. 3. Muramoto R, et al. World J Biol Chem. 2022;13:1-14. 4. Trinchieri G, Scott P. Immunol Today. 1994;15:460-463. 5. Chasset F, Arnaud L. Autoimm Rev. 2018;17:44-52. 6. Gonciarz M, et al. Immunotherapy. 2021;13:1135-11504

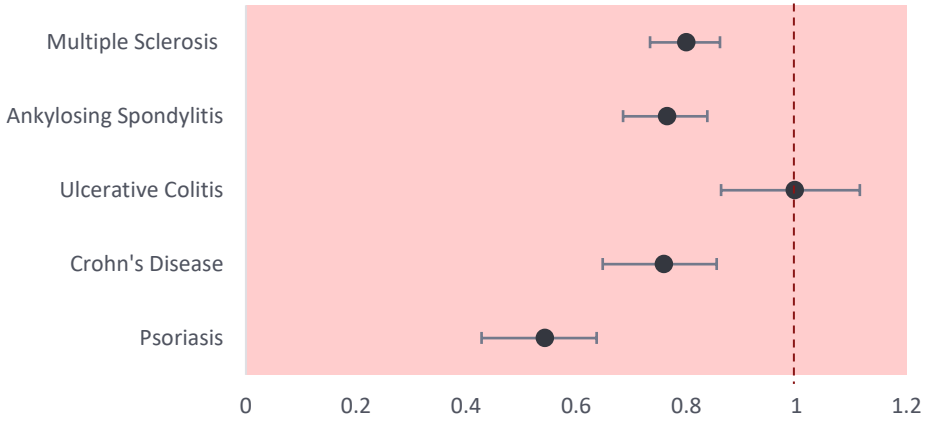
Studies suggest that genetic alteration in TYK2 function protects against inflammatory diseases, without significant adverse outcomes

A common genetic alteration in the *TYK2* gene has been identified and results in an **~80% reduction of TYK2 signaling**[1,2]

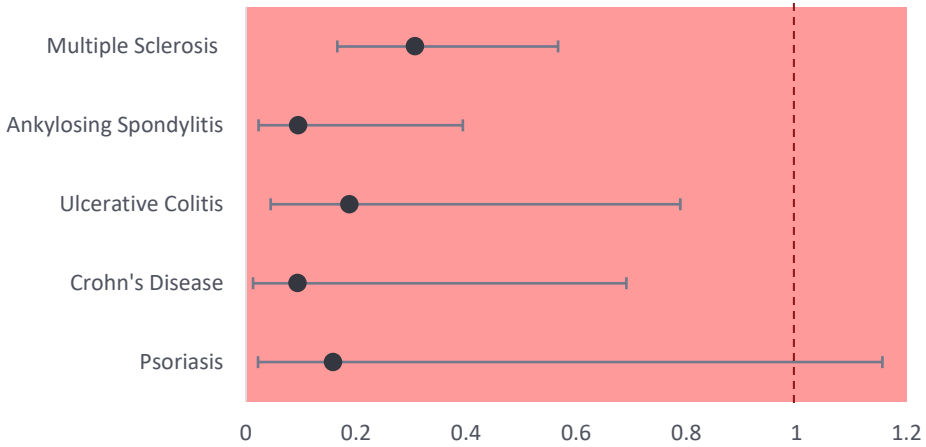
This alteration is **highly protective against inflammatory diseases**[2]

This alteration is **generally well tolerated and safe;** not effecting major health measures (mortality, malignancy, hospitalization due to serious infection)[1]

People with One Altered Copy of *TYK2*



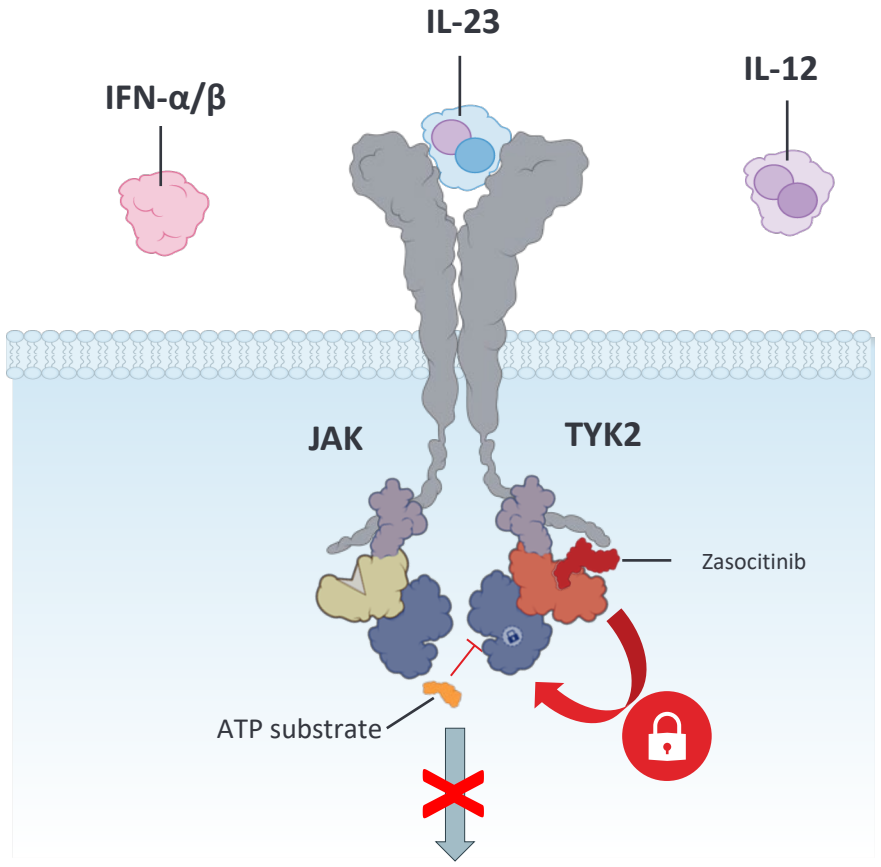
People with Two Altered Copies of *TYK2*



1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6341984/pdf/nihms-1005904.pdf;
2. Sci Transl Med. 2016 November 02; 8(363): 363ra149. doi:10.1126/scitranslmed.aag1974.

Zasocitinib's high selectivity supports the evaluation of a range of doses without concern of JAK1/2/3 inhibition

Zasocitinib binds to the **regulatory domain of TYK2** allowing it to demonstrate **exquisite selectivity**, unlike traditional kinase inhibitors



ATP, adenosine triphosphate; JAK, Janus kinase; TYK2, tyrosine kinase 2.

Highly Selective

Supports the evaluation of a range of doses, important for diseases like IBD which may require higher dosing

Selectivity for TYK2 compared to JAK1

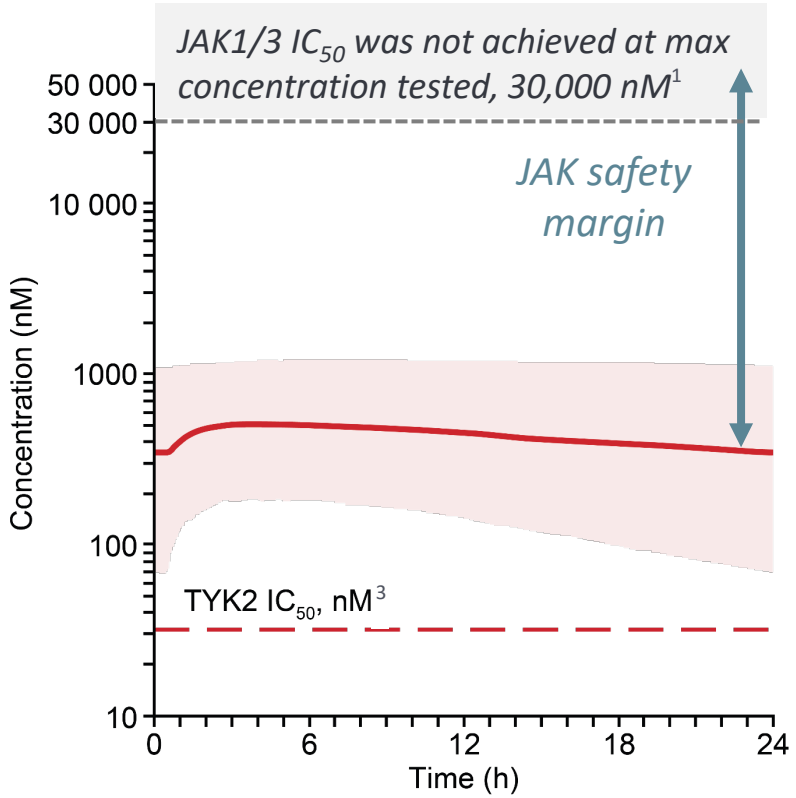
Zasocitinib	Deucravacitinib
> 1.7M	87

~20,000x more selective than Deucravacitinib

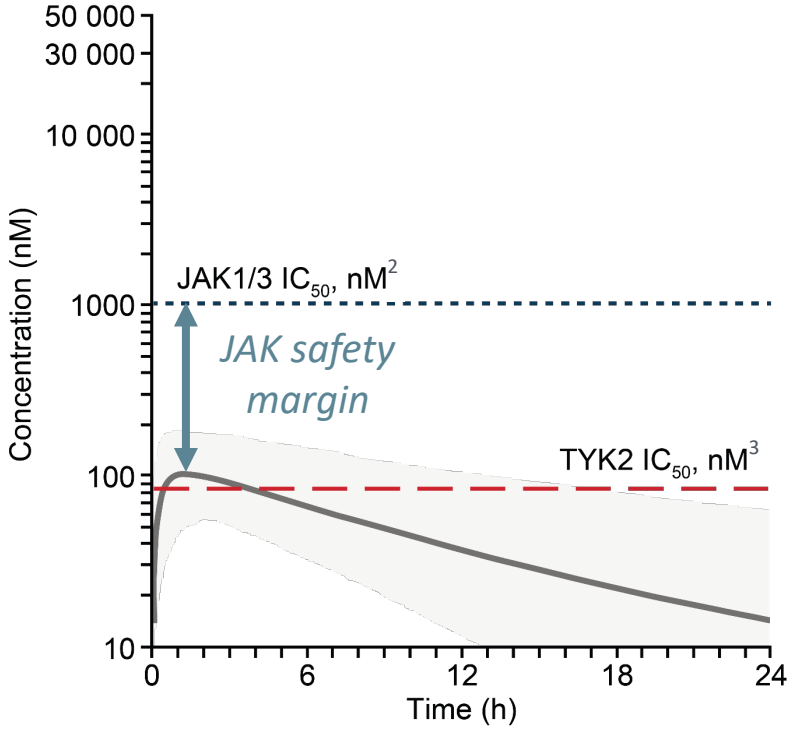
1. Leit S, et al. *J Med Chem*. 2023;66:10473-10496.
2. Mehrotra S, et al. Poster presentation at: European Society for Dermatological Research (ESDR) Conference 2024; 4–7 September 2024; Lisbon, Portugal. Poster LB054

Zasocitinib exhibits greater and longer TYK2 inhibition versus deucravacitinib and no inhibition of JAK1/3

Zasocitinib 30 mg QD



Deucravacitinib 6 mg QD



Greater and Longer Inhibition

Zasocitinib at 30mg QD is **significantly above IC_{50}** with **consistent inhibition over 24 hours**

Wide therapeutic window with no JAK1/3 inhibition up to 30,000nM, upper limit of the test

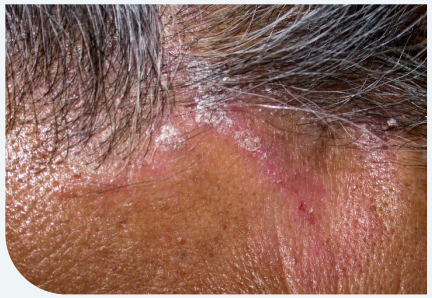
1. The maximum concentration evaluated was 30 000 nM
2. JAK1/3 IC_{50} is based on IL-2 pSTAT5
3. TYK2 IC_{50} is based on IL-12/IL-18-dependent production of IFN-γ; S Mehrotra, Y Sano, P Halkowycz, et al. (Poster LB054). Poster presented at ESDR 2024; 4–7 September 2024; Lisbon, Portugal

Despite numerous treatment options available to patients with psoriatic diseases there is still unmet need for a simple, safe and effective oral treatment

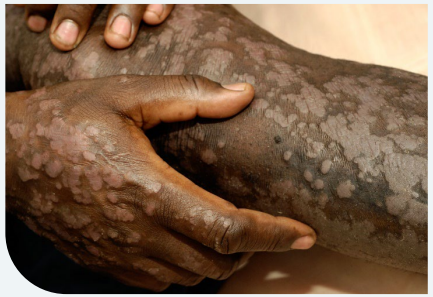
Psoriasis

- Psoriasis is estimated to affect **>60 million** adults[1]
- Lesions are **painful, disfiguring, and disabling**
- Lesions can occur **anywhere on the body**; commonly affected areas include scalp, trunk, gluteal fold, elbows, and knees
- Frequently associated with **several chronic conditions and comorbidities** which may affect lifespan and significantly impair QoL
  - Cardiovascular disease
  - Mental health: Depression and anxiety
  - Obesity

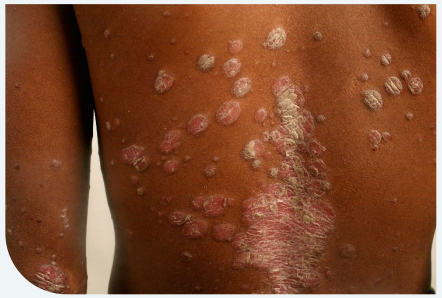
Scalp



Limbs and joints

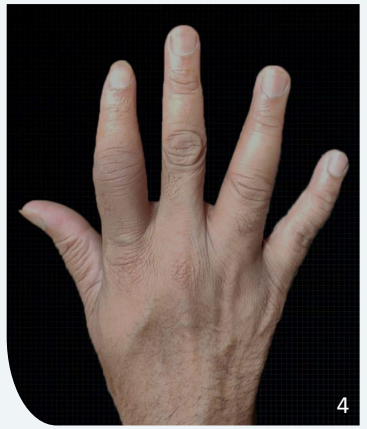


Trunk



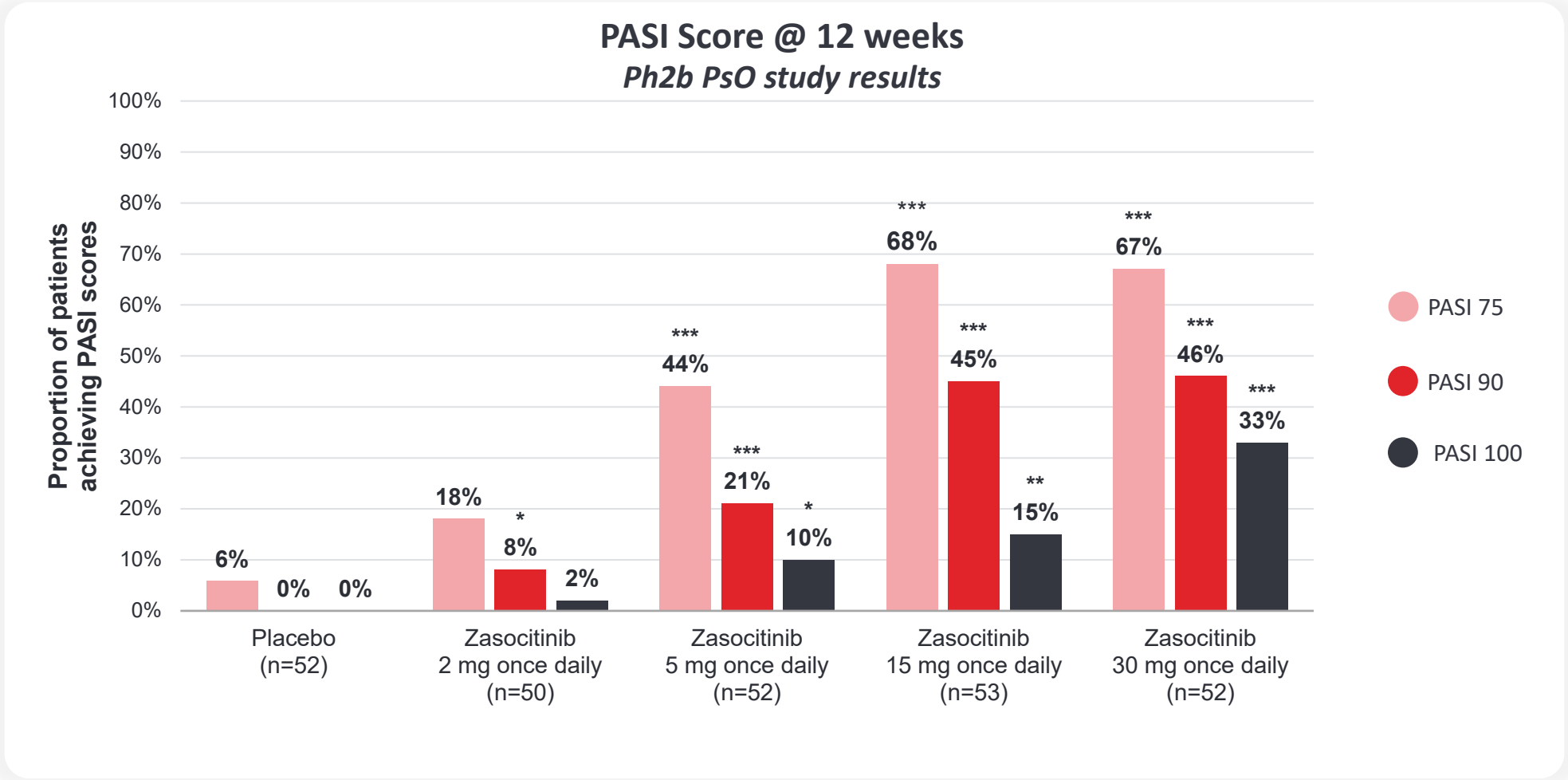
Psoriatic Arthritis

- Psoriatic arthritis is a chronic, progressive, inflammatory disease of the joints
- **Up to 30% of people** with psoriasis develop psoriatic arthritis[2]
- Psoriatic arthritis presents **painful, swollen joints & digits and >80% of patients having skin lesions**[3]
- Early identification, diagnosis and effective disease management are important factors to prevent joint destruction, improve patient outcomes and quality of life



1. AlQassimi S et al. Intl J Dermatol. 2020; 59:566-571; 2. Ritchlin CT, et al. New Engl J Med. 2017;376:957-970; 3. FitzGerald O, et Al Arthritis Res Ther. 17, 115, 2015
4. Pustake M, Vidhale T, Nadgire S. Psoriatic Arthritis With Dactylitis: A Case Report and Concise Review of Treatment Options. Cureus. 2021;13(8):e16966. Published 2021 Aug 6. doi:10.7759/cureus.16966

One-third of patients achieved complete skin clearance at 12 weeks with 30 mg once daily of zasocitinib



P values from a Cochran-Mantel-Haenszel test, with prior biologic treatment included as a stratification factor, comparing the proportion of patients in the treatment group versus placebo. For secondary endpoints (PASI 90 and PASI 100), P values are nominal: *P<0.05; **P<0.005; ***P<0.001. Modified intent-to-treat (mITT) analysis set: all patients who were randomized and received at least one dose of study treatment.; PASI, psoriasis area and severity index.; Armstrong AW, Gooderham M, Lynde C, et al. Tyrosine Kinase 2 Inhibition With Zasocitinib (TAK-279) in Psoriasis: A Randomized Clinical Trial. JAMA Dermatol. Published online August 21, 2024. doi:10.1001/jamadermatol.2024.2701;

No evidence of JAK-related safety signals, consistent with zasocitinib's exquisite selectivity

Ph2b PsO study results **AE, n (%)**	Placebo (n=52)	Zasocitinib 2 mg once daily (n=50)	Zasocitinib 5 mg once daily (n=52)	Zasocitinib 15 mg once daily (n=53)	Zasocitinib 30 mg once daily (n=52)
Deaths	0	0	0	0	0
SAEs	0	0	0	1 (1.9)	0
AEs	23 (44.2)	31 (62.0)	28 (53.8)	28 (52.8)	31 (59.6)
AEs leading to discontinuation	1 (1.9)	1 (2.0)	1 (1.9)	1 (1.9)	2 (3.8)
Most frequent AEs[1]					
COVID-19	1(1.9)	6(12.0)	4(7.7)	6(11.3)	7(13.5)
Acne	0	0	1(1.9)	3(5.7)	2(3.8)
Acneiform Dermatitis	0	0	1(1.9)	1(1.9)	3(5.8)
Diarrhea	1(1.9)	3(6.0)	1(1.9)	1(1.9)	0

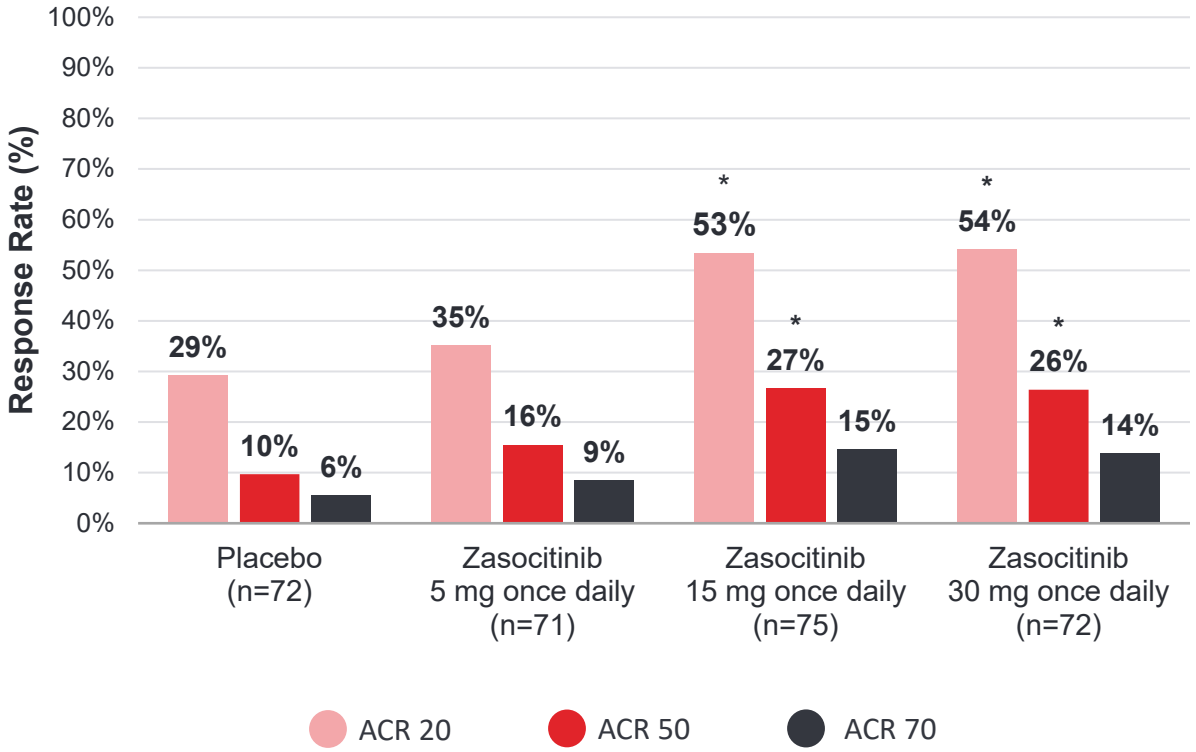
- Zasocitinib was generally well tolerated with a balanced benefit-risk profile.
- The incidence of AEs was higher in the zasocitinib groups compared with placebo, but there was no clear dose dependence.
- No clinically meaningful differences were observed in laboratory parameters for cholesterol, blood cell, liver enzyme, or kidney function with zasocitinib compared with placebo.

1. AEs reported by ≥3 patients in any treatment group (events elicited by laboratory testing are not included).;AE, adverse event; COVID-19, coronavirus disease 2019; SAE, serious adverse event; Armstrong AW, Gooderham M, Lynde C, et al. Tyrosine Kinase 2 Inhibition With Zasocitinib (TAK-279) in Psoriasis: A Randomized Clinical Trial. JAMA Dermatol. Published online August 21, 2024. doi:10.1001/jamadermatol.2024.2701

Strong efficacy across joint and skin endpoints demonstrated in Ph2b PsA study

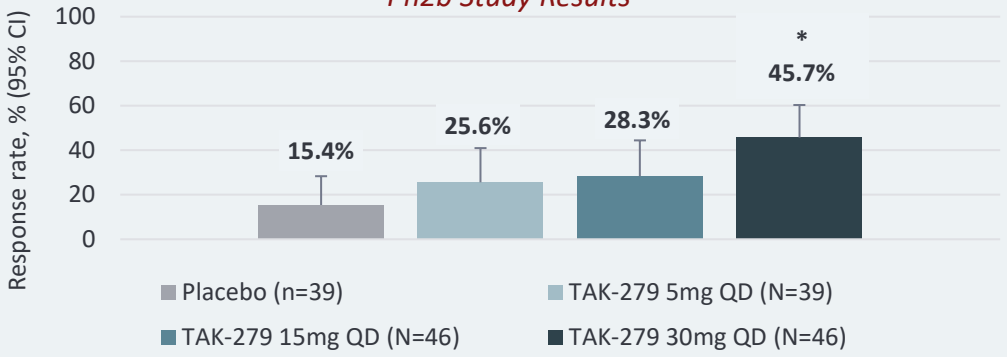
ACR 20, ACR 50, ACR 70 Response at Week 12[1]

Ph2b Study Results



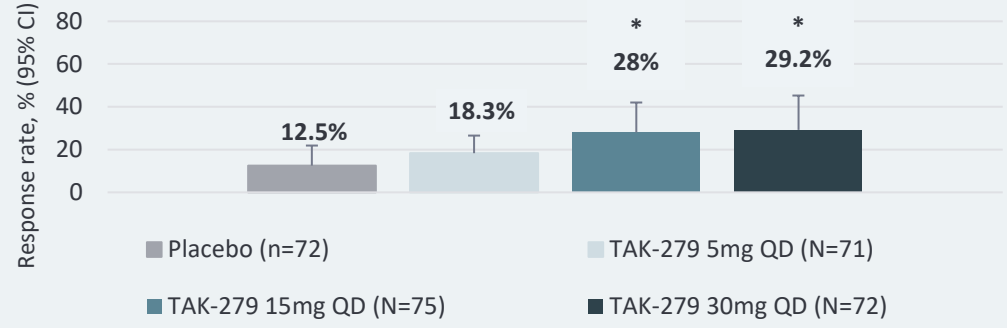
PASI 75 Response at Week 12[1]

Ph2b Study Results



MDA for Psoriatic Arthritis at Week 12[1]

Ph2b Study Results



* p<0.005, vs placebo; p values for secondary endpoints (ACR 50, ACR 70, MDA, PASI 75) are nominal. ; ACR, American College of Rheumatology; CI, confidence interval; MDA, minimal disease activity; QD, once daily.

1. Kivitz A, et al. Poster L12. Presented at: the 2023 American College of Rheumatology Annual Meeting; November 10-15, 2023; San Diego, CA,, USA.

Safety data from psoriatic arthritis Ph2b study supports that zasocitinib is generally well tolerated with a balanced benefit-risk profile

Ph2b PsA study results	Placebo (n=72)	Zasocitinib 5 mg QD (n=71)	Zasocitinib 15 mg QD (n=75)	Zasocitinib 30 mg QD (n=72)
	n (%)	n (%)	n (%)	n (%)
Any TEAEs	39 (54.2)	42 (59.2)	45 (60.0)	56 (77.8)
TEAEs leading to study discontinuation*	1 (1.4)	0	3 (4.0)	5 (6.9)
Serious TEAEs	4 (5.6)	4 (5.6)	3 (4.0)	2 (2.8)
Grade 3 or higher TEAEs	7 (9.7)	6 (8.5)	7 (9.3)	3 (4.2)
TEAEs leading to death	0	0	0	0
Most frequent TEAEs†				
Nasopharyngitis	3 (4.2)	6 (8.5)	7 (9.3)	7 (9.7)
URTIs	2 (2.8)	8 (11.3)	3 (4.0)	7 (9.7)
Headache	3 (4.2)	2 (2.8)	6 (8.0)	4 (5.6)
Rash	0	3 (4.2)	6 (8.0)	4 (5.6)

- The incidence of AEs was higher in the zasocitinib groups compared with placebo, but there was no clear dose dependence.
- No clinically meaningful differences were observed in laboratory parameters for cholesterol, blood cell, liver enzyme, or kidney function with zasocitinib compared with placebo.

*Placebo: psoriatic arthropathy; zasocitinib 15 mg: erythema nodosum, gastrointestinal inflammation, atrial fibrillation/atrial flutter/mitral valve incompetence; zasocitinib 30 mg: dermatitis acneiform, dermatitis allergic, abdominal pain, pharyngitis, Bell's palsy.
†TEAEs occurring at ≥5% by preferred term in any treatment arm.; QD, once daily; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection.;
Kivitz A, et al. Poster L12. Presented at: the 2023 American College of Rheumatology Annual Meeting; November 10-15, 2023; San Diego, CA, USA.

Completed enrollment ahead of schedule in two pivotal Ph3 studies in PsO with plans to begin head-to-head study versus deucravacitinib

Pivotal Studies

LATITUDE-PsO-3001
Moderate-to-Severe Patients
n=600
Randomization 3:1:1

- Zasocitinib 30mg QD
- Apremilast 30mg BID
- Placebo

Co-primary Endpoint:
PASI-75 at week 16

sPGA of clear (0) or almost clear (1) with a >=2-Point decrease from baseline at week 16

LATITUDE-PsO-3002
Moderate-to-Severe Patients
n=1000
Randomization 2:1:1

- Zasocitinib 30mg QD
- Apremilast 30mg BID
- Placebo

Co-primary Endpoint:
PASI-75 at week 16

sPGA of clear (0) or almost clear (1) with a >=2-Point decrease from baseline at week 16

Head-to-Head

LATITUDE-PsO-3004
Protocol under development

- Zasocitinib 30mg QD
- Deucravacitinib 6mg QD

Estimated Study Start:
1H FY2025

Pivotal Ph3 studies Enrollment completed Q3 FY2024

H2H target start 1H FY2025

Target Ph3 Pivotal data readout CY2025

Takeda has advanced zasocitinib into phase 3 for psoriatic arthritis

LATITUDE-PsA-3001
n=1088
Randomization 1:1:1:1

- Zasocitinib 15mg QD
- Zasocitinib 30mg QD
- Apremilast 30mg BID
- Placebo

Primary Endpoint:
ACR20 at week 16

Key Secondary Endpoint:
PASI-75 at week 16
MDA at week 16

LATITUDE-PsA-3002
n=600
Randomization 1:1:1

- Zasocitinib 15mg QD
- Zasocitinib 30mg QD
- Placebo

Primary Endpoint:
ACR20 at week 16

Key Secondary Endpoint:
PASI-75 at week 16
MDA at week 16

Ph2 completed FY2023

Target Ph3 Start FY2024

Target Filing FY28/29

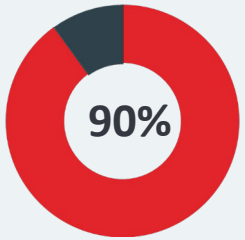
More than 5 million patients globally suffer from IBD

IBD is a chronic inflammatory condition which includes two subtypes: Ulcerative Colitis (UC) & Crohn's Disease

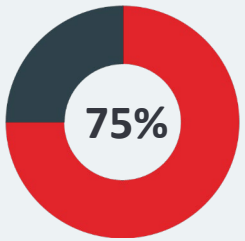
IBD patients experience diarrhea, abdominal pain, and, in the case of UC, perianal bleeding

Patients experience **morbidity** from prolonged medical therapy, particularly as a **consequence of steroid exposure**

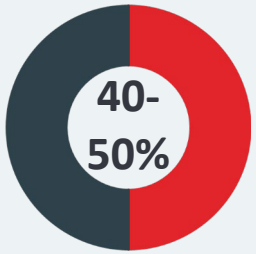
1.4-5x Mortality rates for IBD range from 1.4 to 5 times the general population



of Crohn's disease patients experience relapse within 10 years



of IBD patients do not achieve remission or lose response over time



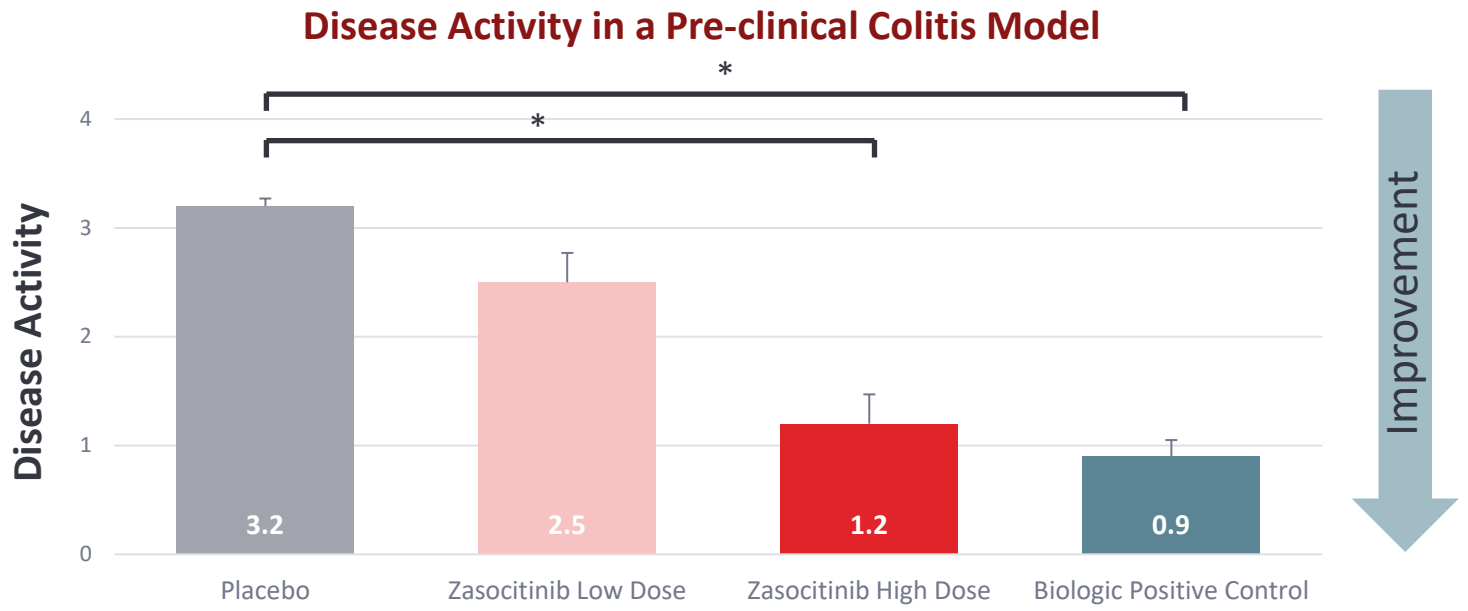
of Crohn's disease patients don't respond to current treatment

Patients are in need of safe, efficacious & convenient novel therapies

Alatab et al, The Lancet Gastroenterol and Hepatol 2020; Jairath et al, The Lancet Gastroenterol and Hepatol 2020; McDowell et al, Inflammatory Bowel Disease. 2024; Xu et al, World J Gastroenterol 2022; Alsoud D. et al. The Lancet Gastroenterol and Hepatol 2021, 6(7):589-595; Barberio B. et al. Dig and Liver Dis 2024, 56(1):7-14; Sandborn W.J., et al. Gastroenterol, 142 (2012): 257-265; Feagan B.G., et al. N Engl J Med, 369 (2013): 699-710; Sandborn W.J., et al. N Engl J Med, 376 (2017): 1723-1736; Bargo D., et al. Inflamm Intestinal Dis. 2021;6(4):186-98; Moens A., et al. Inflamm Bowel Dis. 2022;28(8):1135-42; Dalal R.S. et al. Dig Dis Sci. 2023;68(1):223-32; Sine B., et al. N Engl J Med Evid, 2022;1(8)

Zasocitinib has strong scientific rationale to support exploration in IBD

1. Genetic analysis has identified an alteration in the *TYK2* gene that is highly protective against inflammatory diseases, including Crohn's & UC[1]
2. Zasocitinib can achieve and maintain near-complete TYK2 inhibition[2]
3. Animal models of colitis demonstrate a significant reduction in disease activity at high dose zasocitinib[3]
4. Zasocitinib is highly selective, supporting higher dosing to ensure target tissue coverage in IBD



1. Dendrou CA, et al. Sci Transl Med. 2016;8(363):363ra149.
2. Mehrotra S, et al. Poster presentation at: European Society for Dermatological Research (ESDR) Conference 2024; 4–7 September 2024; Lisbon, Portugal. Poster LB054.
3. Kong KF, et al. Poster presentation at: Congress of the European Crohn's and Colitis Organisation (ECCO) 2024; 21-24 February 2024; Stockholm, Sweden. Poster 143.

Takeda is currently evaluating zasocitinib in phase 2b studies in IBD

LATITUDE-CD-2001

Moderate-to-severe patients

n=268

Randomization 1:1:1:1

- Zasocitinib Dose 1
- Zasocitinib Dose 2
- Zasocitinib Dose 3
- Placebo

Primary Endpoint:

Endoscope response based on SES-CD at week 12

Key Secondary Endpoint:

Clinical remission based on CDAI at week 12

Clinical response based on CDAI at week 12

Endoscopic remission based on SES-CD at week 12

Safety

LATITUDE-UC-2001

Moderate-to-severe patients

n=207

Randomization 1:1:1

- Zasocitinib Dose A
- Zasocitinib Dose B
- Placebo

Primary Endpoint:

Clinic Remission at week 12 based on modified Mayo Score (mMS)

Key Secondary Endpoint:

Clinical Response at week 12 Based on mMS

Endoscopic improvement and Endoscopic remission based on mMS at week 12

Safety

Patients will have the option to move to the long-term extension and followed for safety & remission

SES-CD: Simple endoscopic score for Crohn's disease; CDAI: Crohn's Disease Activity Index

With a deep history in inflammation, Takeda is uniquely placed to advance zasocitinib

Latitude

	PHASE 2b START	PHASE 2b READOUT	PHASE 3	FILING
Psoriasis		✓ Ph2b March 2023	✓ Ph3 Start FY2023 Zaso vs Deucra Start FY2025	Target FY2026
Psoriatic Arthritis		✓ Ph2b September 2023	Target Ph3 Start FY2024	Target FY28/29
Crohn's Disease	✓ Ph2b March 2024	Target FY2026		
Ulcerative Colitis	✓ Ph2b June 2024	Target FY2026		
Others	✓ Planned			

✓ Complete

Zasocitinib

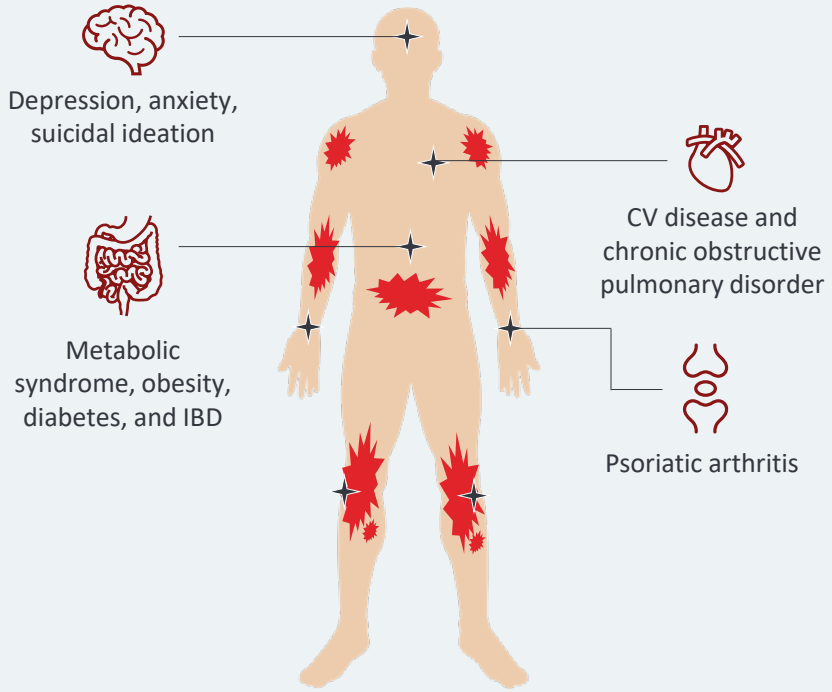
Market Opportunity

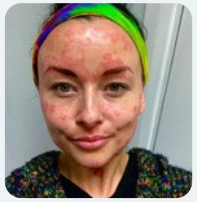
Well-positioned to be the first-choice advanced therapy for psoriatic disease patients, leading the next-generation orals

PsO is much more than just a rash; patients are really suffering

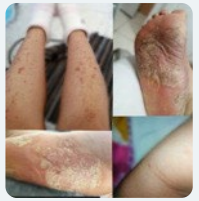
The visible plaques, social stigma and higher risk of comorbidities negatively impact patients' QoL[1]

Associated comorbidities





"Psoriasis first spread over my entire body and then onto my face. For me personally facial psoriasis was the hardest to come to terms with. ***Not because it was the most painful, itchy or sore, but because it could be seen by everyone around me."***

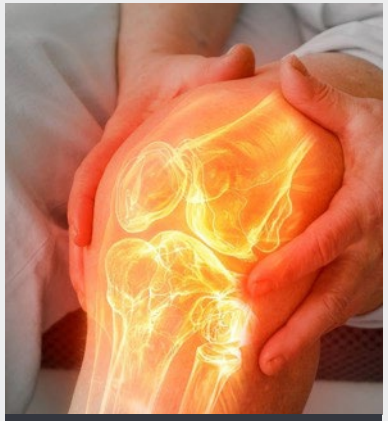


"The pain and itching were severe, and sometimes I couldn't sleep because of it. My life had simply turned into a living nightmare and ***negative thoughts were overpowering everything inside me, making me feel frustrated and hopeless."***

1. The total body inflammatory burden increases the risk of medical comorbidities, including CVD, diabetes and obesity. Symptoms can restrict patients to stay home increasing feeling of disconnect and also cause frustration and embarrassment.

30% of PsO patients develop PsA, which comes with an even higher burden of disease

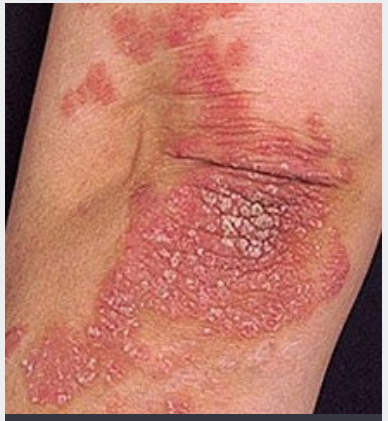
Patients experience unbearable symptoms…



Irreversible joint damage, potentially leading to disability

Chronic pain

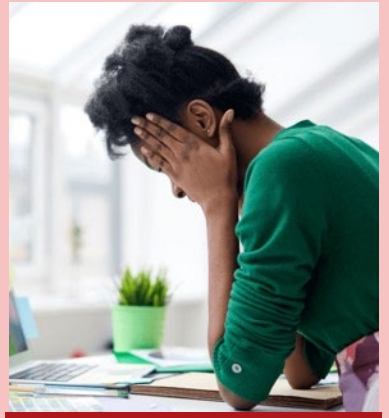
Fatigue



Skin lesions

… with a significant impact on QoL

Social withdrawal from activities

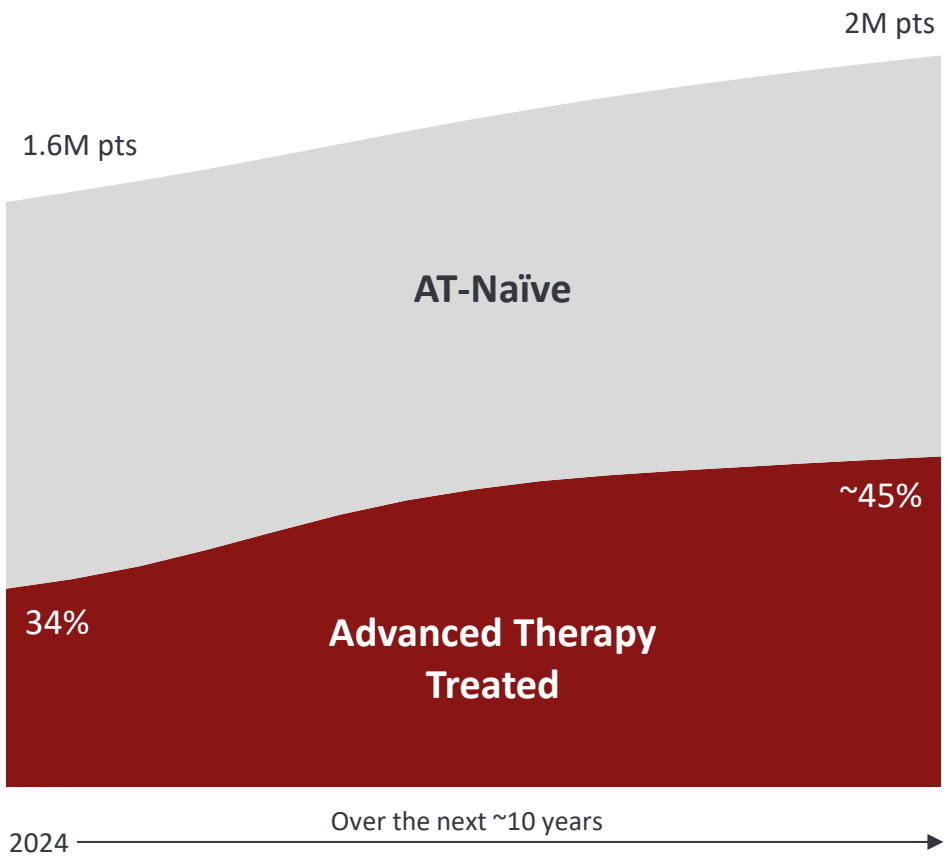


Inability to perform “normal” daily tasks

Rheumatologists are forced to make difficult trade-offs; more aggressive treatments may come with more safety issues

We expect significant growth of advanced therapies in both PsO and PsA markets, both already large at $23B and $7B worldwide, respectively

US Moderate-to-Severe PsO AT Market Projection[2]



Significant headspace for growth of advanced therapy segment in PsO

- WW PsO Advanced Therapy (AT) Market **~$23B**[1] in 2023
- In the US, **only 34%** of patients are being treated with an advanced therapy
- This is even less worldwide, at **only 30%**
- AT penetration is projected to grow to **~45%**

Similar growth opportunity in PsA

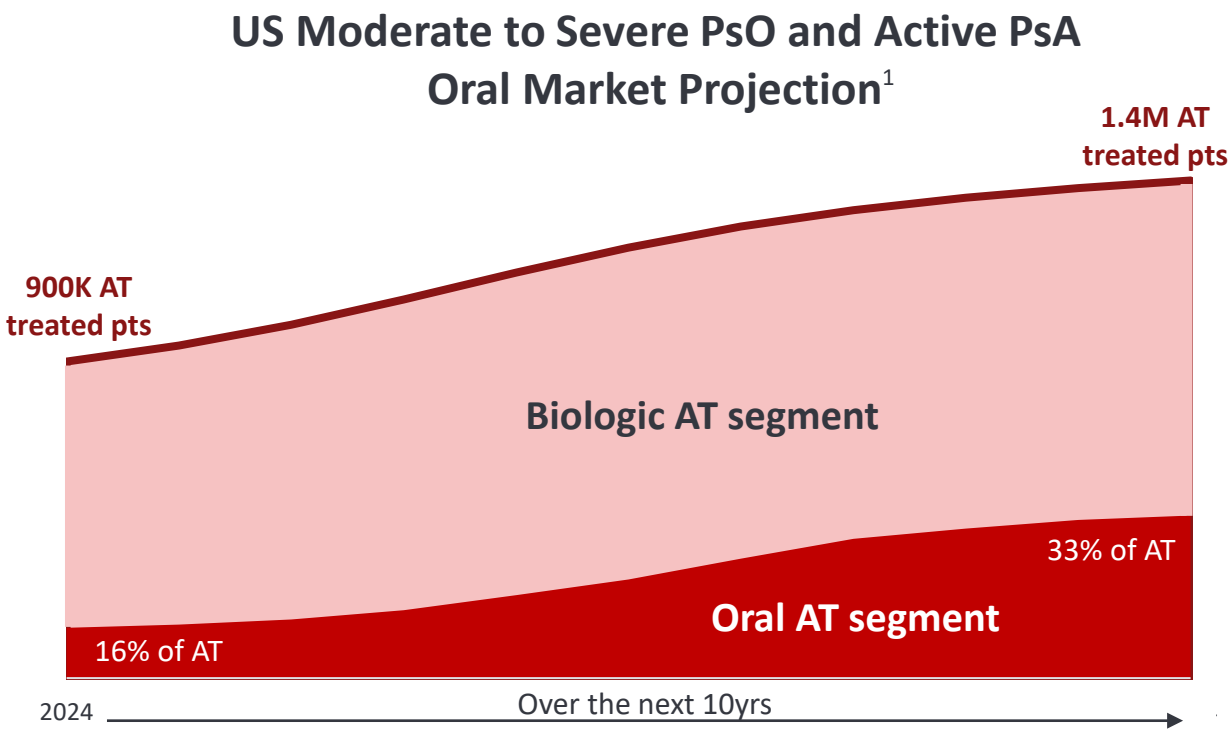
- WW PsA Advanced Therapy Market **~$7B**[1] in 2023
- Somewhat higher penetration of advanced therapy due to physician concern about permanent joint damage
- AT penetration is projected to grow from **50% to 60%**

There is an opportunity to provide better care for so many patients

AT: Advanced Therapy, which includes biologics and targeted orals;
1. Clarivate/Decision Resources (Jun 2024), 2. Based on internal estimates

This growth of advanced therapies is driven by improved oral options

Oral share is expected to double in both PsO and PsA



> *"Orals are where the market is going. It's where all the companies are investing. When a patient comes off of topicals, orals will be next.*
>
> **- US Dermatologist**

1. Based on internal estimates

Zasocitinib aims to…

REDEFINE WHAT IS POSSIBLE WITH AN ORAL THERAPY IN PSORIATIC DISEASE

Patients are seeking safe and effective oral treatment options when topical and conventional treatments aren't enough

WHAT PATIENTS TELL US THEY WANT	Zasocitinib	Apremilast	Deucravacitinib
Clear skin	🟢	🔴	🟡
Safety data	🟢	🟢	🟢
Well-tolerated	🟢	🔴	🟢
Once daily oral / easy to take	🟢	🔴	🟢

Target profile based on Ph2b results

Zasocitinib has the potential to be the first oral treatment option that can address all patient needs

Scoring is based on apremilast and deucravacitinib labels, and target profile of zasocitinib based on Ph2b results. No H2H studies have been performed to date.

Zasocitinib was designed to provide both efficacy & safety, along with a simple and easy treatment experience

A next-generation, highly selective and potent TYK2 inhibitor

A simple & easy treatment experience

- Once daily oral treatment
- Well-tolerated
- Can be taken any time of the day without regard to food

Favorable safety profile

- Highly selective TYK2 inhibitor, with potential for **no JAK effects**
- Strongly favorable benefit-risk profile

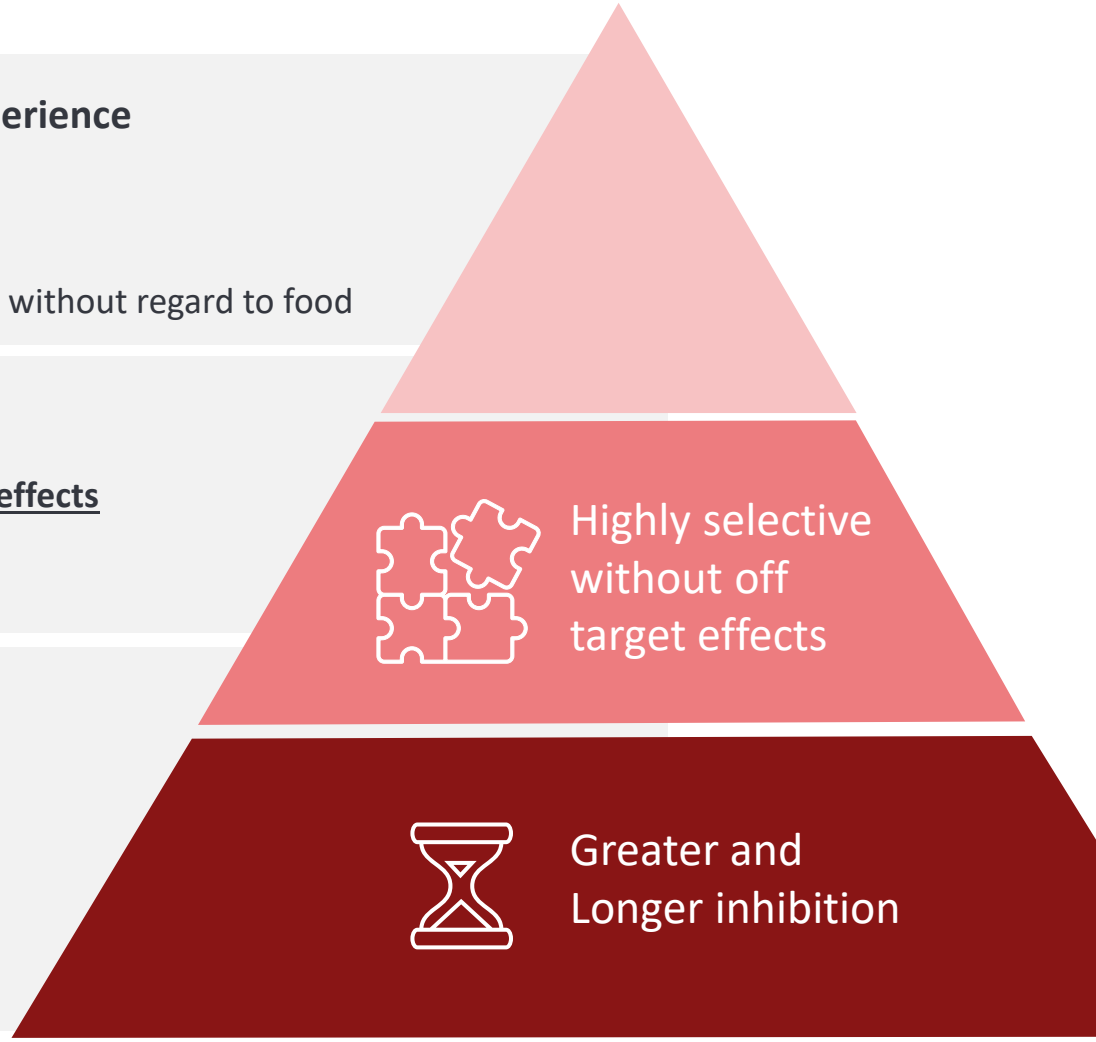
Biologic-like efficacy

PsO

- Potential for rapid, durable and complete skin clearance
- ~1/3 of patients with completely clear skin in 12 wks

PsA

- Reduced pain, swelling and inflammation in joints
- Minimal Disease Activity (MDA) reached in ~1/3 of patients



Target profile based on Ph2b results

PsO & PsA combine for up to $6B of peak revenue, with the potential for additional indications including Crohn's & UC

US PsO + PsA Market Evolution over next ~10 yrs

Diagnosed PsO & PsA Patients	Advanced Therapy Treated	Oral treated	**Zasocitinib 1st Choice AT**
2.2M → **~2.8M**	39% → **~50%**	16% → **~33%**	

Global Peak Revenue Potential

PsO and PsA $3 - 6B

Plus Crohn's & UC

Plus potential additional indications

Targeting the right patients and physicians

Simple and streamlined onboarding

Winning access strategy

Head-to-head superiority trials vs currently marketed orals

Please refer to the Important Notice at the start of this presentation for more information about peak revenue estimates.

Unique opportunity for zasocitinib

Large, growing market in PsO/PsA with only **~30-50% of moderate-to-severe patients** currently on advanced therapy

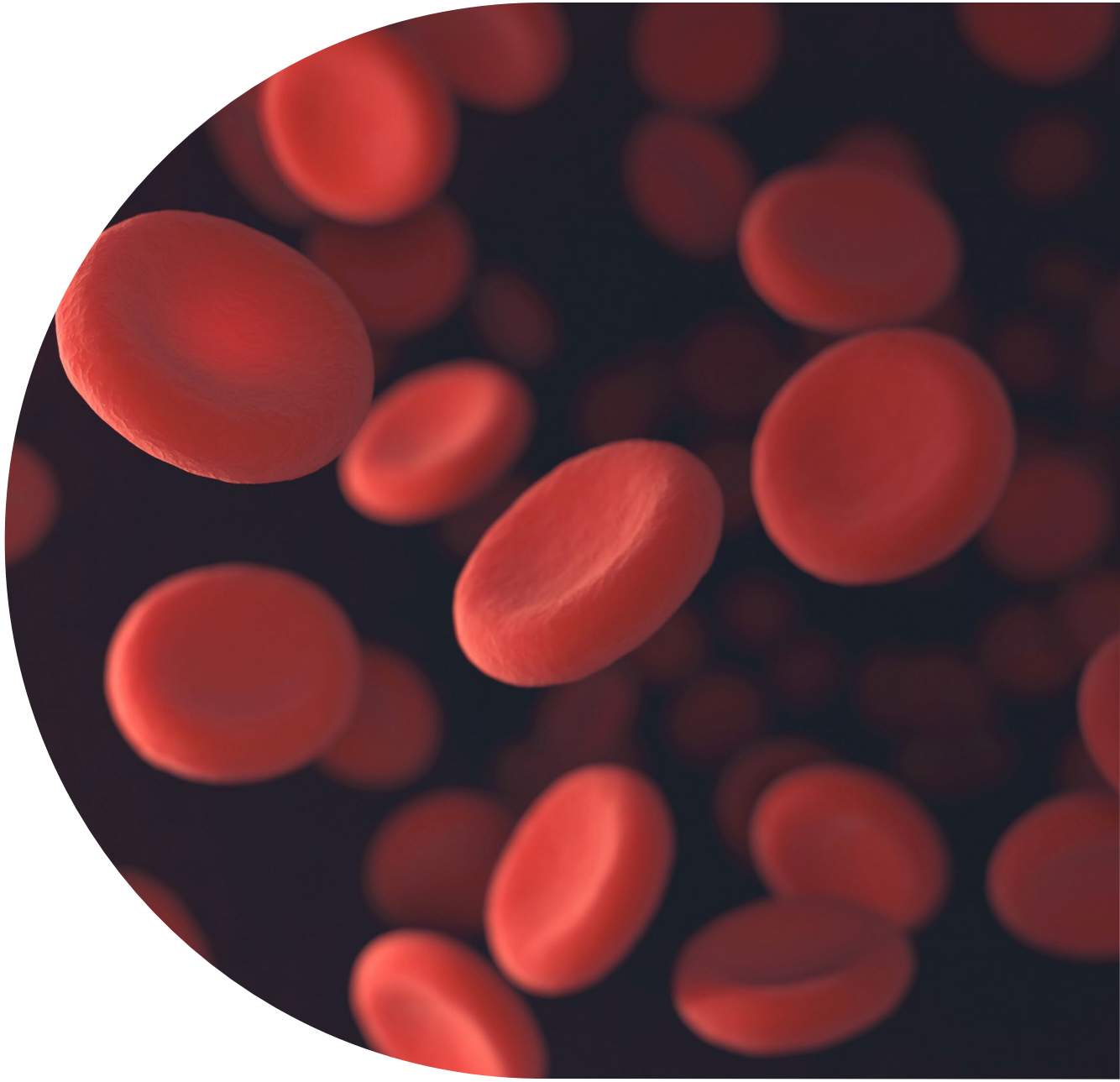
Opportunity for improved oral options to expand the use of advanced therapy and more than double the share of AT patients on orals

As a next-generation, highly selective TYK2 inhibitor, Zasocitinib has the potential **to deliver biologic-like efficacy with favorable tolerability & safety**, in a simple once-daily oral formulation

Zasocitinib is poised to be the first-choice advanced therapy, with global peak revenue potential of $3-6B

Please refer to the Important Notice at the start of this presentation for more information about peak revenue estimates.

Rusfertide: Advancing Polycythemia Vera (PV) Treatment for Superior Hematocrit Control



Better Health, Brighter Future

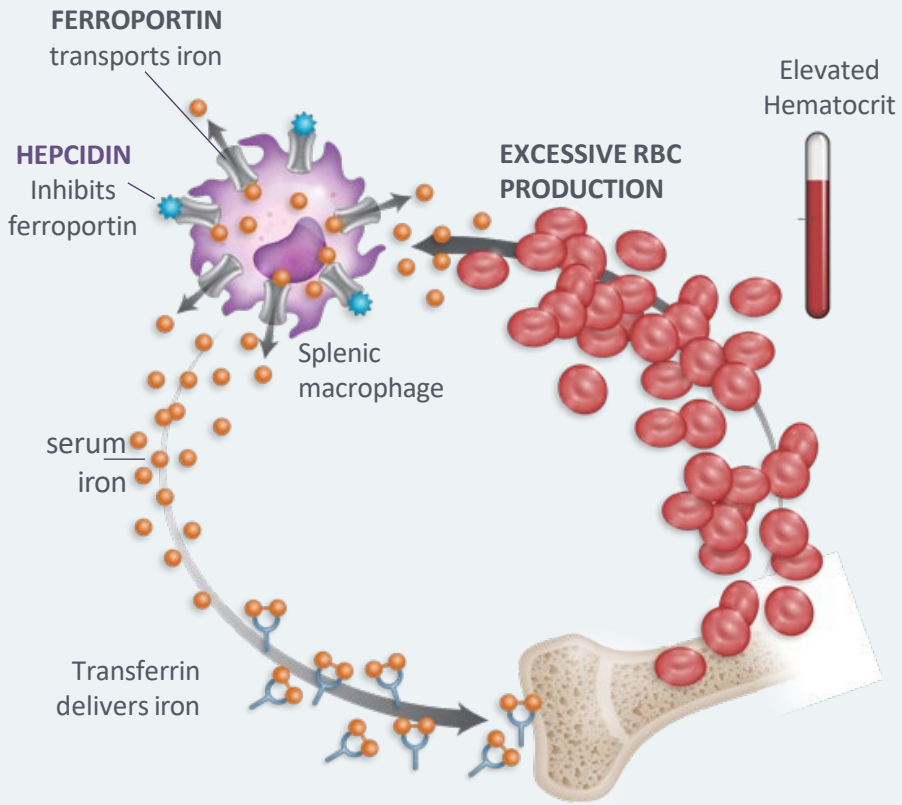
Elevated hematocrit is the hallmark of polycythemia vera (PV) and its clinical challenges

PV – Rare Myeloproliferative Neoplasm Characterized by Excessive Production of Red Blood Cells[1]

PV is a **rare myeloproliferative neoplasm** characterized by elevated hematocrit (HCT)[1,2]

Elevated HCT is due to overproduction of red blood cells[2]

There are ~155,000 PV patients in the US, with a median survival of 14 years[1]



PRIMARY TREATMENT GOAL
is to maintain
HCT <45%[3,4]

1. NORD Rare Disease Database, Polycythemia Vera. https://rarediseases.org/rare-diseases/polycythemia-vera/
2. Spivak JL. Ann Hematol 2018; 19(2):1-14.; 3. Marchioli R, et al. N Engl J Med 2013; 368:22-33. 4. Barbui, T, et al. Leukemia 2018, 32(5), 1057-1069.

There remains significant unmet need in polycythemia vera treatment

Inconsistent HCT Control

- **Consistent HCT <45% is critical**, as uncontrolled HCT is associated with ~4 times higher risk of death from cardiovascular causes or thrombotic events[1]
- Real-world data shows that **78% of patients have uncontrolled** HCT[2]

Increased Risk of Thrombotic Events

- **34-41% of patients experience thrombotic** events[3-5]
- Common events include acute coronary syndrome, stroke, deep vein thrombosis, and pulmonary embolism[3,5]

Significant Burden

- **PV impacts daily activities and productivity**[6]
- 84% of patients report fatigue, and 23% report spending full days in bed because of symptoms[6]
- Patients with PV often present with iron deficiency that can be further exacerbated due to iron loss from phlebotomy[7]

1. Marchioli R, et al. *N Engl J Med* 2013; 368:22-33; 2. Verstovsek S, et al. *Ann Hematol* 2023 Mar;102(3):571-581; 3. Kaifie A, et al. *J Hematol Oncol* 2016;9:18.; 4. Griesshammer M, et al. *Ann Hematol* 2019;98(5):1071-1082.; 5. Polycythemia vera: the natural history of 1213 patients followed for 20 years. Gruppo Italiano Studio Policitemia. *Ann Intern Med* 1995;123(9):656-664.; 6. Mesa R, et al. *BMC Cancer* 2016;16,167. 7. Ginzburg et al. *Leukemia* 2018;32:2105-2116.

Mechanistic rationale of rusfertide in managing polycythemia vera

Rusfertide helps address the overproduction of red blood cells (RBCs) in patients with polycythemia vera (PV) through,

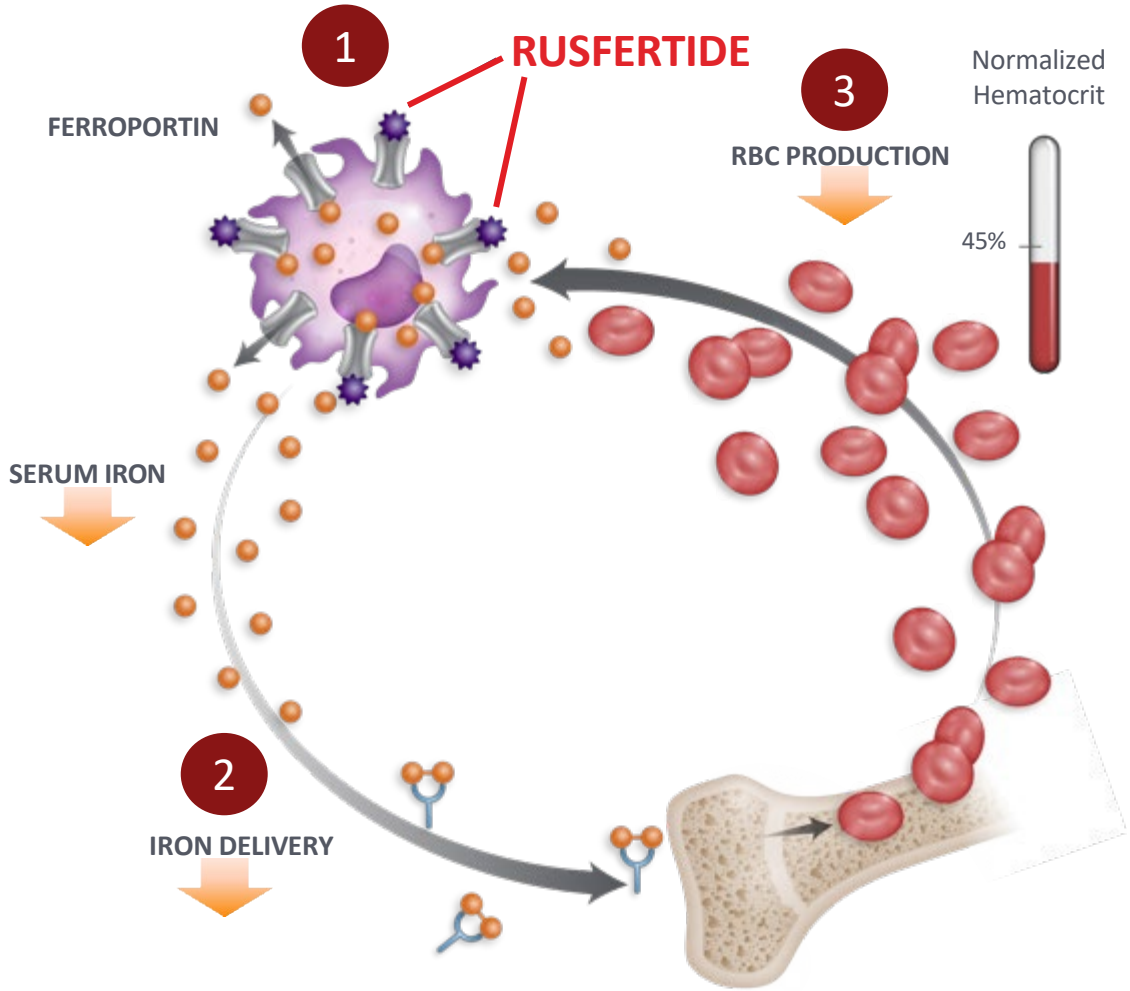
1. **Restricting availability of iron by closing the ferroportin channel, which reduces serum iron**
2. **Decreasing iron delivery to bone marrow**
3. **Controlling RBC production**

Key Outcomes of Rusfertide's Mechanism:

- **Consistent and Sustained Hematocrit Control**
  - HCT levels < 45%
  - Reduced risk of cardiovascular and thrombotic events
- **Stabilizes iron metabolism**

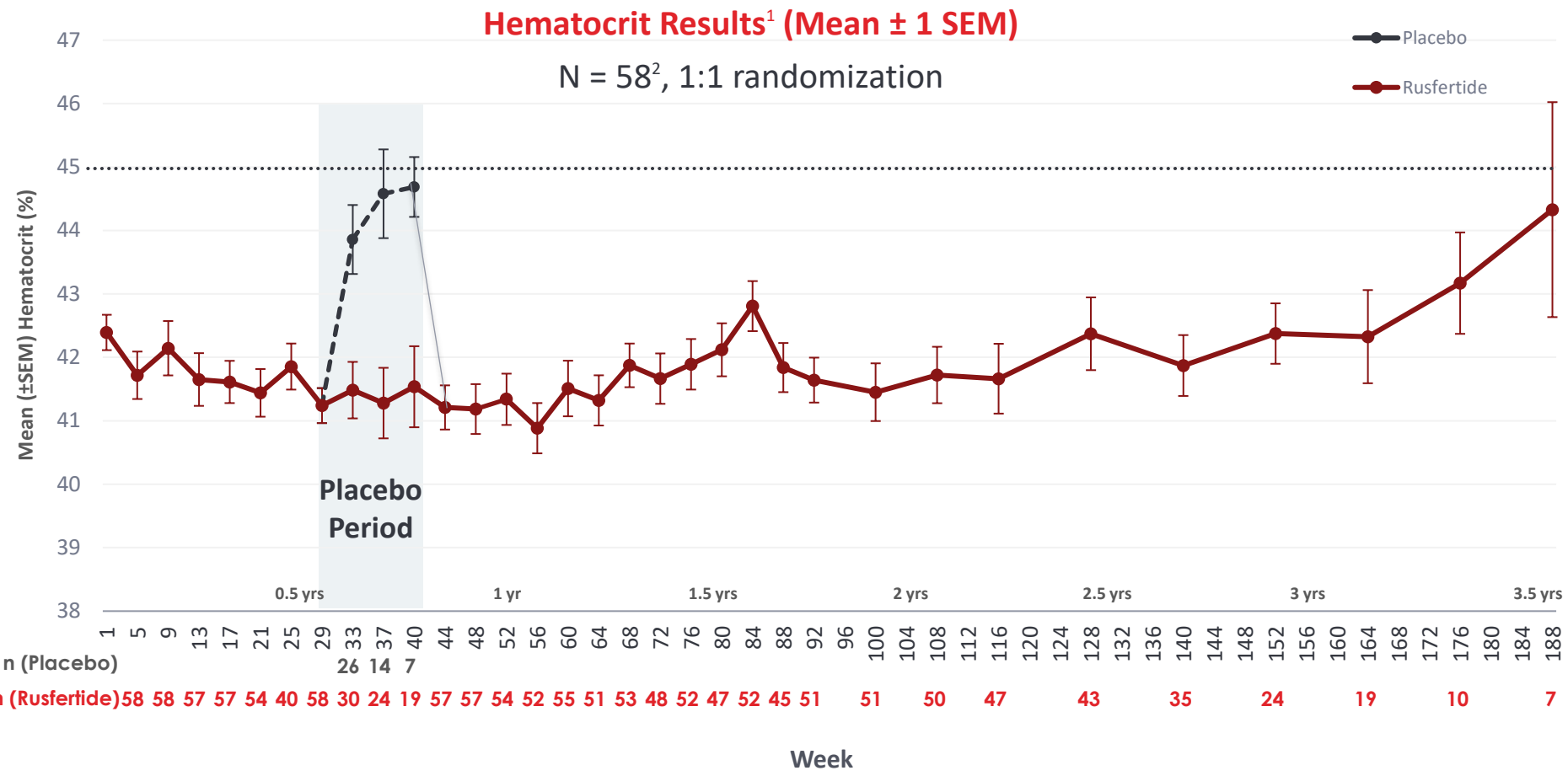
MOA of Rusfertide

Leveraging Hepcidin Mimetic to Target Excessive RBC Production



Clinical efficacy of rusfertide: rapid, sustained and durable hematocrit control

REVIVE Study: PV patients requiring frequent phlebotomy ± cytoreductives; 90% phlebotomy free



- **Rapid, Sustained and Durable** hematocrit control
- **Robust efficacy** for all patient categories
- **Positive** improvements in **symptom scores**[3]

- **HCT levels rise** during **placebo period** (wk 29-37)
- HCT levels **revert to being controlled** when **rusfertide is restarted** (wk 37-41)

1. Local laboratory results; Data on file
2. Includes all REVIVE patients who continued to Part 3
3. improvement in symptom scores were in patients with moderate or severe symptoms at baseline assessed by the MPN-SAF

REVIVE demonstrated a favorable long-term safety profile

Most common (≥20%) TEAEs

- Injection site reactions, fatigue, COVID-19, pruritus, arthralgia, dizziness, nausea, anemia, and headache
  - Grade 3 TEAEs occurred in 25.7% of patients and there were no Grade 4 or 5 TEAEs

Serious AEs

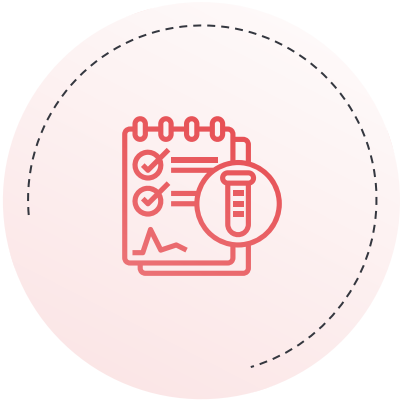
- 18 patients (26%) experienced SAEs
- Most SAEs were unrelated and likely associated with underlying disease; 1 SAE was assessed as treatment-related by the investigator

Thromboembolic events (TE)

- No TEs occurred in low-risk patients
- 40 patients entered the study with high-risk PV and 14 patients had a TE prior to study entry
  - 6 patients with high-risk PV developed 7 TEs on study (2 of these patients had a TE prior to study entry)

Patients in REVIVE were eligible to roll over to the open-label extension THRIVE study

which will continue to assess the long-term safety and efficacy of rusfertide



Data cutoff: 9 April 2024; COVID-19, coronavirus disease; PV, polycythemia vera; SAE, serious adverse event; TE, thromboembolic event; TEAE, treatment-emergent adverse event. ; Adapted from: Pettit KM, et al. Abstract Presented at the 29th European Haemotology Association Congress, June 13-16, 2024, Madrid, Spain.

Rusfertide phase 3 ongoing: target data readout CY2025

Verify Study (Ph3) Design

N = 250
Randomization 1:1

INCLUSION CRITERIA

≥3 PHL[3] due to inadequate HCT control in 28 weeks before randomization

OR ≥5 PHL due to inadequate HCT control within 1 year prior to randomization

Part 1A: Double-Blind[1, 2]
Duration - 32 weeks
(Weeks 0-32)

- **Rusfertide + ongoing therapy**
- **Placebo + ongoing therapy**

Part 1B: Open-Label[1, 2]
Duration - 20 weeks
(Weeks 32-52)

- **Rusfertide + ongoing therapy**

Background therapy may be decreased or stopped but not increased

Primary endpoint:

Response Rate at wk 20 to wk 32 (inclusive) vs placebo

- Response is the absence of PHL eligibility defined as,
  - HCT ≥45% and ≥3% higher than the baseline HCT
  - *or,* HCT ≥48%

Key Secondary endpoints:

- Mean number of PHL wk 0 to wk 32 (inclusive)
- Proportion of patients with all HCT values <45% wk 0 to wk 32 (inclusive)
- Safety / Adverse Events

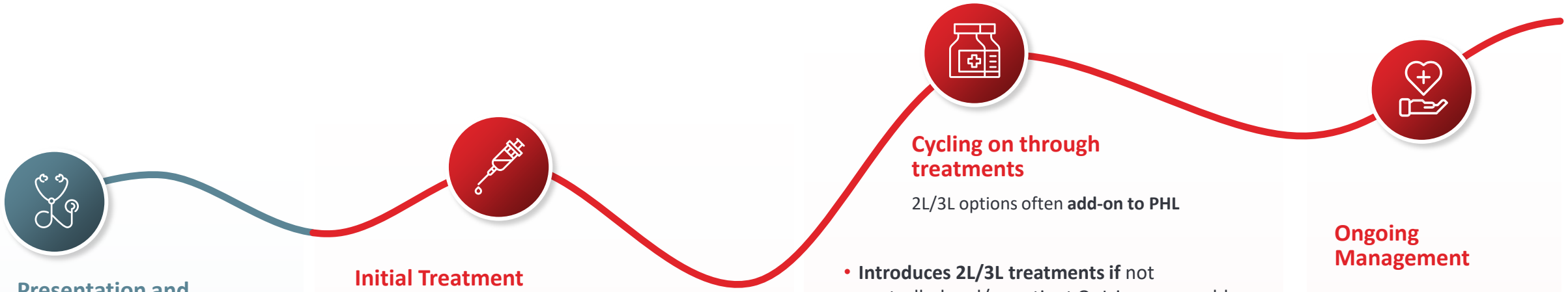
1. ClinicalTrials.gov. NCT05210790. https://clinicaltrials.gov/ct2/show/NCT05210790
2. ASCO'24: Bankar A, et al. VERIFY: A randomized controlled phase 3 study of the hepcidin mimetic rusfertide (PTG-300) in patients with polycythemia vera (PV). J Clin Oncol;2024;42;16_suppl. TPS6592
3. PHL is an abbreviation for phlebotomy.

Rusfertide

Market Opportunity

Advancing care in polycythemia vera by targeting critical unmet needs

Patient Journey in PV identifies unmet need in current treatment paradigm as patients cycle through options with inconsistent HCT and tolerability



Presentation and Diagnosis

Initial Presentation: Routine blood work or thrombotic event

Work Up: **Blood tests** prompt a referral to Hematology/Oncologist

Diagnosis: Hem/Onc diagnoses PV and assesses risk

Initial Treatment and Management

Immediate: Phlebotomy (PHL) after diagnosis

- **LOW RISK: Regular PHL** to reduce HCT
  - PHL inconsistently, temporarily reduces HCT
  - PHL results in iron deficiency; amplifies PV symptoms
- **HIGH RISK: PHL with HU or Interferon** if PHL alone is insufficient

"I don't love phlebotomy. Most patients hate it. It's exchanging PV for symptomatic iron deficiency…nobody can sustain that."

- MPN Specialist

Cycling on through treatments

2L/3L options often **add-on to PHL**

- **Introduces 2L/3L treatments if** not controlled and/or patient QoL is unmangable
- **2L HU** an off-label[1] cytoreductive chemotherapy
- **Ruxolitinib or Ropeg-interferon** added for HCT control or tolerability and/or based on HCP preference

Current 2L+ therapies may have side effects and *safety* concerns

*"There's **side effects that make HU impossible to take for some patients**…30% of patients drop off."*

- MPN Specialist

Ongoing Management

Monitor blood counts and treatment side effects

Adjusts treatment as necessary

HCPs also educate patients on lifestyle modifications, symptom surveillance, and treatment adherence through the management of PV

*Recommended threshold levels for hematocrit = 45% in men and 42% in women

1. HU is an off-label treatment in the US

Rusfertide aims to deliver rapid, consistent & sustained HCT control and is expected to be used at each step of the treatment landscape

~155k diagnosed patients in the US with **~78K treated**

Patients are often on polytherapy and will cycle through various treatments

~41K Phlebotomy (PHL) And/Or **~26K** Hydroxy Urea (HU) And/Or **~6K** Ruxolitinib And/Or **~3K** Ropeg-interferon

Unmet needs exist at each step of the treatment landscape, with potential for rusfertide to reach up to 10% of the treated population.

Driving awareness of the unmet needs in PV › Working broad access and inclusion in guidelines › Engaging with key stakeholders to promote use of Rusfertide ‹› Exploring digital solutions for optimal patient onboarding

Rusfertide may provide consistent hematocrit control and reduce treatment burden to achieve peak revenue potential of $1-2B

Source: Komodo Health closed claims dataset (2016-2023); Note: ~2,000 patients are treated via a combination of other therapies; Please refer to the Important Notice at the start of this presentation for more information about peak revenue estimates.

Unlocking the full potential of rusfertide for polycythemia vera patients

Advancing Care In The PV Space By Targeting Critical Unmet Needs

Approximately **155,000 patients diagnosed with PV** with only 78,000 currently being treated

Hematocrit control (<45%) is the primary goal of physicians in treating patients with PV

Patients cycle through treatment options according to guidelines and 78% of patients remain uncontrolled; HCT >45% increases risk of TE and CV

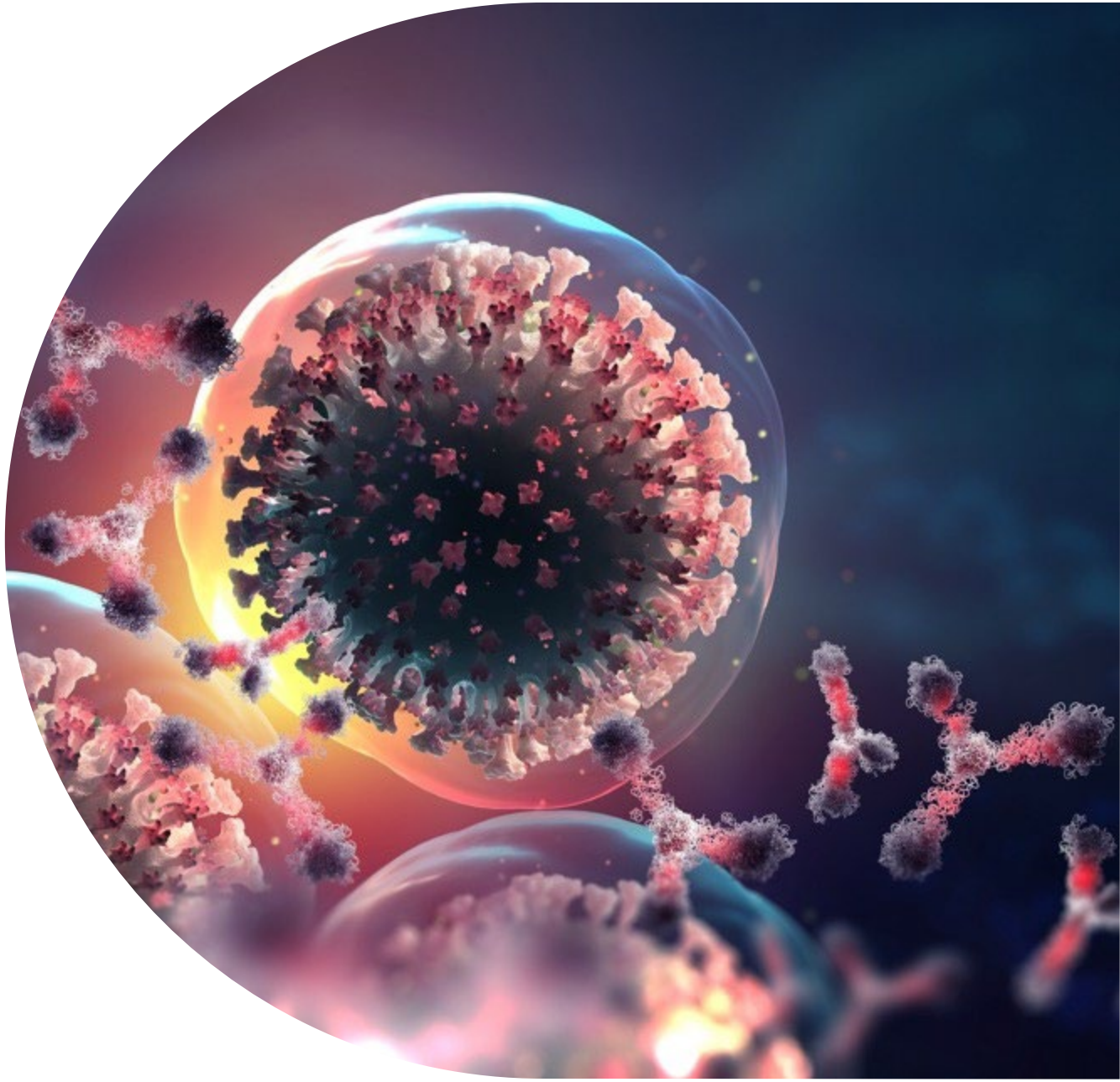
Current treatment options can exacerbate PV Symptoms and/or cause significant side effects

Rusfertide has the potential to provide rapid, consistent & sustained hematocrit control with favorable tolerability – Peak revenue potential $1-2B

Please refer to the Important Notice at the start of this presentation for more information about peak revenue estimates.

Mezagitamab (TAK-079)

Transformative Potential for Chronic Auto-immune Diseases



Better Health, Brighter Future

Mezagitamab: New unique anti-CD38 antibody with disease modifying potential providing rapid, safe, selective & sustained depletion of disease-causing immune cells

01

Potential best-in-class anti-CD38 agent

Leadership in immune modulation

02

Pipeline in a product

Potential for multiple indications in auto-immune diseases

03

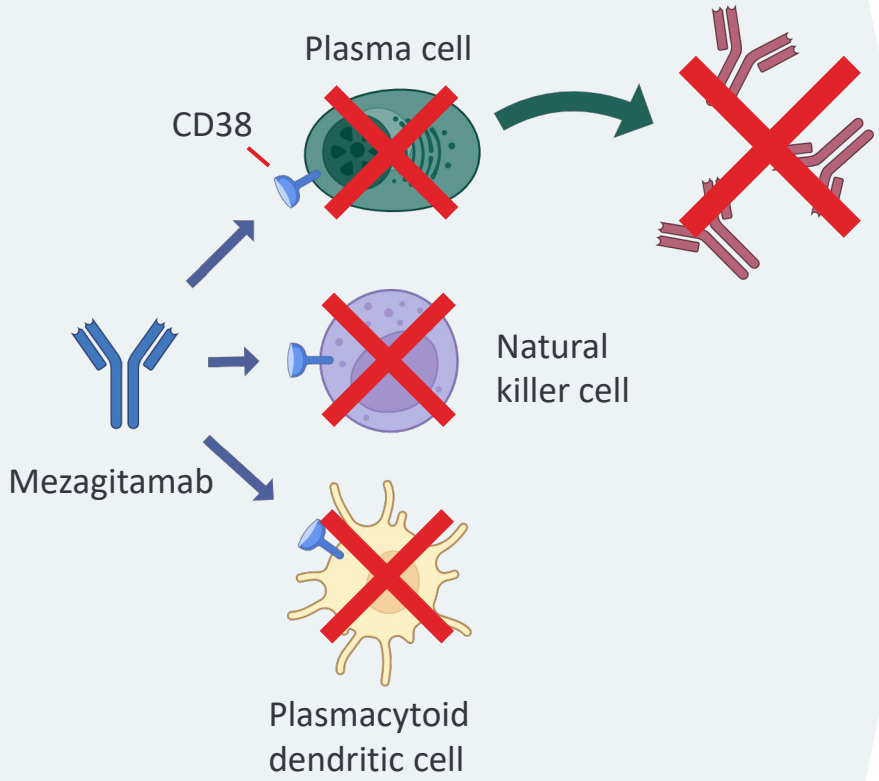
Proof of concept in ITP and IgAN

Setting new standard for ITP and IgAN patients

Mezagitamab is designed for rapid, selective, safe and sustained depletion of immune cells

Selective targeting of CD38 **directly depletes long and short-lived plasma cells** which produce pathologic autoantibodies

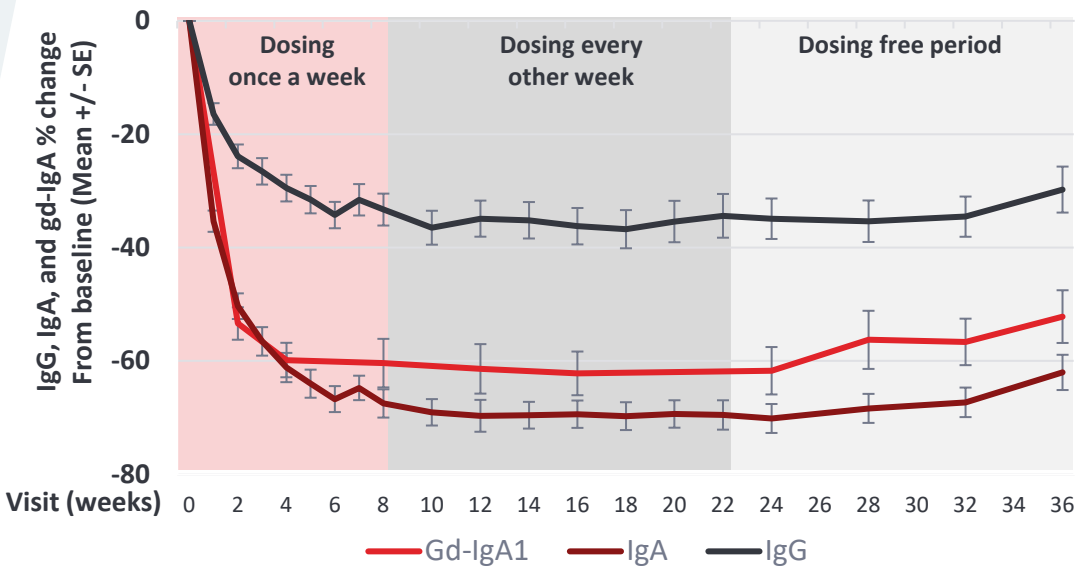
High efficacy & **sustained response** with **disease modifying potential**



Rapid and robust antibody reduction observed in multiple indications[1]

- IgG up to **41%**
- IgA up to **70%**
- Gd-IgA1 up to **62%**

Antibody reduction in patients with IgAN[1]

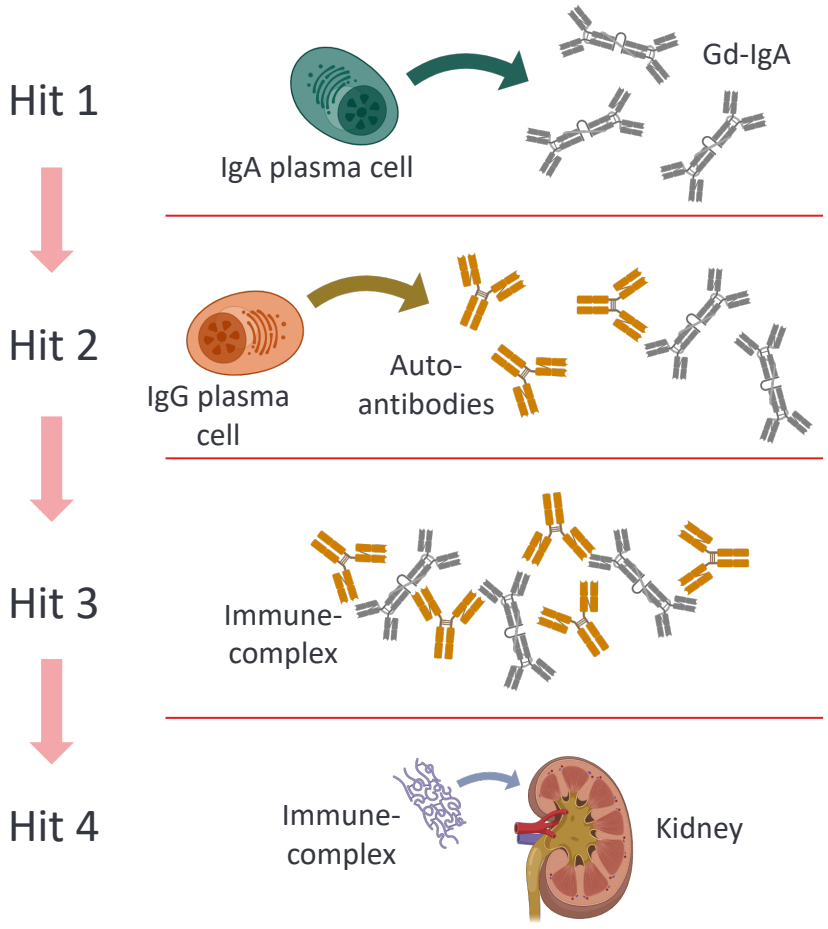


1. Barratt J, et al. ASN 2024 Poster FR-PO857, Oct 25, 2024

Understanding IgA Nephropathy (IgAN) pathophysiology and the consequences for patients

- IgAN is a **chronic progressive autoimmune mediated kidney** disease usually diagnosed between the ages of 16 and 35
- Patients with IgAN may present with hematuria, proteinuria, nephrotic syndrome, rapidly progressing glomerulonephritis and even **kidney failure**

4-hit model of IgAN pathophysiology[1-3]



Plasma cells produce circulating galactose-deficient (Gd-) IgA1

Other plasma cells produce IgG & IgA autoantibodies against Gd-IgA1

Formation of pathogenic immune-complexes of IgG and Gd-IgA1

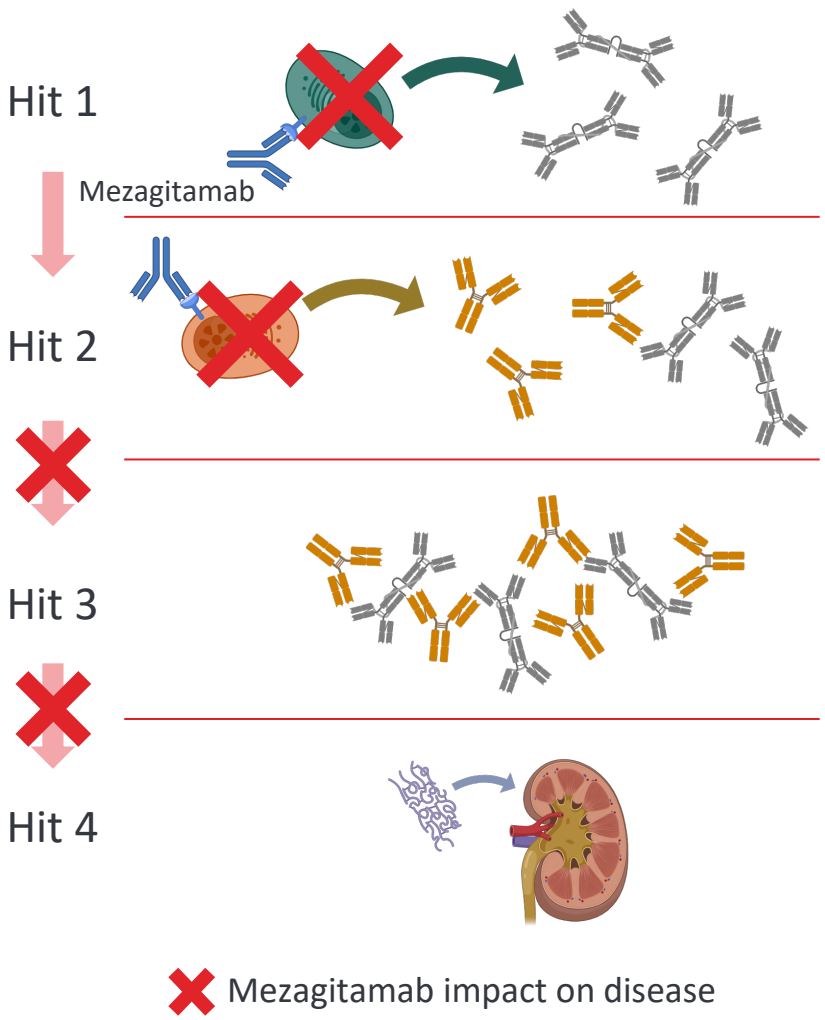
Deposition of pathogenic immune-complexes in kidney leading to IgA Nephropathy

1. Suzuki H, et al. J Am Soc Nephrol. 2011; 22(10):1795–1803.
2. Karoui K EL, et al. JASN 2024; 35: 103-116.
3. Cheung CK, et al. Frontiers in Nephrol. 2024 review

Mezagitamab addresses the root causes of IgAN, thereby delivering a sustained disease-modification (including off-treatment)

Mezagitamab treatment leads to profound and sustained reduction in levels of pathogenic auto-antibodies by depleting plasma cells

4-hit model of IgAN pathophysiology[1-3]



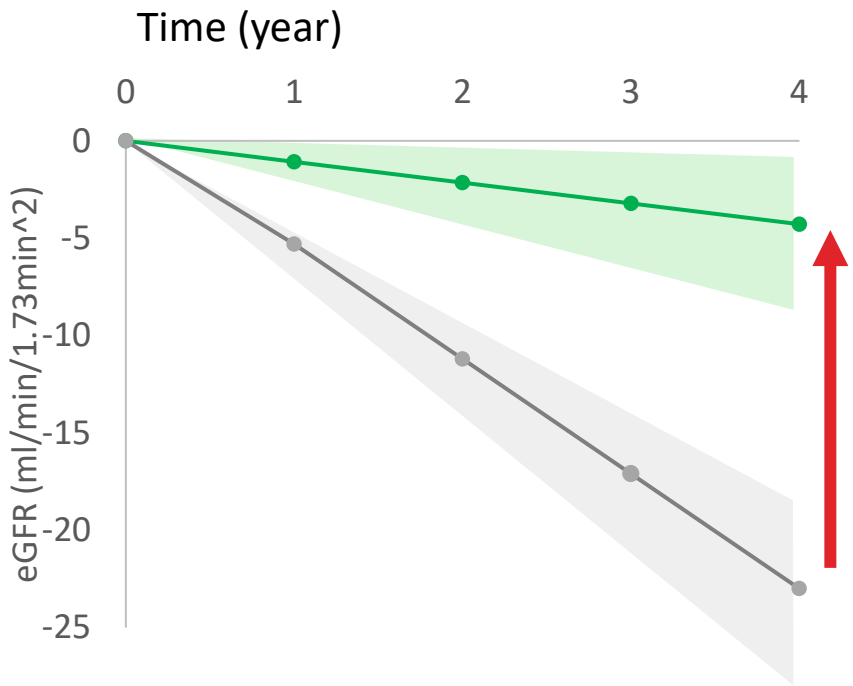
Mezagitamab targets the initial steps in IgAN pathophysiology (Hit 1 and 2)[1-3]

- Binding to CD38, mezagitamab depletes IgA and IgG producing plasma cells
- This suppresses the production of the abnormal IgA and the IgG autoantibodies.
- Disrupts the formation of pathological immune-complexes and
- Thus, prevents further damage to/loss of nephrons, thereby preserving kidney function (stabilization of eGFR).

1. Suzuki H, et al. J Am Soc Nephrol. 2011; 22(10):1795–1803.
2. Karoui K EL, et al. JASN 2024; 35: 103-116.
3. Cheung CK, et al. Frontiers in Nephrol. 2024 review

Unmet need in IgAN is for a transformative disease modifying treatment that preserves kidney function

The primary goal of IgAN treatment is to halt the chronic kidney injury thereby preserving renal function (eGFR)



Mezagitamab's goal:

Functional cure[1]

Goal is to significantly improve over SoC nearing or achieving functional cure

Current SOC and approved IgAN treatments[2-10]

Unmet needs remain

Need for disease modifying treatment that,

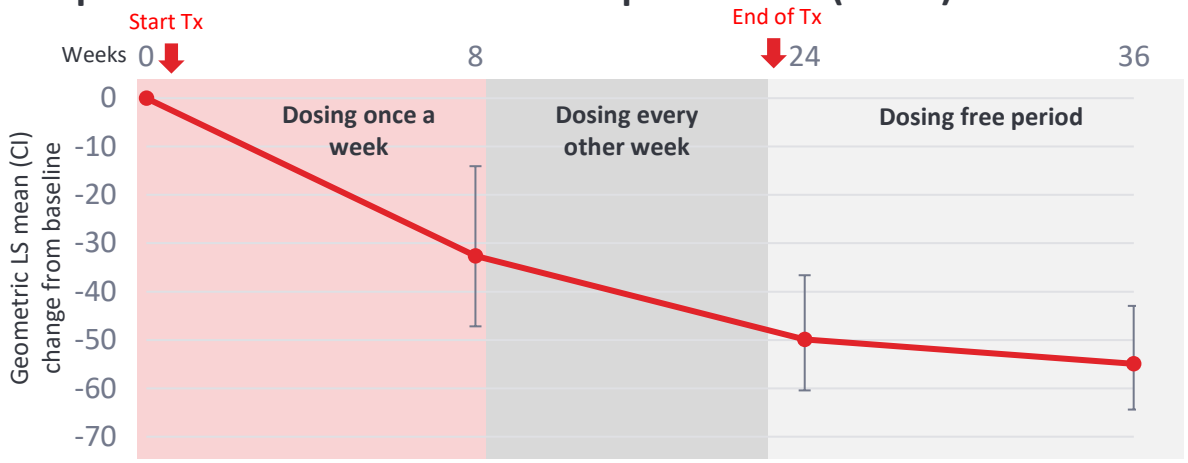
- **Stops the chronic kidney damage**
- **Prevents** the progressive **loss** of **renal function** (eGFR)
- Is **safe** and **well-tolerated**
- Allows for **convenient dosing and extended dosing-free intervals**

1. Baba M, et al. PLoS ONE 2015; 10 (6): e0129036. 2. Lafayette R, et al. Lancet 2023; 402: 859-70. 3. Rovin BH, et al. Lancet 2023; 402 (10417): 2077-2090; 4. Li PK-T, et al. Am J Kidney Dis 2006; 47 (5): 751-60; 5. Manno C, et al. Nephrol Dial Transplant 2009; 24 (12): 3694-3701; 6. Lv J, et al. JAMA 2017; 1; 318 (5) 432-442; 7. Wheeler DC, et al. Kidney Int 2021; 100 (1): 215-224; 8. Lv J, et al. JAMA 2022; 327 (19) 1888-1898; 9. Zhang H, et al. ASN Kidney Week 2023, poster TH-PO1123; 10. Mathur M, et al. N Engl J Med 2023; 390: 20-31.

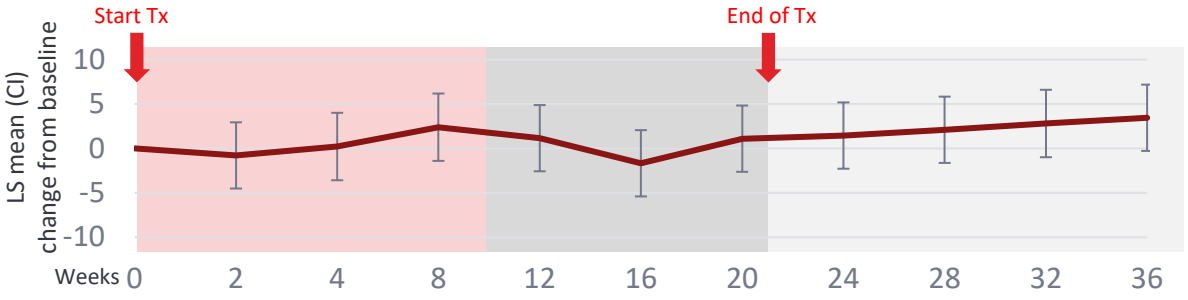
Mezagitamab in POC study was well tolerated and showed rapid, sustained best-in-class UPCR reduction in patients with IgA nephropathy

Mezagitamab IgAN Phase 1 data[1]

Rapid and sustained reduction in proteinuria (UPCR)



Stable renal function (eGFR)



Best-in-Class Efficacy

- Mezagitamab demonstrated **rapid and sustained reduction of serum IgA, IgG and gd-IgA1** over time during the treatment period
- Urinary protein creatine ratio **(UPCR) was reduced by 55%**
- **Renal function (eGFR) was stable** over 36 weeks, including 14 weeks off-treatment (follow-up ongoing)

- **No discontinuations of study**; 6 patients (35%) had a related hypersensitivity TEAEs mostly mild events. No grade 3 or more infections.

Regulatory interactions ongoing
Target Phase 3 start FY2025

1. Barratt J, et al. ASN 2024 Poster FR-PO857, Oct 25, 2024

Potential best in class (anti-CD38) disease modifying agent in IgAN

Not Disease Modifying	Disease Modifying Potential	
	Targeting B-cells	Targeting Plasma Cells
Corticosteroid *Complement inhibitors* *ETA(AT1) inhibitors* *ACE/ARB* *SGLT2 inhibitors*	*Anti-APRIL* *Anti-APRIL/BLyS*	*Anti-CD38*
✗ **Acts upstream (Hit 1/Hit 2)**	✓ **Acts upstream (Hit 1/Hit 2)**	✓ **Acts upstream (Hit 1/Hit 2)**
✗ **Stops eGFR loss**	✓ **Stops eGFR loss**	✓ **Stops eGFR loss**
✗ **Treatment holiday**	✗ **Treatment holiday**	✓ **Treatment holiday**

Mezagitamab

- ☑ **Stabilizing** renal function
- ☑ **Efficacy** maintained **off-treatment**
- ☑ **NOT** targeting memory B cells
- ☑ **Best-in-class** antibody reduction

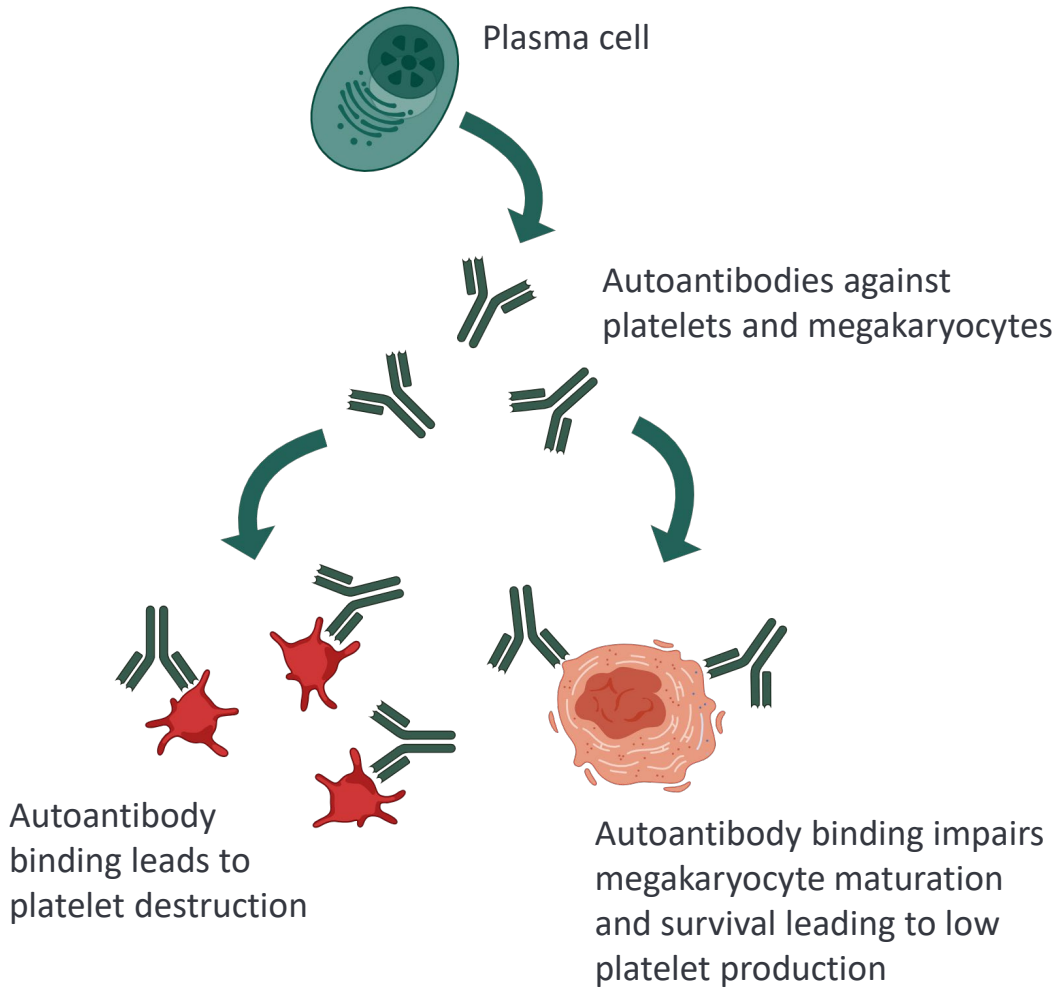
Target profile based on Ph2 results

Scoring is based on either approved label and/or clinical data to date. Mezagitamab's target profile is based on Ph2 results. There have been no head-to-head studies to date.

Understanding immune thrombocytopenia (ITP) and its consequences for patients

- ITP is a rare **chronic disorder** characterized by an **autoimmune** response **against platelets** and megakaryocytes leading to low platelet count in the blood
- ITP patients have an **increased risk of bleeding**, including risk of fatal hemorrhage. Disease is also accompanied by fatigue and reduced QOL.

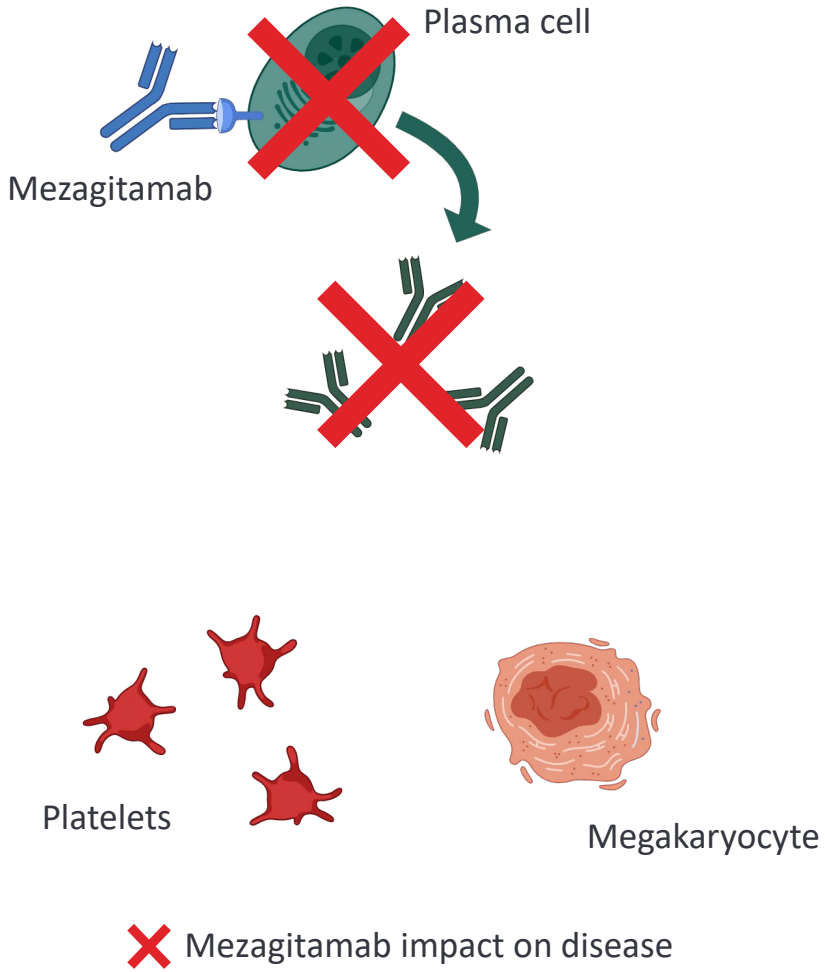
ITP pathophysiology[1-8]



1. Fedyk ER, et al. Brit J Clin Pharmacol. 2020;86(7):1314–25; 2. Audia S, et al. Hemasphere. 2021;5(6):e574; 3. Singh A, et al. J Clin Med. 2021;10(4):789; 4. Zufferey A, et al. J Clin Med. 2017;6(2):16; 5. Alabbad S, et al. Biodrugs. 2020;34(5):557–66; 6. Cooper N, Ghanima W. N Engl J Med. 2019;381(10):945–55; 7. Vollenberg R, et al. Haematologica. 2019;104(6):1237–43; 8. Roepcke S, et al. Pharmacol Res Perspect. 2018;6(3):e00402.

Mezagitamab addresses the root causes of ITP, delivering a sustained disease-modifying treatment

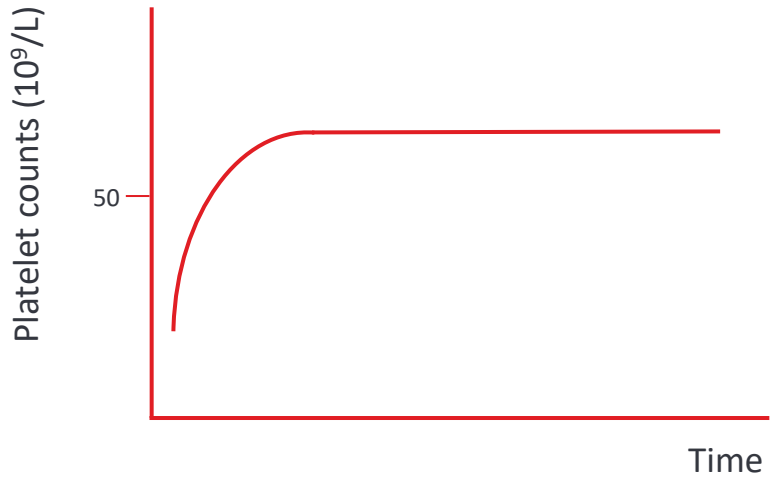
- Binding to CD38, mezagitamab **depletes IgG** producing **plasma cells**
- This **suppresses the production of the IgG autoantibodies** and leads to a profound and **sustained reduction** in levels of pathogenic auto-antibodies **against platelets and megakaryocytes**



Current ITP treatments leave clinical unmet needs

The primary goal of ITP treatment is to quickly and sustainably restore safe levels of platelets

Stable platelet count over time[1]



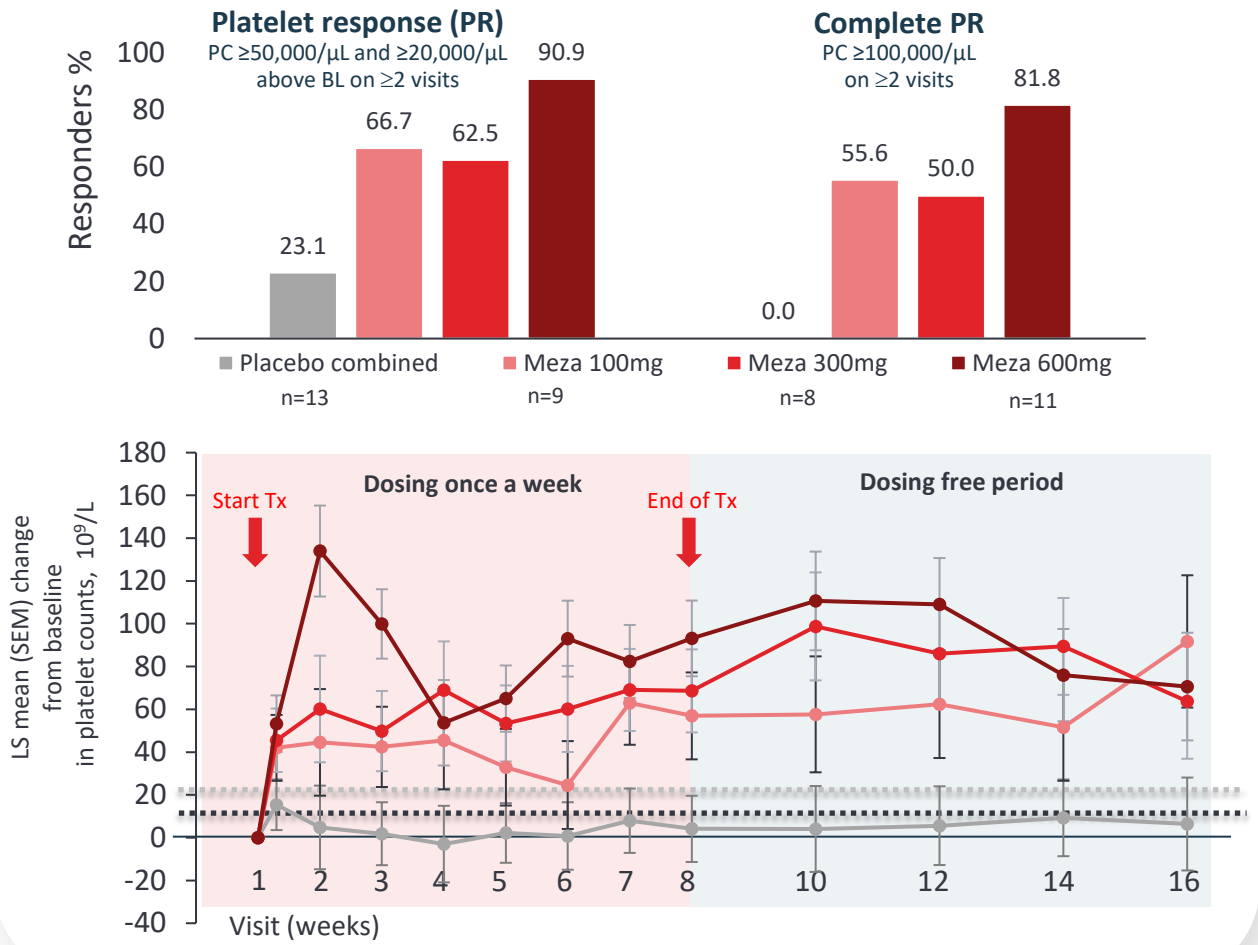
Patients want new novel treatments that deliver

- Durable platelet response
- Long-term remission off-treatment
- No bleeding events
- Favorable safety profile
- Improved QOL

1. Provan D, et al Blood Advances 2019; 3 (22) 3780-3817

Mezagitamab demonstrated rapid and sustained improvement in multiple efficacy measures of durable platelet response in patients with immune thrombocytopenia

Mezagitamab ITP Phase 2b data[1]



Robust and Sustained Efficacy and Favorable Safety[1]

- Efficacy was demonstrated in highly refractory patients **with many previous ITP treatments** (1-13 previous treatments)
- **No bleeding events** reported in patients on 600 mg mezagitamab vs 14 on placebo arm
- ~1/3 of patients who had received mezagitamab had a **sustained platelet** response at week 24 off-treatment (up to 16 weeks **off-treatment)**
- Overall, the **incidence of TEAEs was similar** between patients treated with **mezagitamab** and patients on **placebo**

1. Kuter D, et al. ISTH 2024 Oral Presentation, June, 2024

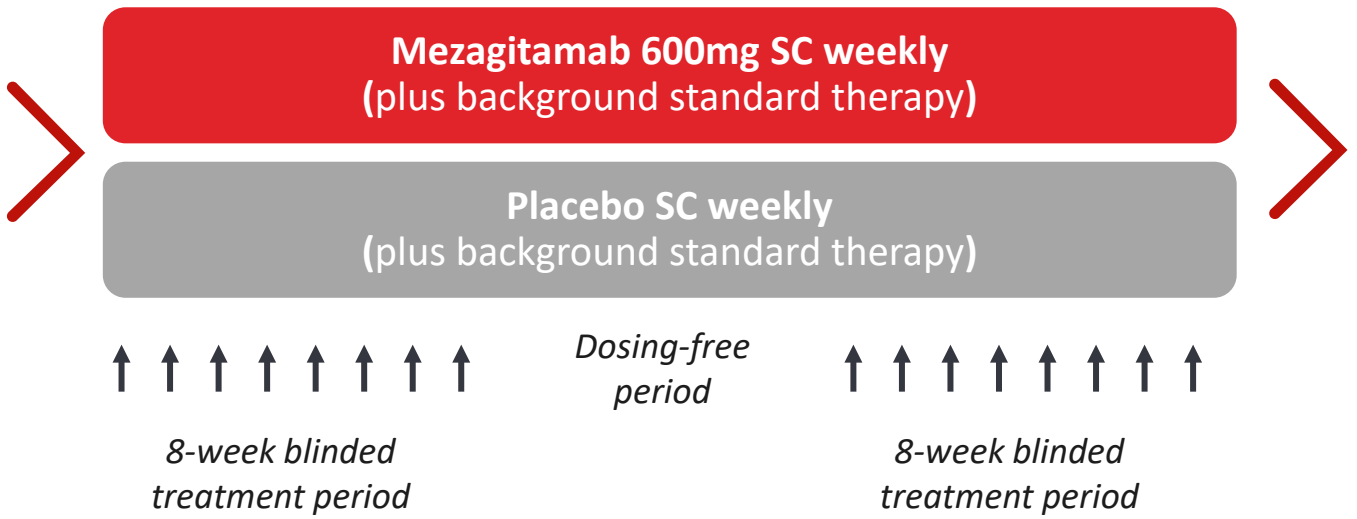
ITP phase 3 pivotal study – expected to start Q4 FY2024

Mode of action permits cyclic dosing thus allowing patients to have extended treatment free periods

Inclusion criteria:
ITP pts with insufficient response or intolerance to ≥2 prior treatments

N=171

Randomization
2:1



Primary Endpoint:

Durable platelet response
- Response is, platelet count ≥50,000/µL on ≥4 of 6 weekly platelet measurements (wk 19 to wk 24)

Key Secondary Endpoints:

Durability of response
- Durability is, cumulative number of wks that a platelet count was ≥50,000/µL up to wk 24

Time to platelet response

Complete platelet response

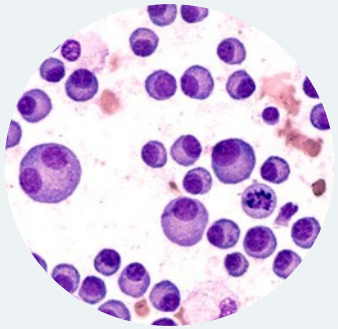
Target filing in ITP – FY28/29

Mezagitamab

Market Opportunity

Well positioned to be the best-in-class anti-CD-38 agent to transform the IgAN and ITP markets by setting new standard for patients

Mezagitamab: a transformative approach to combat autoimmune diseases



Targets plasma cells

The direct source of auto-antibodies production

Disease modifying treatment potential

Rapid and sustained disease remission

Dosing holiday enhances potential for safety and convenience

Subcutaneous dosing with extended treatment-free periods

Pipeline in a Product

Proof of concept in IgAN & ITP and potential for multiple new indications

IgAN patients often experience progressive and irreversible loss of kidney function leading to end stage kidney disease

ILLUSTRATIVE PATIENT EXPERIENCE WITH IgAN

1 …First visible symptoms **Blood in urine**

2 …Diagnosis often in **teens or young adults**

Initiation of supportive care therapies (1L)

3 … Progressive **loss of renal function** and **irreversible kidney damage**

~1 in 2 patients experience loss of kidney function while on SOC[1]

4 …End stage kidney disease Need for **dialysis and kidney transplant -** Significant impact on QOL and mortality

~ 1 in 5 patients experience renal failure within a decade[2]

There are no approved therapy that specifically target the underlying cause of the disease and stop the disease progression

1. Therapy of IgA nephropathy: time for a paradigm change; Jonathan Barratt 1, Richard A. Lafayette 2 and Jürgen Floege 3
2. https://www.niddk.nih.gov/health-information/kidney-disease/iga-nephropathy#what. Accessed October 2024.

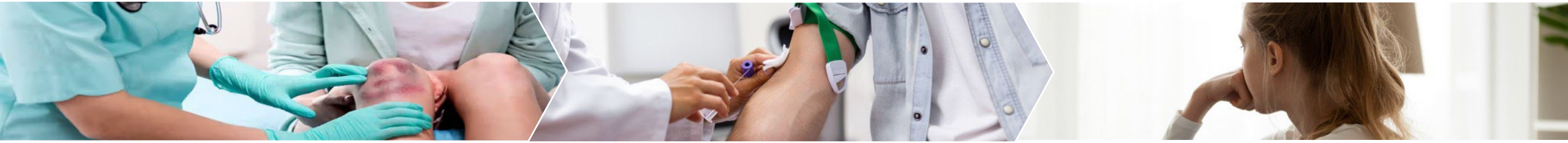
Mezagitamab has the potential to stop the disease progression and address the root cause of the disease in IgAN

Establish the CD38 class as a new transformative approach to combat IgAN disease, a plasma cell driven disease

Differentiate mezagitamab as best-in-class CD38 in a subcutaneous dose

1. Internal estimates based on exhaustive Literature review
2. Clinical characteristics and treatment pattern of children and adults with IgA Nephropathy or IgA Vasculitis: Findings from the CureGN study, 2018

In ITP, current therapies leave many patients struggling with their disease and looking for improved treatment options in 3L



ILLUSTRATIVE PATIENT EXPERIENCE WITH ITP

…**Newly Diagnosed ITP**
(0-3 months post Dx)

1

…Diagnosis (Dx) following severe bleeding or routine check-up

initiate short course of steroids

…**Persistent / Chronic ITP**
(>3 months post Dx)

2

…Chronic treatment initiation

…**Refractory** to 2 lines of therapies

3

…Platelet count defines patients' life

Significant impact on QOL

1 Line | 2 Line | 3 Line

*"I would love to **see the underlying disease process stopped.** My treatment is good, but my body is still targeting and destroying my platelets."*
– ITP Patient

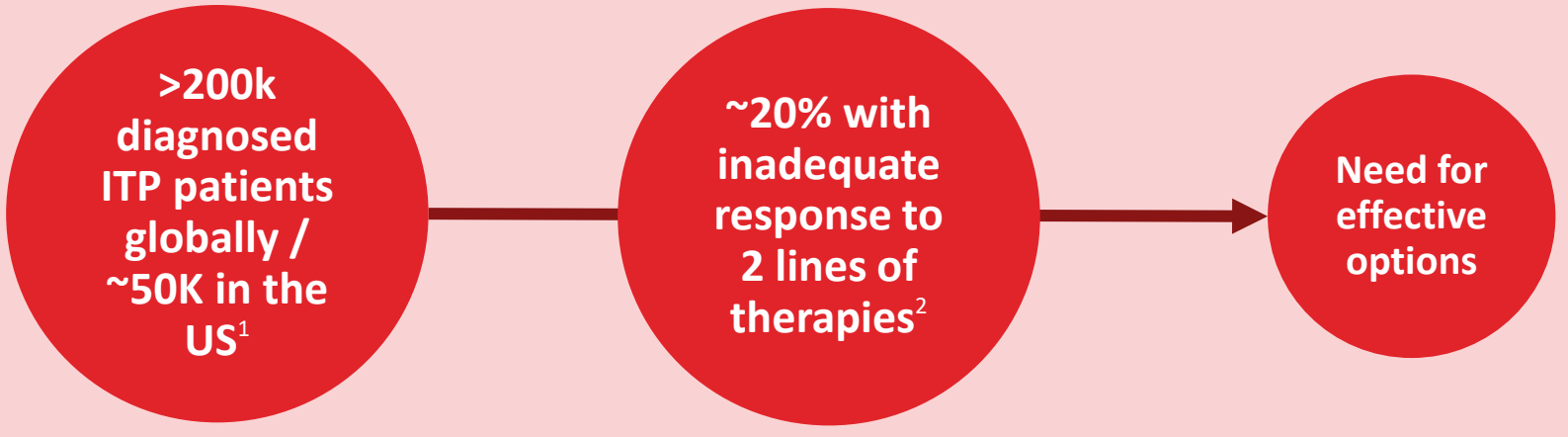
*"We need therapies that allow us to achieve **treatment-free remission; being able to stop treatment is important.**"*
– KOL

*"Treatment beyond second-line does not give both a **complete and a lasting response….**"*
– ITP Treater

***"My veins are shot from all the blood tests** and I bruise all over my arms. It is hard to have the constant draws."*
– ITP Patient

Efficacy of 3L agents are limited

The need for effective treatment for patients not responding well to current standard of care in ITP creates an opportunity for mezagitamab



Redefine what success looks like

Differentiate mezagitamab as 1st choice in patients not responding well to current standard of care

1. Internal estimates based on exhaustive Literature review
2. 2024 Komodo Claims analysis

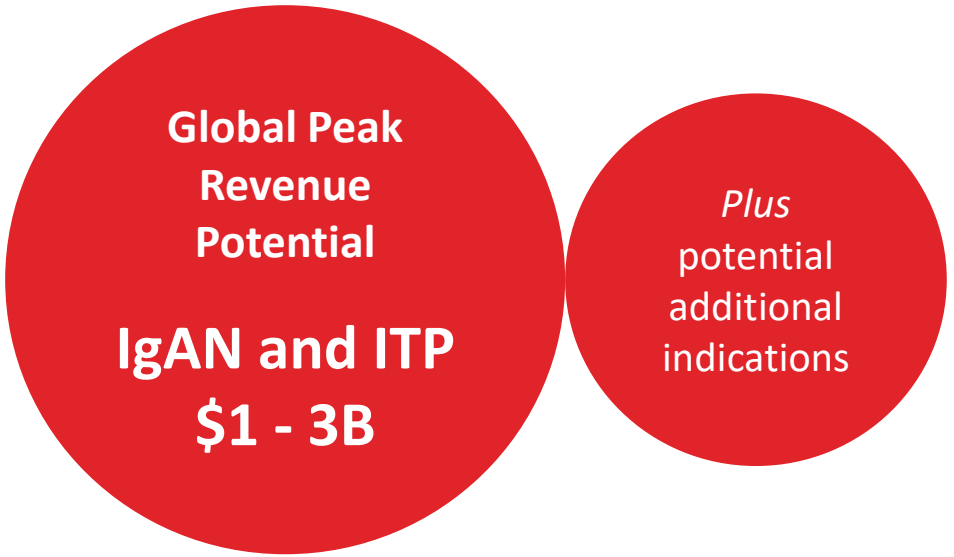
Potential to deliver a transformative profile, addressing the root cause in auto-immune diseases

IgAN ambition

- 1st anti-CD38 choice
- Stop progression of disease (eGFR stabilization) with sustained kidney protection off-treatment
- Promise of treatment holiday (half of year)
- Favorable safety and tolerability profile

ITP ambition

- 1st choice in patients not responding well to current standard of care
- Sustained platelet restoration with treatment-free remission periods
- Favorable safety and tolerability profile



Please refer to the Important Notice at the start of this presentation for more information about peak revenue estimates.

Unlocking the full potential of mezagitamab in autoimmune diseases – Summary Slide

Mezagitamab is well positioned to be the **best-in-class anti-CD38** agent with disease modifying potential and treatment holiday to **transform the IgAN and ITP treatment** by setting new standard for patients

POC studies demonstrated **stabilization of kidney function (eGFR)** in IgAN and **restoration of platelet count** in ITP, **with durable response off-treatment** and **favorable safety**

Continue **expanding the asset potential beyond IgAN and ITP** by prioritizing the most relevant indications to mezagitamab

Global peak revenue potential: $1-3B with IgAN and ITP alone with potential upside through new indications

Please refer to the Important Notice at the start of this presentation for more information about peak revenue estimates.

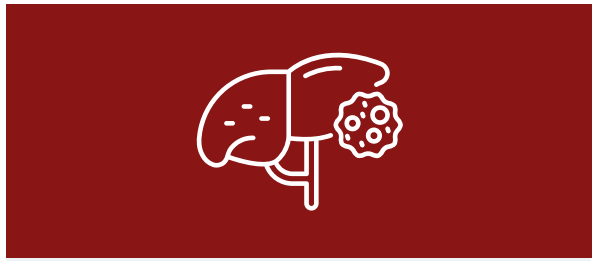
Fazirsiran

The potential of a transformative therapy for patients living with Alpha-1 Antitrypsin Deficiency Liver Disease (AATD-LD)

Better Health, Brighter Future

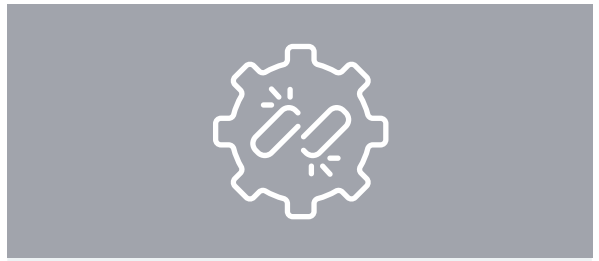
There are no treatment options available to Alpha-1 Antitrypsin Deficiency liver disease (AATD-LD) patients today

AAT Deficiency (AATD), a genetic disease, often results in a misfolded AAT protein and increases risk of liver and lung disease



AATD-LD is caused by to the aggregation of misfolded abnormal protein (Z-AAT) in the liver **leading to inflammation and fibrosis**[1, 2]

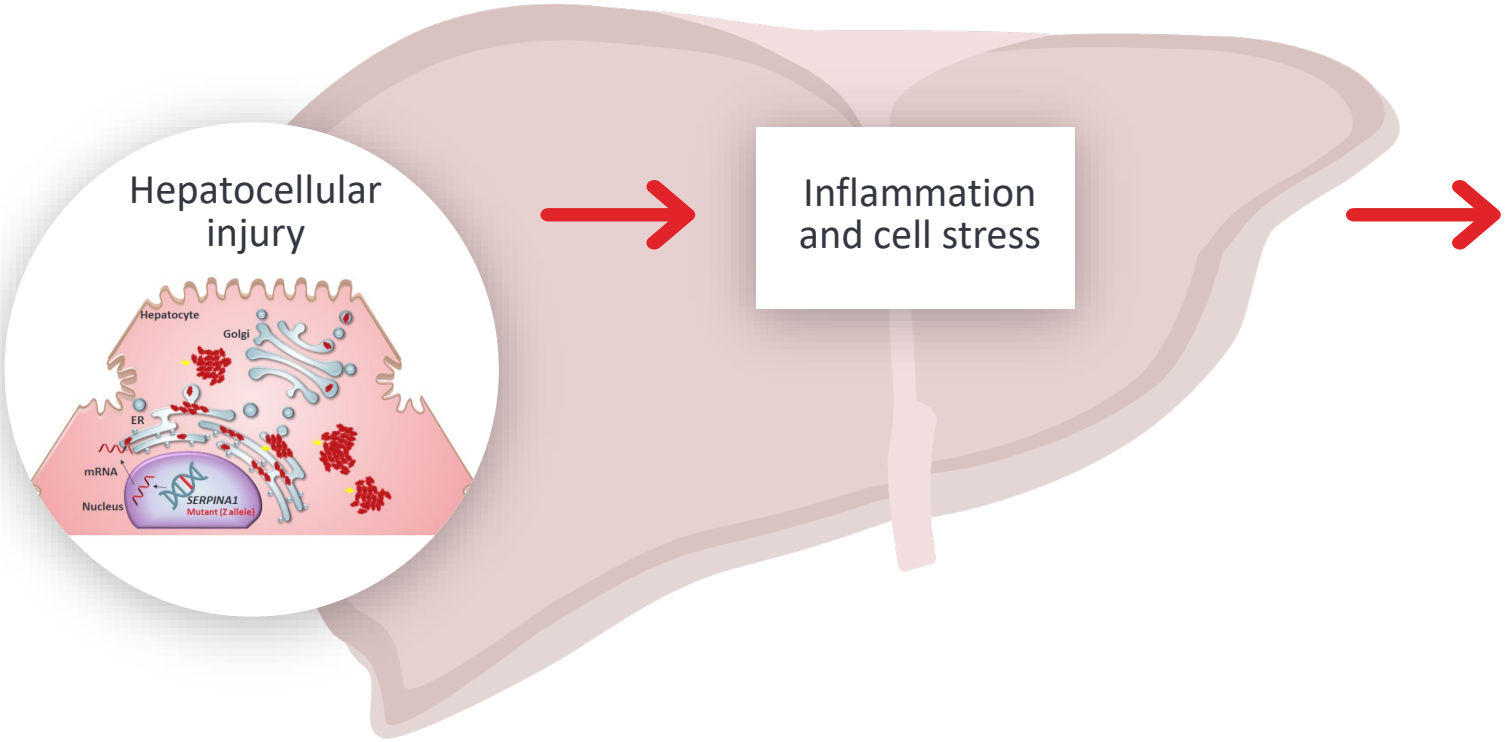
AATD-LD is a largely asymptomatic and **progressive chronic liver disease** that **has no approved treatments**[2]

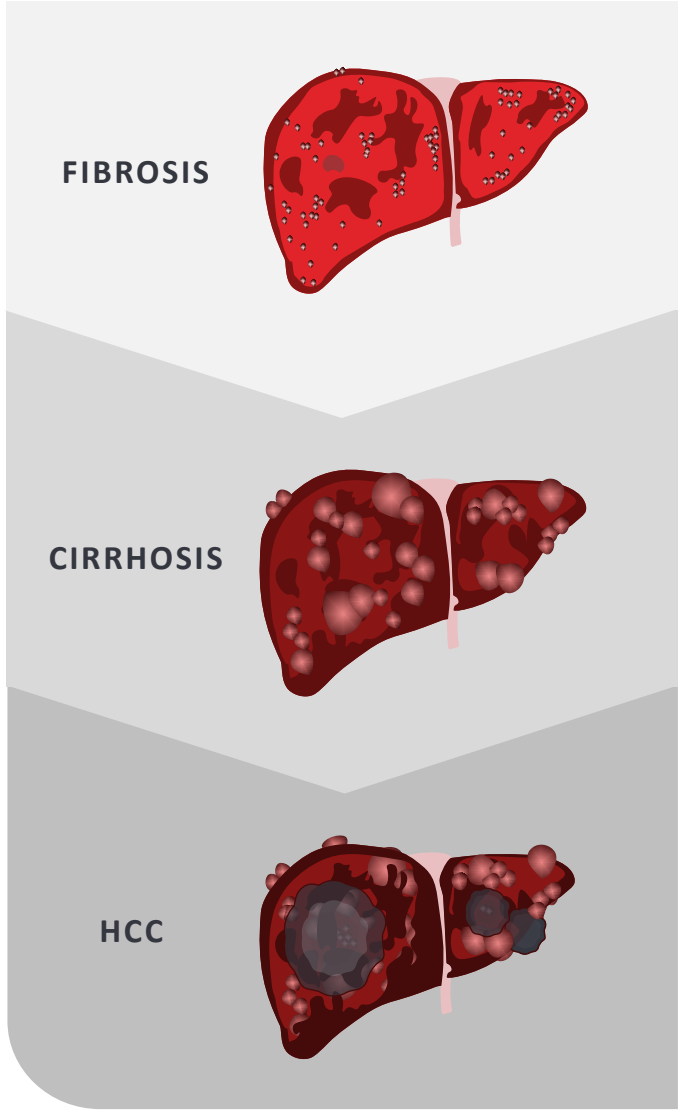


Fazirsiran treatment reduces/eliminates Z-AAT production, **removing the trigger for fibrosis** thereby **preventing progression to end-stage liver disease**[3, 4]

1. Teckman JH. *COPD.* 2013; 10 (Suppl 1):35-43; 2.Strnad P, et al. *N Engl J Med.* 2020;382(15):1443-55; 3. Strnad P, et al. *N Engl J Med.* 2022; 387(6):514-24; 4. WooddellCI, et al. *JCI Insight.* 2020;5(12):e135348.

Z-AAT polymer accumulation is known to cause fibrosis and end stage liver disease





Accumulation of **aggregated misfolded Z-AAT polymers** within hepatocytes causes **ER (proteotoxic) stress** which over time leads to chronic liver injury, with **fibrosis**, **cirrhosis**, and **HCC**[1,2]

ER: endoplasmic reticulum; HCC: hepatocellular carcinoma; Z-AAT: alpha-1 antitrypsin produced by the Pi*Z *SERPINA1* allele

1. Teckman JH. *COPD.* 2013;10(Suppl 1):35-43; 2. Strnad P, et al. *N Engl J Med.* 2020;382(15):1443-55.

Fazirsiran's mechanism of action stops the production of Z-AAT, directly addressing the pathology in AATD liver disease

1. **Fazirsiran** is a liver-targeted, **double-stranded siRNA**[1-3]
2. Fazirsiran leads to ***Z-AAT* mRNA degradation**[1,2]
3. Z-AAT protein **accumulation is reduced**[1,2]
4. The **liver can clear existing Z-AAT polymers** and **restore liver health**[2]

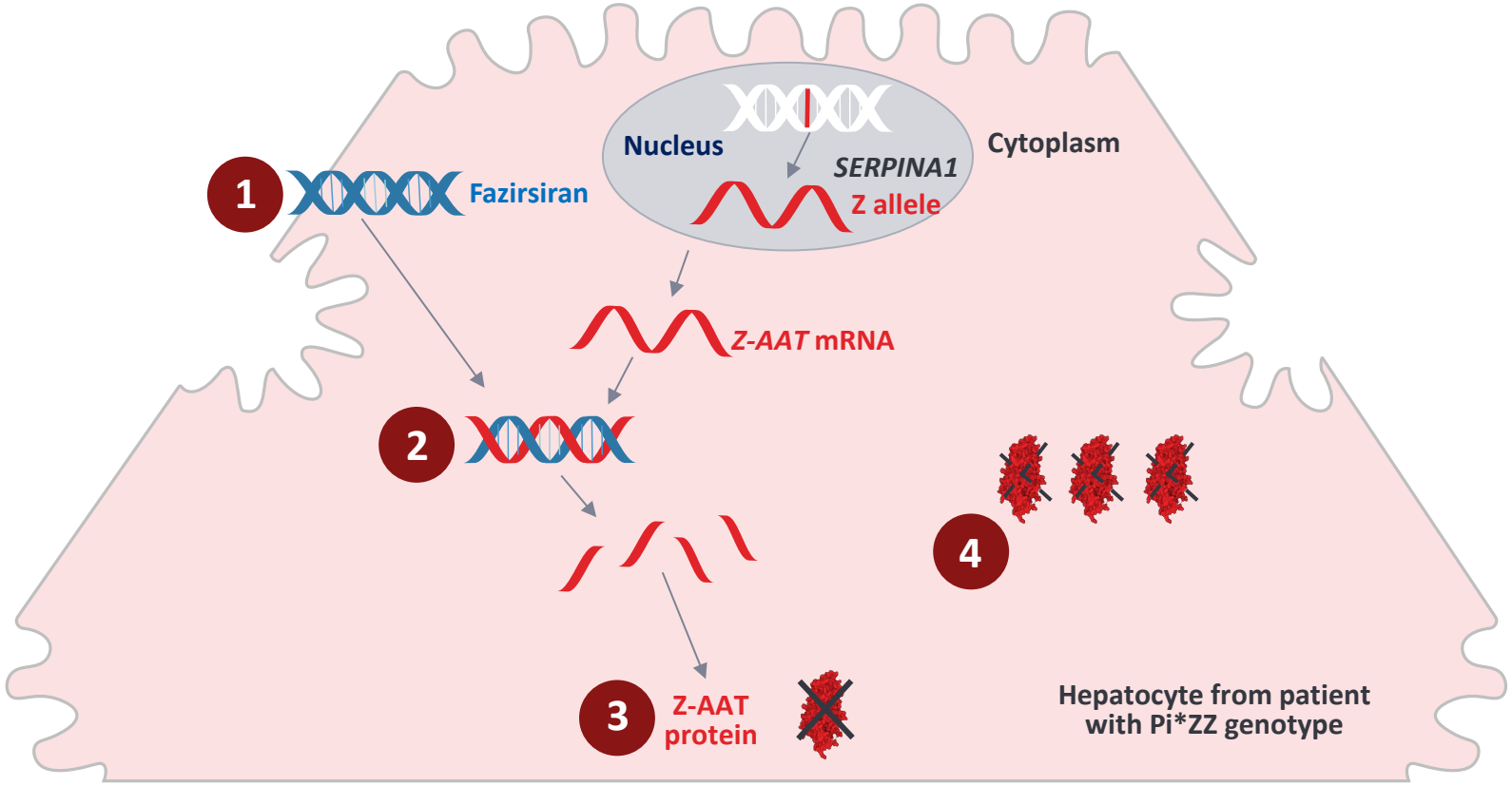


Figure adapted from Hu B, et al. *Signal Transduct Target Ther*. 2020;5(1):101.

AAT, alpha-1 antitrypsin; AATD, alpha-1 antitrypsin deficiency; DNA, deoxyribonucleic acid; GalNAc, N-acetylgalactosamine; mRNA, messenger ribonucleic acid; siRNA, small-interfering ribonucleic acid; Z-AAT, alpha-1 antitrypsin produced by the Pi*Z *SERPINA1* allele.

1. Wooddell CI, et al. *JCI Insight*. 2020;5(12):e135348; 2. Strnad P, et al. *N Engl J Med*. 2022;387(6):514-24; 3. Hu B, et al. *Signal Transduct Target Ther*. 2020;5(1):101.

Ph2 study intended to demonstrate reduction of liver Z-AAT

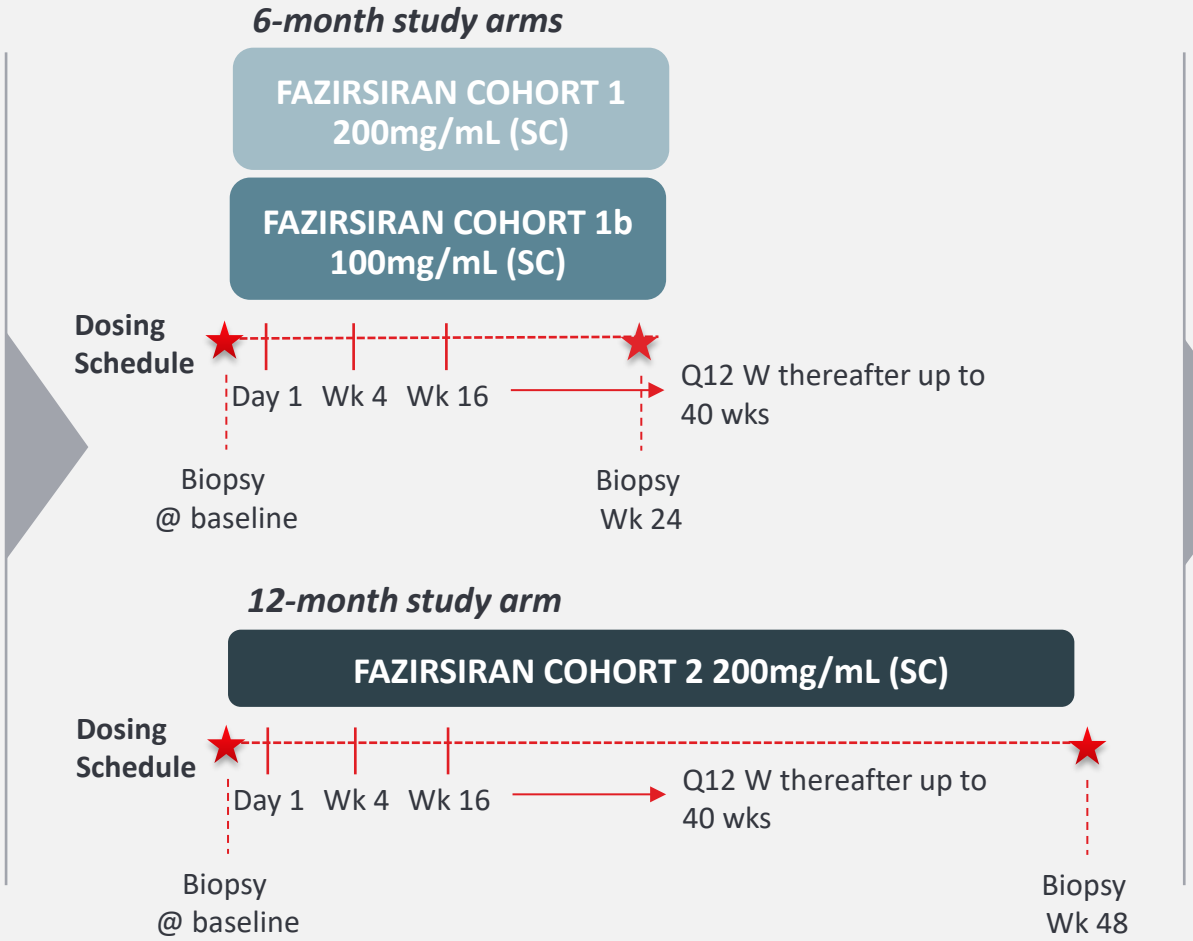
AROAAT2002: Ph2 study design[1,2]

Cohort 1 (n = 4)

Cohort 1b (n = 4)

Cohort 2 (n = 8)

Includes stage F1 – F3 patients



Primary Endpoint:

- Change from baseline in liver Z-AAT @ wk 24/48

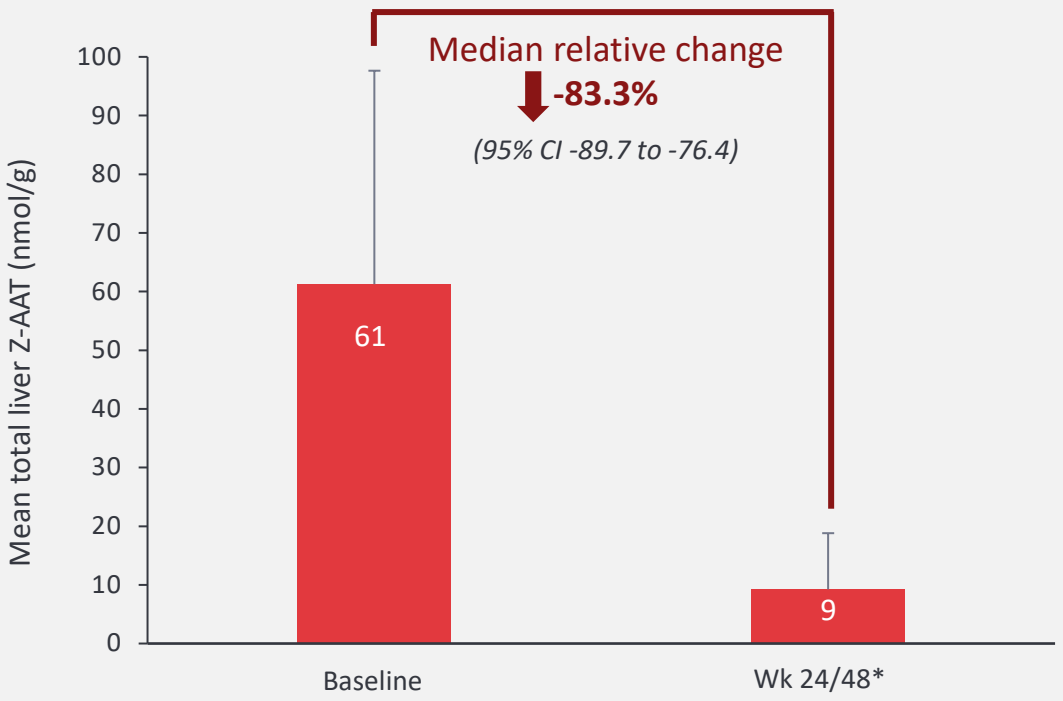
Secondary Endpoints include:

- Change from baseline in serum Z-AAT
- Treatment emergent AEs

1. Strnad P, et al. *N Engl J Med.* 2022;387(6):514-24; 2. Strnad P, et al. *N Engl J Med.* 2022;387(6):514-24 (Supplement).

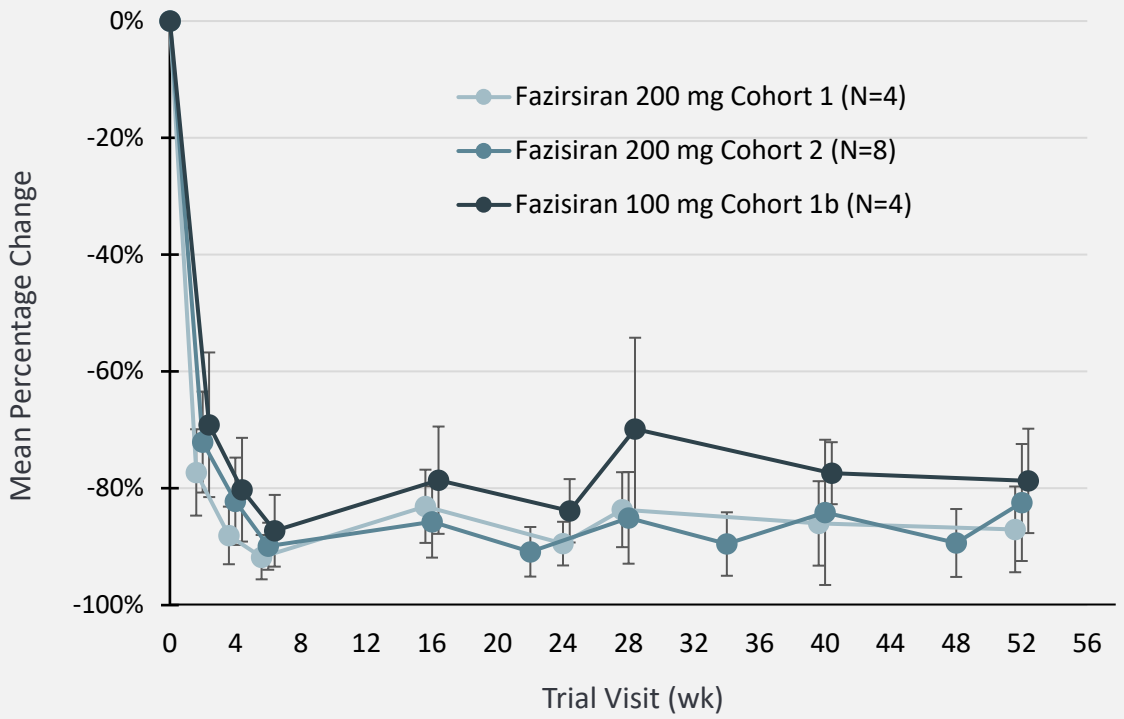
Ph2 POC study showed that fazirsiran treatment leads to significant reductions in serum and liver Z-AAT concentrations

Primary endpoint: Change from baseline in liver Z-AAT



Reductions in total accumulated liver Z-AAT were seen in all patients (n=14 evaluable)

Change from baseline serum Z-AAT



CI: confidence interval; Z-AAT: alpha-1 antitrypsin produced by the Pi*Z *SERPINA1* allele

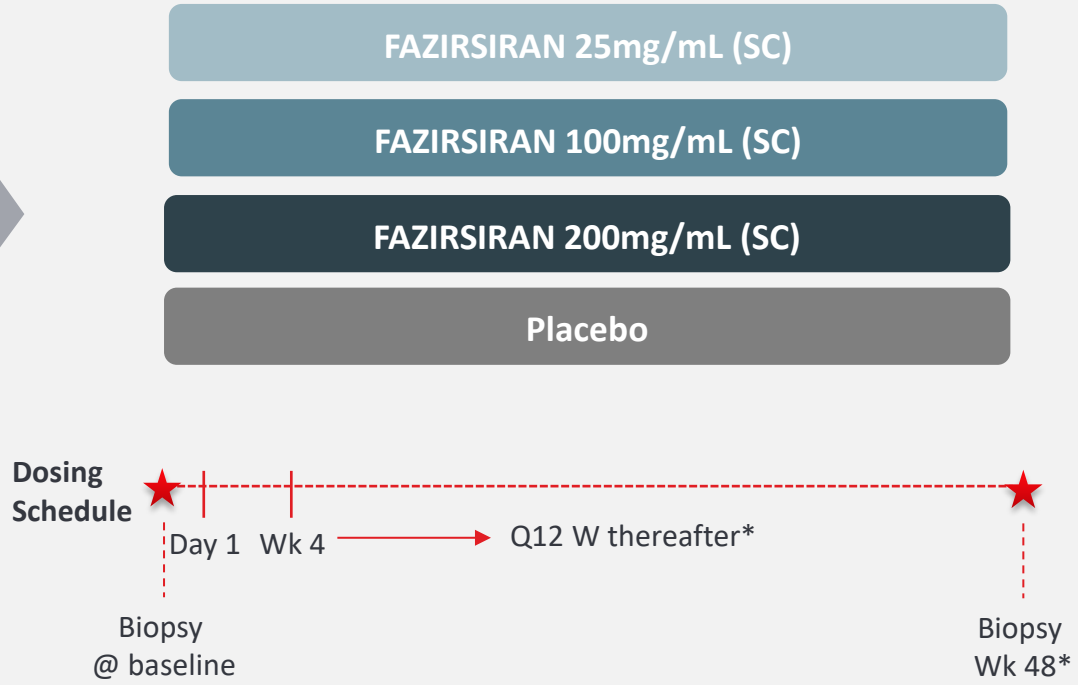
Strnad P, et al. *N Engl J Med.* 2022;387(6):514-24; *Week 24 in Cohorts 1/1b, Week 48 in Cohort 2

Randomized dose ranging placebo-controlled study that laid the foundation for Ph3 development

AROAAT2001 (SEQUOIA): Ph2 study design[1,2]

N = 40

Fibrosis <F4 or no fibrosis (based on previous liver biopsy)



Primary Endpoint:

- Percent change in serum Z-AAT @ wk 16

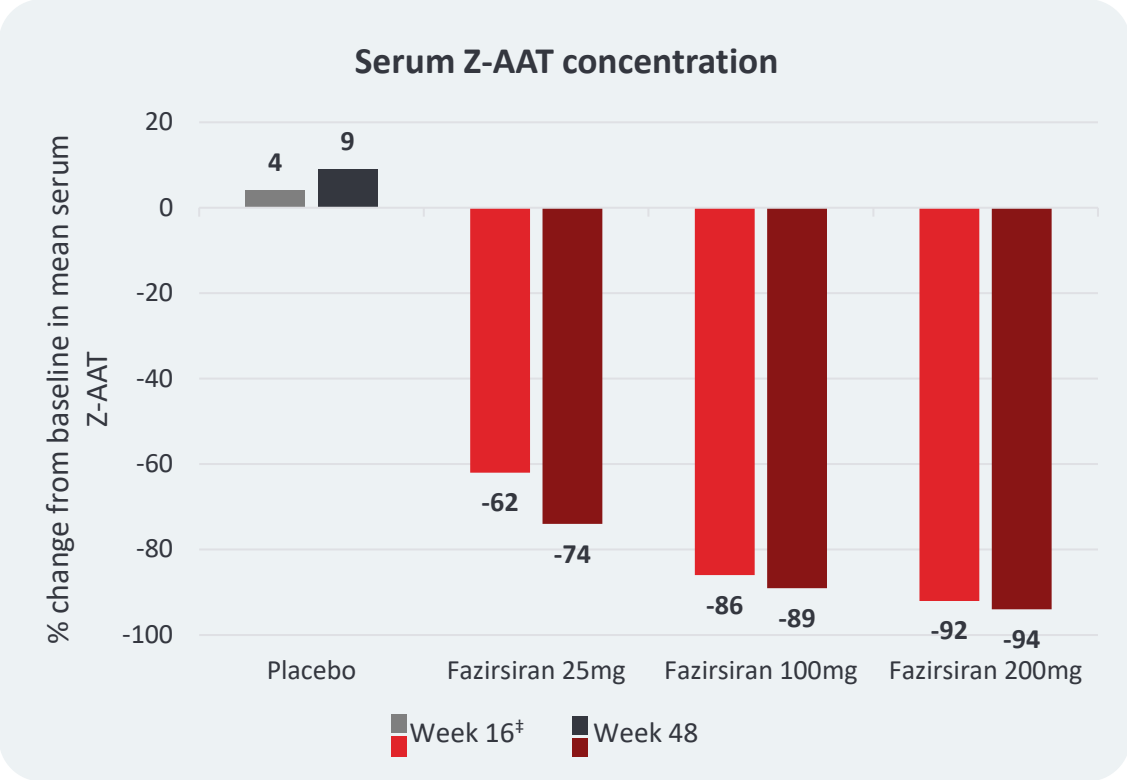
Secondary Endpoints include:

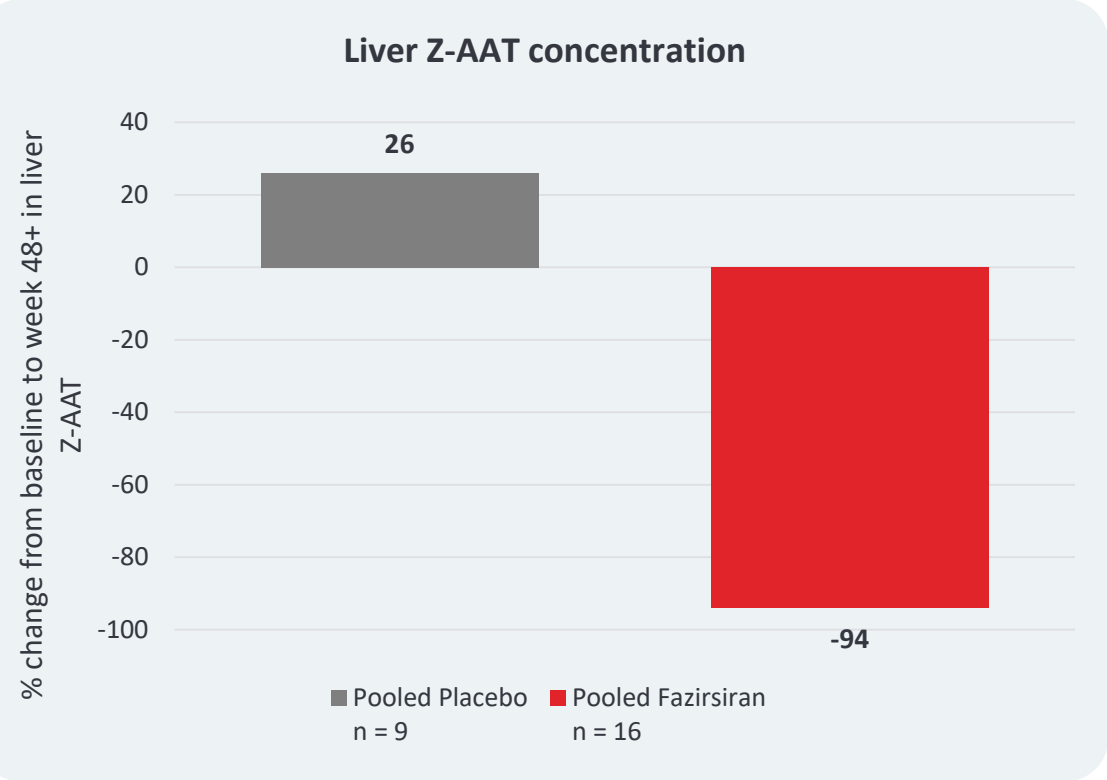
- Change from basline in serum and liver Z-AAT
- Treatment emergent AEs

*Patients with fibrosis at baseline had a post dose biopsy at week 48, 72, or 96. Q 12wk dosing after wk 4

1. ClinicalTrials.gov Identifier: NCT03945292. https://clinicaltrials.gov/ct2/show/NCT03945292; 2. Clark VC, et al. *Gastroenterology*. 2024; 2:S0016-5085(24)05181-3. online ahead of print.

Ph2 Placebo controlled study demonstrates fazirsiran's transformative potential in reducing Z-AAT





Fazirsiran reduced serum Z-AAT concentration in a dose-dependent manner

Fazirsiran reduced liver Z-AAT concentrations versus placebo from baseline to Week 48+

‡N=40 to Week 16; Reference: Fazirsiran SEQUOIA Topline Results. Arrowhead Pharmaceuticals website. https://ir.arrowheadpharma.com/static-files/ffc86cc4-7005-4f02-a538-ebcf0ed7de0a.

Strong safety profile demonstrated in Ph2, with no TEAE-related discontinuations, dose interruptions, or study withdrawals

Treatment emergent adverse events (TEAE)
AROAAT2001 (NCT03945292; Phase 2) [1]

Incidence, n (%)	Fazirsiran 25 mg (n=9)	Fazirsiran 100 mg (n=8)	Fazirsiran 200 mg (n=9)	Placebo (n=14)
TEAEs	9 (100)	8 (100)	9 (100)	13 (93)
Treatment-related TEAEs	2 (22)	4 (50)	4 (44)	8 (57)
Serious TEAEs	0 (0)	0 (0)	2 (22)	3 (21)
TEAEs in 4 or more subjects				
COVID 19	0 (0)	2 (25)	6 (67)	2 (14)
Headache	4 (44)	1 (13)	2 (22)	3 (21)
Procedural pain	1(11)	0 (0)	4 (44)	3 (21)
Arthralgia	2(22)	2 (25)	0 (0)	3 (21)
Diarrhea	2 (22)	1 (13)	0 (0)	2 (14)
Nausea	1 (11)	0 (0)	1 (11)	3 (21)
Back pain	1 (11)	1 (13)	2 (22)	0 (0)
Fatigue	1 (11)	1 (13)	0 (0)	2 (14)

- Serious TEAEs on fazirsiran 200 mg (infective exacerbations of bronchiectasis in participants with history of pulmonary disease receiving AAT augmentation therapy)
- Serious TEAEs on placebo [one patient with acute pancreatitis, influenza and staphylococcal wound infection; one patient (on AAT augmentation therapy) with decreased PFT and hypertensive crisis; and one with presyncope]

Consistent safety profile demonstrated in AROAAT2002:
Patients followed for 1.5-year, there were no deaths, discontinuations, or dose interruptions[2]

AAT: alpha-1 antitrypsin; PFT: pulmonary function test; TEAE: treatment-emergent adverse event; 1. Clark VC, et al. *Gastroenterology*. 2024; 2:S0016-5085(24)05181-3. online ahead of print. 2. Strnad P, et al. *N Engl J Med.* 2022;387(6):514-24

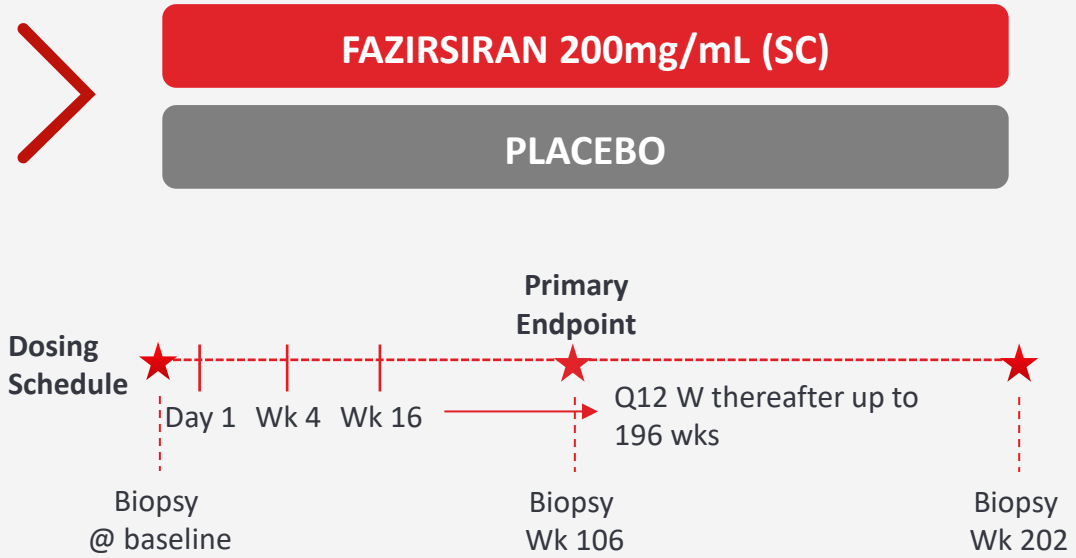
Fazirsiran Ph3 ongoing: target filing FY2028

Redwood Study (Ph3) Design[1]

n=160

Randomization 1:1

Includes stage F2 – F4 patients



Primary Endpoint:

- ≥ 1 point reduction in fibrosis score (F2-F3) by liver biopsy @ wk 106

Secondary Endpoint include:

- Percent change in total liver Z-AAT (F2-F3) @ wk 106
- ≥ 1 point reduction in fibrosis score (F2-F4) by liver biopsy @ wk 202
- Treatment emergent AEs

Exploratory Innovative Endpoints:

- Change in fibrosis as evaluated by AI

1. ClinicalTrials.gov Identifier: NCT05677971; https://clinicaltrials.gov/ct2/show/NCT05677971

Fazirsiran

Market Opportunity

Well positioned to be the first available treatment indicated for AATD associated Liver Disease

Fazirsiran represents an opportunity to offer hope in the form of a transformative therapy for patients living with AATD-LD

"I had lived a perfectly healthy life for 50 years when I suddenly became unwell with several subtle changes, then suddenly became jaundiced.

*I was **diagnosed with Alpha-1 Antitrypsin Deficiency [Liver Disease] and became very ill very fast**. I was only sick for 5 months before I was at a 40 MELD (Model for End-Stage Liver Disease) and earnestly dying.*

*I was given a **liver transplant** on April 1, 2017 with only hours left. I never thought about my liver until it got sick. **Your liver affects every part of your body and it won't tell you it's sick till it's very sick.***

*My family never knew we had the Alpha gene. Since my diagnosis, several have been tested and a **niece and nephew are diagnosed**, but thankfully they are aware and asymptomatic as of now."*

Linda K.

Source: American Liver Foundation: https://liverfoundation.org/about-your-liver/patient-stories/linda-k/

AATD-LD, an asymptomatic disease progression coupled with higher risks for cancer and liver transplant

ILLUSTRATIVE PATIENT EXPERIENCE WITH AATD -LD

Silently progressive liver disease

End stage liver disease

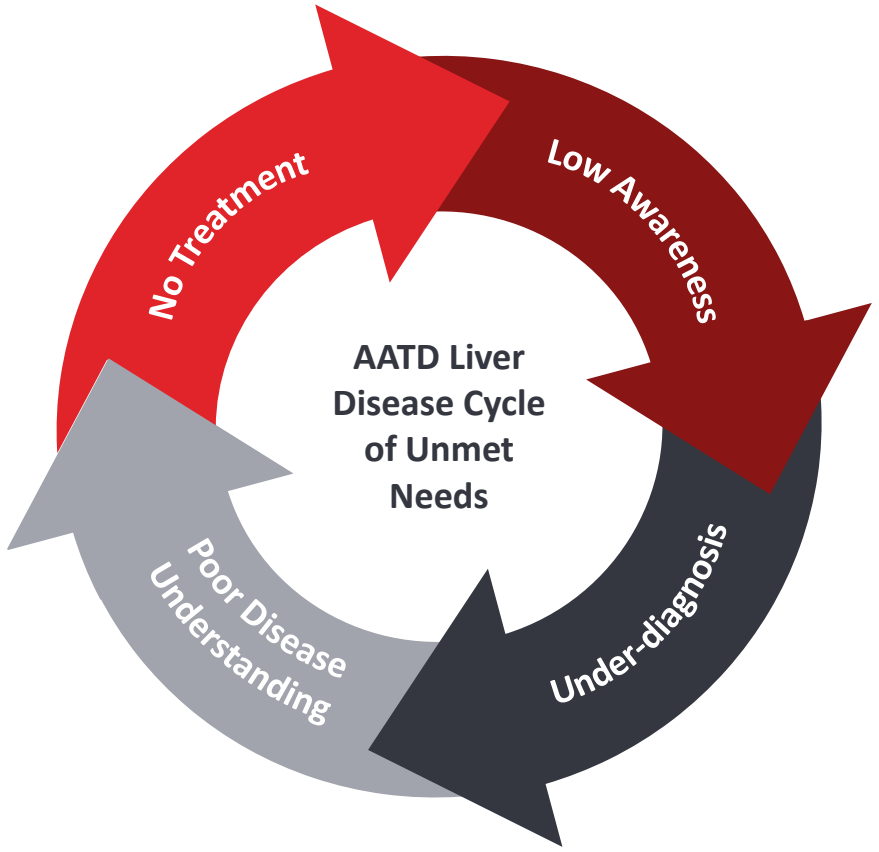
Undiagnosed → **+10 years** → **Diagnosed** → **+6 months** → **+1 year**

- Undiagnosed: Potential elevated LFTs; Misdiagnosis (e.g. MASH); Identification of lung disease?
- +10 years: Referral to hepatologist; Definitive AATD-LD diagnosis
- +6 months: Severe burden including e.g. jaundice, swelling, bleeding, confusion
- +1 year: Transplant; Liver cancer; Death

Patients living with AATD-LD have 20x risk of cancer[1] & 40x risk of liver transplant[2]

1. Fromme M, Schneider CV, Trautwein C, et al. Alpha-1 antitrypsin deficiency: A re-surfacing adult liver disorder. Journal of hepatology. 2022;76(4):946-58.
2. P S, CV S, V C. Clinical approach to liver disease in adults. In: Pavel S, Mark LB, Robert B, editors. α1-Antitrypsin Deficiency (ERS Monograph). Sheffield: European Respiratory Society,; 2019. p. 114–26..

AATD-LD has significant unmet needs anchored around the lack of available treatments, low awareness & low diagnostic rates



There are **no treatments available** to slow or stop progression to end-stage liver disease and liver failure in AATD patients

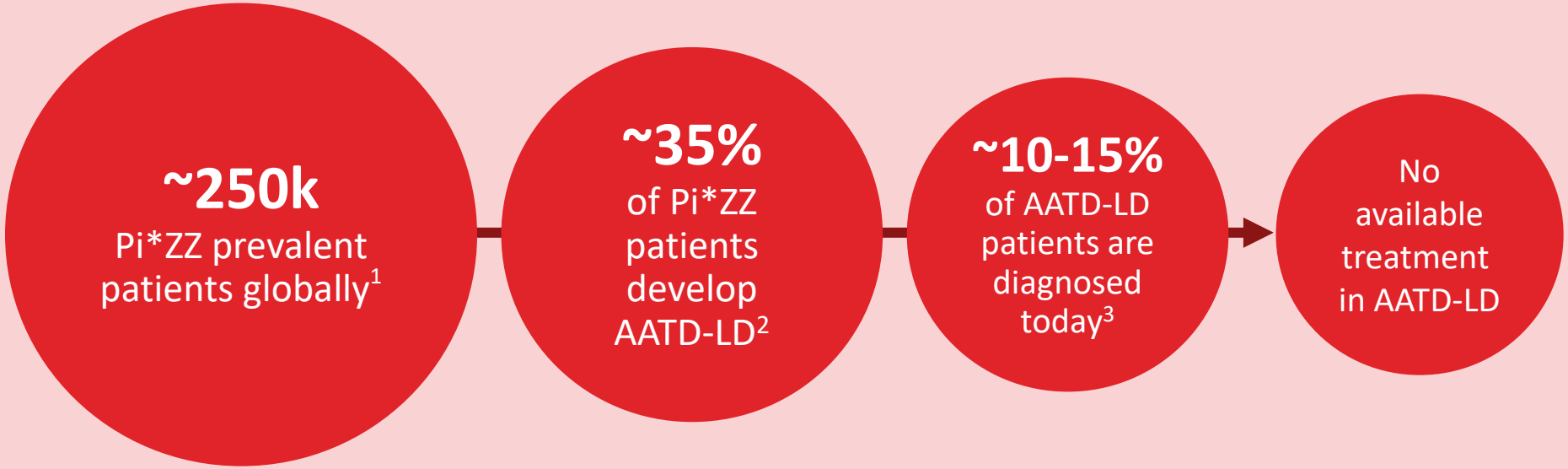
Disease awareness is low as a consequence of relatively low incidence and lack of treatment options

AATD liver disease **often goes undiagnosed** or misdiagnosed as other-cause liver disease (e.g., MASH)

Disease understanding and management standards are underdeveloped due to low diagnosis and awareness

Opportunity to fundamentally transform management of AATD liver disease with Fazirsiran

The AATD-LD market & Fazirsiran's potential are poised to benefit from the advancements in MASH & diagnosis acceleration upon availability of an effective treatment in AATD



Advancement in liver disease management (i.e. MASH) › Elevate awareness on AATD-LD & prognosis › Accelerate adoption of diagnosis in AATD-LD upon approval of Fazirsiran ‹› Elevate Fazirsiran as the Standard of Care in AATD-LD

Fazirsiran's (TAK-999) global peak revenue potential : $1-3B

1. Blanco I, Bueno P, Diego I, Pérez-Holanda S, Casas-Maldonado F, Esquinas C, Miravitlles M. Alpha-1 antitrypsin Pi*Z gene frequency and Pi*ZZ genotype numbers worldwide: an update. Int J Chron Obstruct Pulmon Dis. 2017 Feb 13;12:561-569; 2. Clark VC, Marek G, Liu C, Collinsworth A, Shuster J, Kurtz T, Nolte J, Brantly M. Clinical and histologic features of adults with alpha-1 antitrypsin deficiency in a non-cirrhotic cohort. J Hepatol. 2018 Dec;69(6):1357-1364; 3. Horvath, I. et all ERJ Open Res 2019 Mar 11;5(1):00171-2018, Takeda physician research; Please refer to the Important Notice at the start of this presentation for more information about peak revenue estimates.

Fazirsiran (TAK-999): The 1st Potential Treatment for AATD-LD with global peak revenue opportunity of $1-3B

Fazirsiran is on track to be the **1st available treatment** indicated for AATD associated liver disease

Strong Phase 2 clinical data demonstrates Fazirsiran **reduces** Z-AAT, **reverses** fibrosis, and **restores** liver health

Fazirsiran has been granted **Breakthrough Therapy Designation** by the FDA and **Orphan Designation** from European Commission

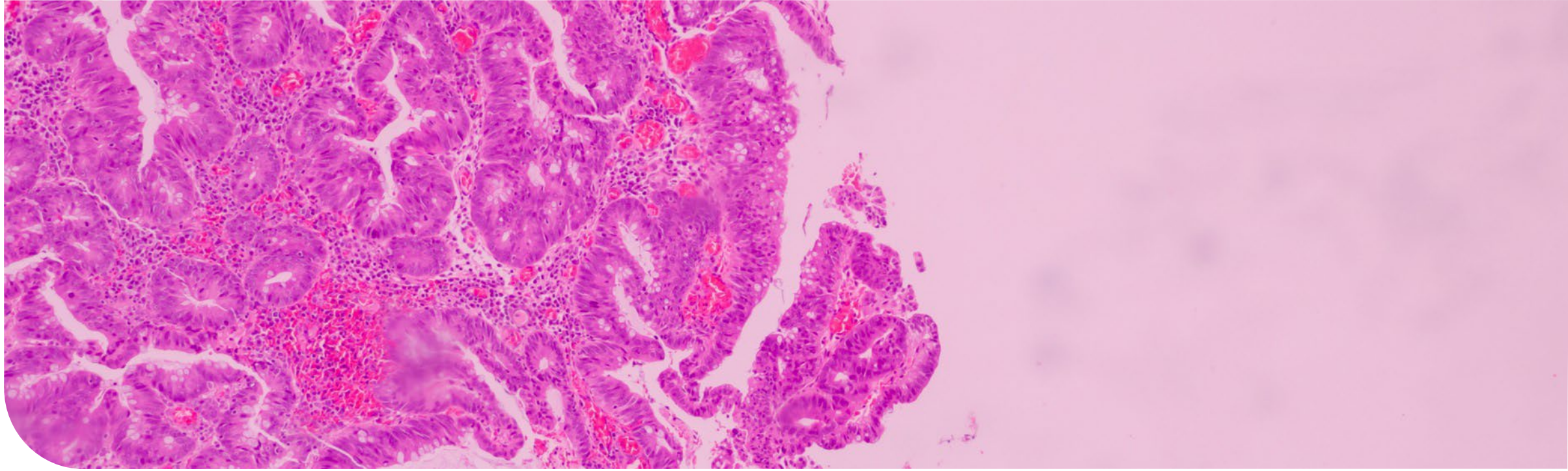
Takeda is **well-poised to transform the patients' journey** by **elevating awareness and accelerate diagnosis of AATD**

Global peak revenue potential: $1-3B

Please refer to the Important Notice at the start of this presentation for more information about peak revenue estimates.

Today's Agenda

TIME (JST)	AGENDA
8:30-8:40	**A Global, Innovation-driven Biopharmaceutical Company** *Christophe Weber, President & CEO*
8:40-9:00	**R&D Strategy and Pipeline Highlights** *Andy Plump, President Research & Development*
9:00-9:50	**Neuroscience: Deep-dive on Orexin Franchise** *Sarah Sheikh, Head of Neuroscience Therapeutic Area Unit and Head of Global Development* *Ramona Sequeira, President of Global Portfolio Division*
9:50-10:00	*Break*
10:00-11:30	**Gastrointestinal and Inflammation (GI&I): Deep-dive on Zasocitinib, Rusfertide, Mezagitamab, Fazirsiran** *Chinwe Ukomadu, Head of GI&I Therapeutic Area Unit* *Ramona Sequeira, President of Global Portfolio Division*
11:30-12:00	Lunch
12:00-12:20	**Oncology: Deep-dive on Elritercept – newly announced BD deal** *P.K. Morrow, Head of Oncology Therapeutic Area Unit* *Teresa Bitetti, President of Global Oncology Business Unit*
12:20-13:15	**Q&A Session**
13:15-14:00	*Reception*



Oncology: Deep dive on Elritercept – newly announced BD deal

P.K. Morrow
Head of Oncology Therapeutic Area Unit

Teresa Bitetti
President, Global
Oncology Business Unit

Better Health, Brighter Future

Please refer to the Important Notice at the start of this presentation for more information about the Elritercept license agreement

Late-stage programs have significant value potential; oveporexton, zasocitinib, rusfertide phase 3 data expected in 2025

Three Phase 3 Data Readouts Over the Next 12 Months

- Oveporexton in Narcolepsy Type 1
- Zasocitinib in Psoriasis
- Rusfertide in Polycythemia Vera[1]

>70% PTRS[2] to approval

Late-Stage Peak Revenue Potential

$10 - 20B

Target Filing Dates by Indication

FY25 / FY26

Oveporexton
Narcolepsy Type 1

Zasocitinib
Psoriasis

Rusfertide
Polycythemia Vera

FY27 - FY29

Zasocitinib
Psoriatic Arthritis

Mezagitamab
IgA Nephropathy
Immune Thrombocytopenia

Fazirsiran
AATD Liver Disease

Elritercept
Myelodysplastic Syndromes

1. Our partner Protagonist Therapeutics is responsible for Phase 3 development of Rusfertide and has stated Phase 3 data may be available as soon as March 2025 which is our Q4 FY24
2. Please refer to the Important Notice at the start of this presentation for more information about PTRS and peak revenue estimates

Please refer to the Important Notice at the start of this presentation for more information about the Elritercept license agreement

Oncology strategy is focused on leveraging internal and external innovation to address unmet medical need

Vision

We aspire to cure cancer with inspiration from patients and innovation from **everywhere**

Areas of Focus

- **ENRICH** mid- and late-stage pipeline through internal and external innovation, and create a robust, sustainable and risk-balanced portfolio in areas of high unmet patient need
- **FOCUS** our R&D efforts on three disease areas (thoracic, gastrointestinal, hematologic cancers), and four modalities (small molecules, complex biologics, ADCs, gamma delta T cell therapies)
- **OPTIMIZE** our portfolio of approved medicines via robust life cycle management
- **DOUBLE DOWN** on data, digital and technology

Oncology R&D efforts focus on three disease areas and four modalities

Oncology Disease Areas	
Heme	ALL, AML/MDS, CML/MF
GI	CRC, Gastric, Pancreatic, HCC
Thoracic	NSCLC, SCLC, SCCHN

Modalities
Small Molecules
Complex Biologics
Antibody–drug conjugates (ADCs)
Gamma Delta Cell Therapies

ALL: Acute Lymphoblastic Leukemia, AML: Acute Myeloid Leukemia, CML: Chronic Myeloid Leukemia, CRC: Colorectal Cancer, HCC: Hepatocellular Carcinoma, MDS: Myelodysplastic Syndrome, MF: Myelofibrosis, NSCLC: Non-Small Cell Lung Cancer, SCCHN: Squamous Cell Carcinoma of Head and Neck, SCLC: Small-Cell Lung Cancer.

Recent business development transactions enhance realization of Takeda's Oncology strategy

Aligning our disease focus, exploring diverse modalities and addressing high unmet patient needs

Fruzaqla® (Fruquintinib)

In-licensing of fruquintinib[1] from **HUTCHMED**
Takeda leads development and commercialization **globally** (ex-China, Hong Kong and Macau)

- ✓ **Aligned with gastrointestinal cancer focus**
- **Establishes foundation in CRC**
- **Small molecule modality**

Mirvetuximab soravtansine-gynx

Licensing agreement with **AbbVie** (formerly ImmunoGen) to develop and commercialize mirvetuximab soravtansine-gynx in **Japan**

- ✓ **Strong strategic fit with existing expertise**
- **Antibody-drug conjugate (ADC) modality**

Olverembatinib

Option agreement with Ascentage Pharma to enter license[2] for olverembatinib, a third-generation BCR-ABL tyrosine kinase inhibitor (TKI)

- ✓ **Aligned with hematologic cancer focus**
- **Potential to maintain Takeda's leadership in CML**
- **Small molecule modality**

Elritercept

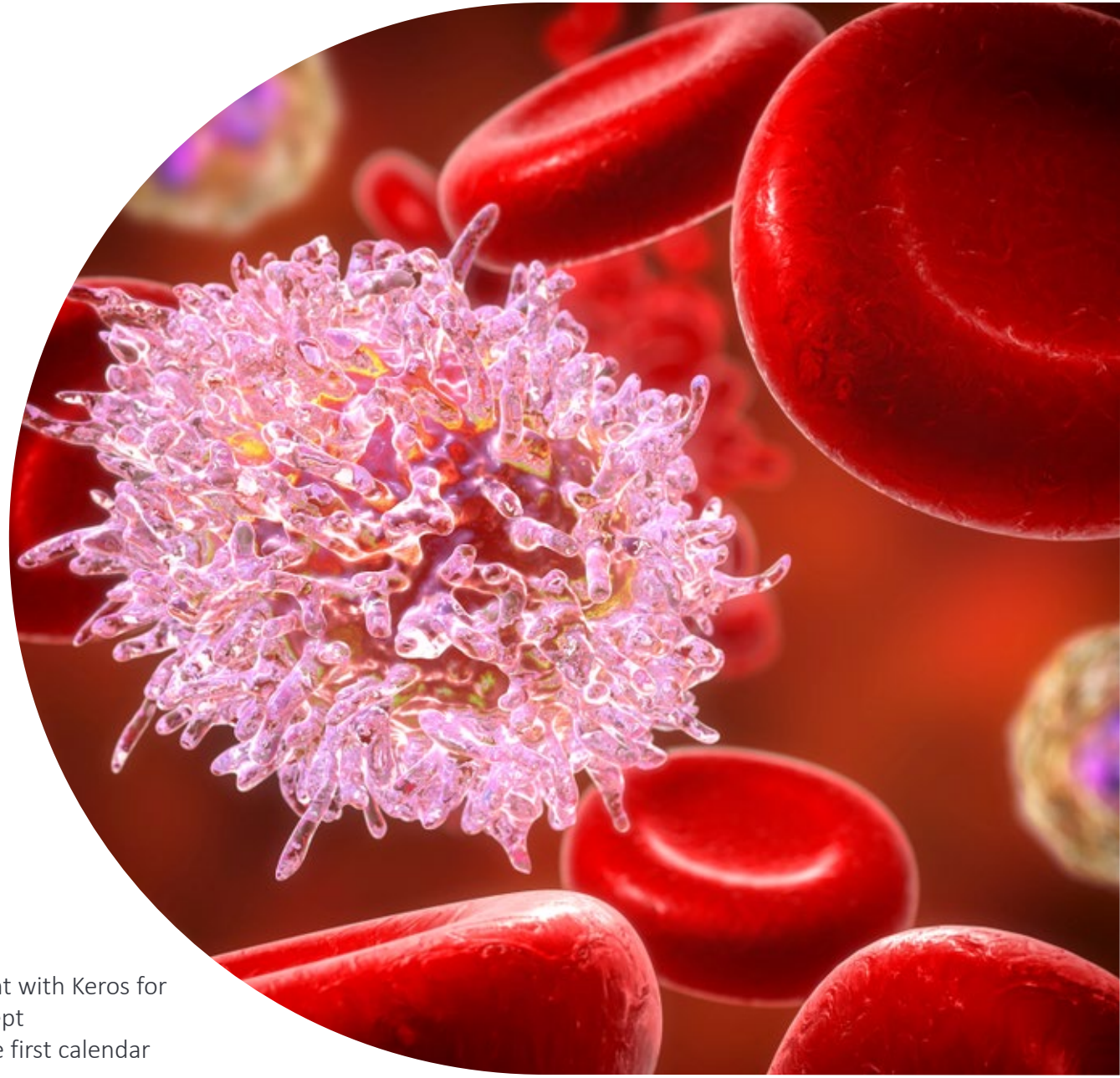
Entered into agreement with Keros Therapeutics to in-license elritercept[3]
Opportunity to realize synergies with existing capabilities

- ✓ **Initial indications aligned with hematologic cancer focus**
- **Complex biologic modality**

1. Worldwide license outside of mainland China, Hong Kong and Macau
2. Olverembatinib/HQP-1351 is included for reference only. Ascentage Pharma retains ownership of this asset and is solely responsible for its clinical development prior to Takeda's potential exercise of its option to exclusively license the asset (global rights in all territories outside of mainland China, Hong Kong, Macau, and Russia), which is subject to customary conditions including regulatory approval
3. Please refer to the Important Notice at the start of this presentation for more information about the Elritercept license agreement

Elritercept

Potentially best-in-class activin inhibitor for treatment of anemia associated with hematologic diseases, including myelodysplastic syndromes (MDS) & myelofibrosis (MF)



Elritercept is included for reference only. Takeda entered into an exclusive license agreement with Keros for global rights, in all territories outside of mainland China, Hong Kong and Macau, to Elritercept
The closing of the transaction is subject to receipt of regulatory approval(s), expected in the first calendar quarter of 2025. Takeda does not currently have rights to Elritercept

Elritercept represents a foundational opportunity to further realize Takeda's Oncology strategy and grow our footprint in hematologic cancers

01

Best-in-Class Potential

Differentiated mechanism of action supported by strong clinical data[1]

02

Pipeline in a Molecule

Potential to help patients suffering from Anemia-Associated (AA) MDS, MF, and other hematologic conditions across patient segments and lines of therapy

03

Strong Strategic Fit

Strong strategic fit into our existing hematology-oncology disease area framework

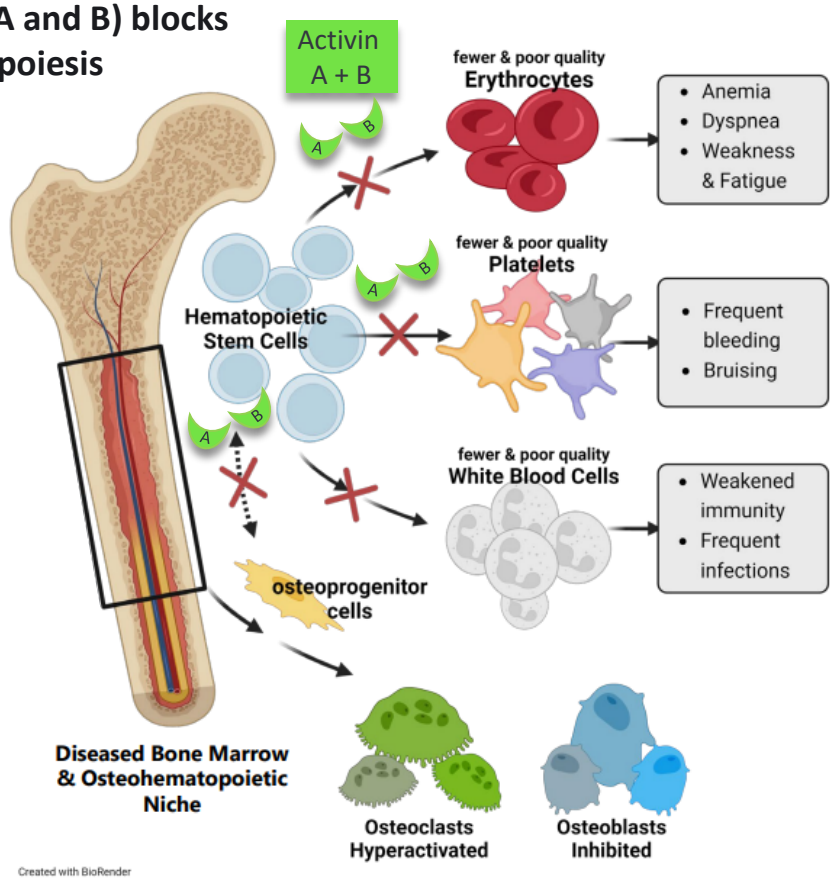
1. Feigenson, M et al. European Hematology Association. 2001.

MDS: Myelodysplastic Syndrome, MF: Myelofibrosis

Please refer to the Important Notice at the start of this presentation for more information about the Elritercept license agreement

High unmet need remains for MDS patients despite advances

In MDS, overactivation of the TGF-β superfamily (e.g., Activin A and B) blocks hematopoiesis



MDS comprises several bone marrow disorders characterized by ineffective hematopoiesis and peripheral cytopenias, which may arise from overactivation of the TGF-β superfamily

Anemia-Associated LR-MDS

- MDS patients frequently have anemia, requiring chronic blood transfusions, which impact QoL and may lead to complications
  - Poor outcomes may include infection, hemorrhage, and progression to AML (10-15% of LR-MDS[1])
- High unmet need remains in anemia-associated (AA) low-risk MDS as the treatment landscape is highly fragmented
  - Patients with high transfusion burden and patients with ringed sideroblast negative (RS-) disease represent segments with poorest outcomes and the highest unmet need today

1. Jain, et al. Haematologica. 2024

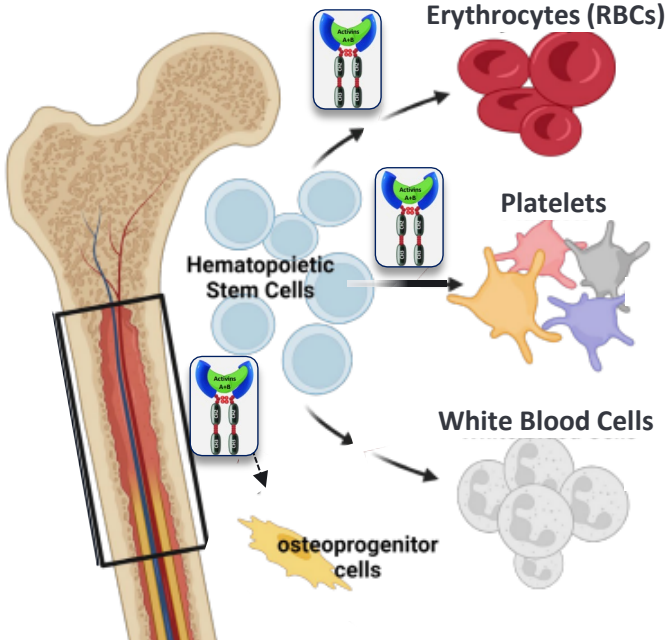
AA: Anemia-Associated; QoL: Quality of Life.; TGF-β: Transforming Growth Factor Beta.

Diez-Campelo, et al. ASH. 2023; Zhou, et al. Blood. 2008; Garcia-Manero. AJH 2023; Steensma. Mayo Clin Proc. 2015; Dayyani et al., Cancer 2013; UpToDate; Leukemia and Lymphoma Society.

Elritercept is a potentially best-in-class treatment for anemia-associated diseases

Elritercept

Elritercept inhibits Activin A and B, restoring a balanced early and late hematopoiesis process



Elritercept has the potential to address significant clinical unmet need that persists despite currently available anemia-associated LR-MDS treatments

- Potent inhibitor of both Activin A and B impacting early and late stages of blood cell development
- Effect on the osteohematopoietic niche – targeting a broad range of pathways - improving in both red blood cells and platelet counts
- Potential to treat a broad set of LR-MDS patients including:
  - RS+ and RS-
  - High or low transfusion burden
- Generally well tolerated safety profile

Diez-Campelo, et al. ASH. 2023.
LR-MDS: Low-Risk Myelodysplastic Syndrome; RBCs: Red Blood Cells; RS: Ring Sideroblast.

Elritercept demonstrated strong responses across AA LR-MDS segments, supporting the potential to treat a broad proportion of patients

% Responders[1]	EPO < 500 U/L[2]	
	All (N=71)	HTB (N=39)
Overall Response[3]	**60.6%**	**56.4%**
Modified IWG 2006 HI-E[4]	**52.1%**	**53.8%**
RS+	*55.8%*	*53.3%*
RS-	*42.1%*	*55.6%*
TI ≥8 weeks[5]	**26/55 (47.3%)**	**15/39 (38.5%)**
RS+	*21/41 (51.2%)*	*12/30 (40%)*
RS-	*5/14 (35.7%)*	*3/9 (33.3%)*

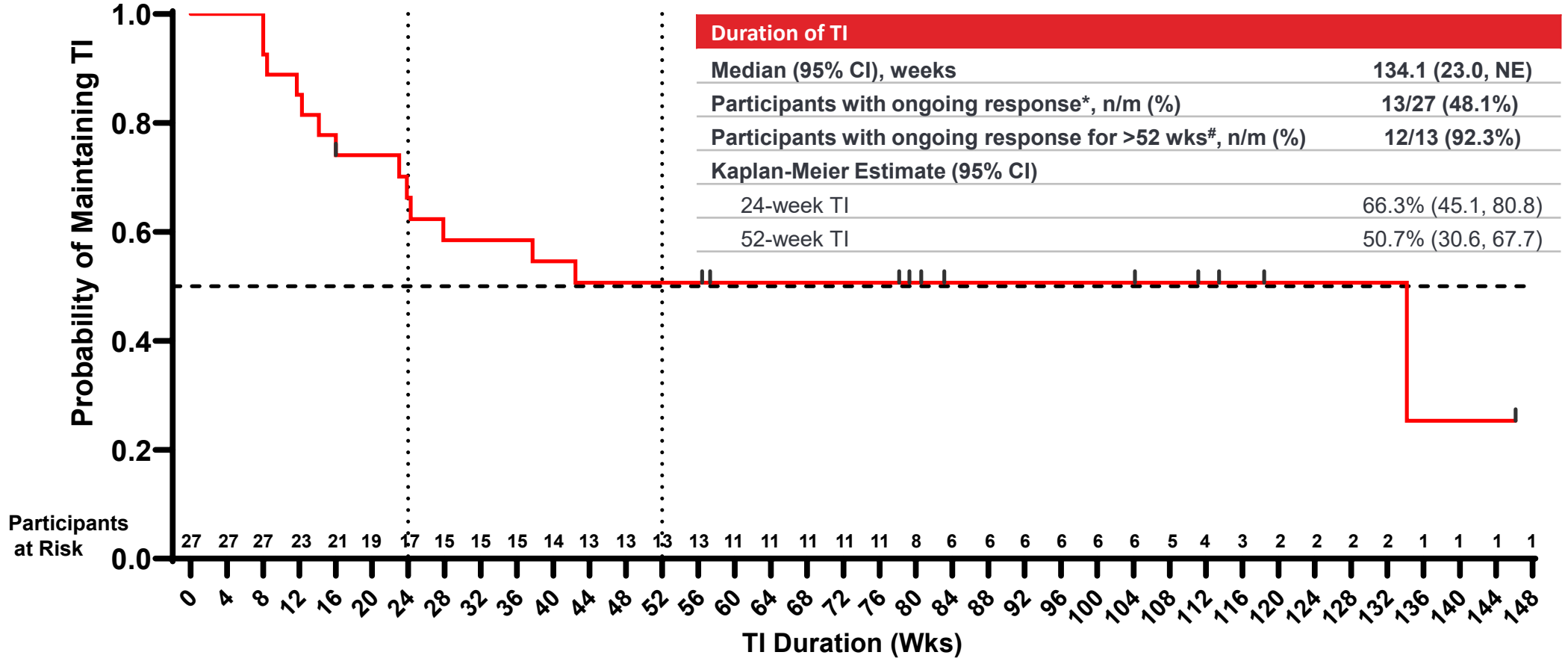
- Response rates in patients with high transfusion burden (HTB) were similar to those observed in the overall population
- Sustained transfusion independence intervals observed regardless of RS status

Giagounidis, et al. ASH. 2024. Data cutoff 30Aug2024. 1. Response data are presented for the modified intent to treat 24 week population (mITT24) that includes recommended Ph2 dose patients who had at least 24 weeks of elritercept treatment or who have discontinued (n=81); 2. Includes data for Weeks 0-24 in $mITT_{24}$ participants with baseline EPO < 500 U/L, excluding one participant with del5q MDS; 3. Defined as achieving modified IWG 2006 HI-E and/or TI; 4. Modified IWG 2006. HI-E = mean increase in hemoglobin ≥1.5 g/dL (NT+LTB) or reduction in transfusion of ≥4 RBC units (HTB) over 8 weeks on treatment compared to 8-week pre-treatment period; 5. TI-evaluable participants received at least 2 RBC units in the 8-week pre-treatment period

AA: Anemia-Associated; EPO: Erythropoietin; HI-E: Erythroid Response; HTB: High Transfusion Burden; IWR: International Working Group; LR-MDS: Low Risk Myelodysplastic Syndrome; $mITT_{24}$: Modified Intent to Treat 0-24 weeks; RS: Ring Sideroblastic; TI: Transfusion Independence.

Elritercept resulted in prolonged and durable transfusion independence (TI) in Ph2 study

Longest TI interval in mITT$_{24}$ participants who achieved TI ≥ 8 wks from baseline through Wk 24**



Duration of TI	
Median (95% CI), weeks	134.1 (23.0, NE)
Participants with ongoing response*, n/m (%)	13/27 (48.1%)
Participants with ongoing response for >52 wks#, n/m (%)	12/13 (92.3%)
Kaplan-Meier Estimate (95% CI)	
24-week TI	66.3% (45.1, 80.8)
52-week TI	50.7% (30.6, 67.7)

Giagounidis, et al. ASH. 2024. Data cutoff 30Aug2024. Participants with ongoing TI response (i.e. without transfusion event) at time of cutoff are censored and denoted by vertical lines. *Red Blood Cell (RBC) transfusions for elective surgery and intercurrent disease (i.e. bleeding events) were recorded but were not counted towards baseline requirement or efficacy assessment. **Due to ongoing TI responses as of the data cutoff date, the median duration of TI is expected to change as data continues to accumulate.
#6/12 (50%) participants with ongoing TI for > 52 weeks were HTB, including participants who had received up to 11 RBC U/8 weeks at baseline.
CI: Confidence Interval; mITT$_{24}$: Modified Intent to Treat 0-24 weeks; NE: Not Evaluable; TI: Transfusion Independence.

Elritercept showed a generally well tolerated safety profile and has resulted in improvements in QoL in AA LR-MDS patients

Safety	**Majority of the treatment-emergent adverse events (TEAEs) were mild to moderate (Gr 1-2)**
	Investigator and sponsor assessed that there were no treatment related fatal adverse events
QoL	**Patients who achieved TI ≥24 weeks showed greater improvement in QoL as compared to those who did not achieve TI ≥24 weeks**

Giagounidis, et al. ASH. 2024. Data cutoff 30Aug2024.
AA: Anemia-Associated; Gr: Grade; QoL: Quality of Life; TI: Transfusion Independence

Elritercept Ph3 in 2L+ AA LR-MDS – Target study start FY2024

RENEW Ph3 Study Design

N = 225

Randomization 2:1

Elritercept + BSC*

Placebo + BSC*

Stratification

- Transfusion Burden (high vs low)
- RS Status (positive vs negative)

Primary endpoint

- TI ≥ 8 weeks within the first 24 weeks (ITT population)

Secondary endpoint

- Safety/tolerability

Target study start FY2024

*Best Supportive Care includes Red Blood Cell transfusions, as needed.
RS: Ring Sideroblast; TI: Transfusion Independence.
Clinicaltrials.gov (NCT06499285); Keros Corporate Presentation, Aug. 2024.

Elritercept is a molecule that has the potential to benefit patients across a wide portfolio of hematologic indications

Anemia-Associated (AA) LR-MDS

- Potential best-in-class asset, based on Ph2 results, showing strong efficacy across heme lineages, and a generally well tolerated safety profile
- Potential to treat a broad range of patients with Low-Risk MDS, across lines of therapy, agnostic of RS status and transfusion burden

AA Myelofibrosis

- Promising clinical activity and a generally well tolerated safety profile seen in early clinical studies
- Ph2 RESTORE study in MF is ongoing

Additional Hematologic Indications

- Takeda is evaluating further opportunities in other heme indications

Please refer to the Important Notice at the start of this presentation for more information about the Elritercept license agreement

Elritercept
Commercial Opportunity

Well positioned to be the best-in-class agent for treating anemia associated with LR-MDS across treatment lines

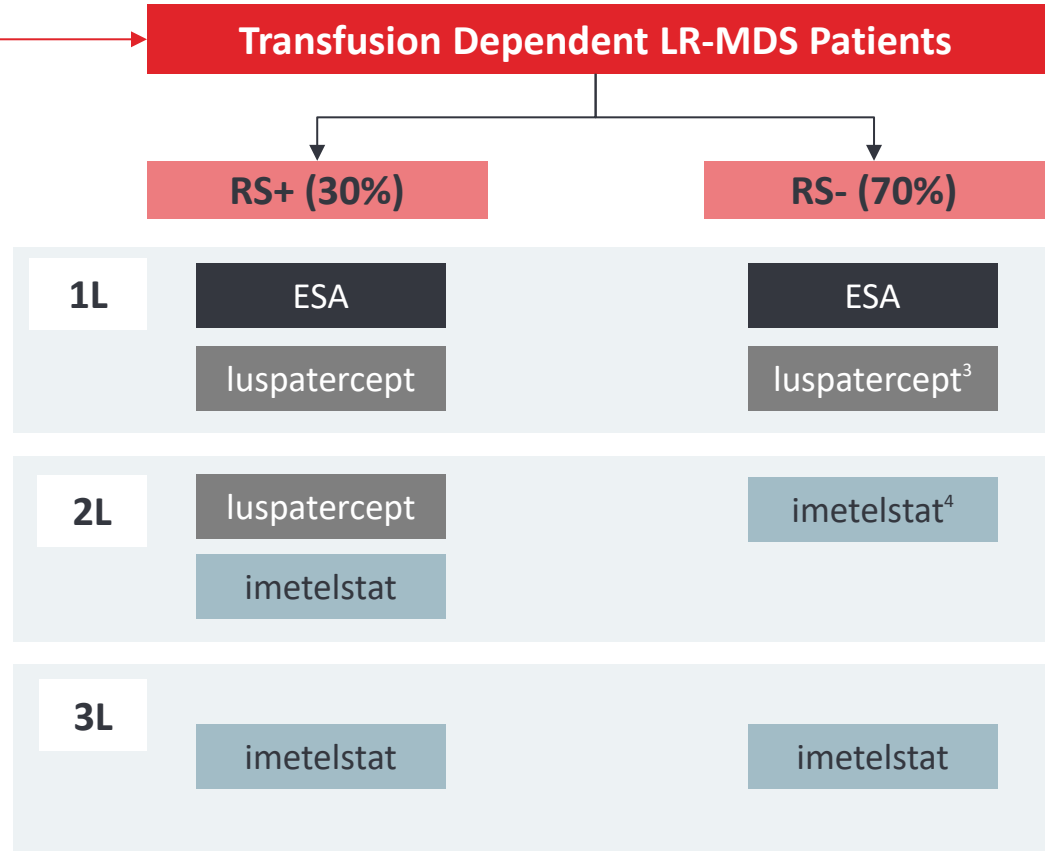
Please refer to the Important Notice at the start of this presentation for more information about the Elritercept license agreement

LR-MDS is a large growing space with significant unmet medical need

50k+
Incident[1] MDS patients *(US, EU-4[2] and JP)*

37k+
Classified as ***low risk***

25k+
Transfusion dependent LR-MDS patients[5]



- ~40% of patients will not respond to ESA in 1L and will progress within a year
- Majority of patients in later lines have high transfusion burden (HTB)
- RS- and HTB patients represent the segments with the poorest outcomes and highest unmet need

MDS sales currently estimated at $2B+ with estimated growth to $6B+ by 2030
Majority of sales coming from lower-risk[6,7]

1. Per annum
2. Germany, France, Italy, Spain
3. Luspatercept indicated for 1L treatment however use in RS- patients is limited; Source HealthVerity US claims data pulled October 2024
4. Indicated for the treatment of adult patients with low- to intermediate-1 risk myelodysplastic syndromes (MDS) with transfusion-dependent anemia requiring 4 or more red blood cell units over 8 weeks who have not responded to or have lost response to or are ineligible for erythropoiesis-stimulating agents (ESA); only approved in US
5. Patients ESA eligible, not including patients with del(5q)
6. Landscape & Forecast Myelodysplastic Syndromes August 2023
7. EvaluatePharma Myelodysplastic syndrome

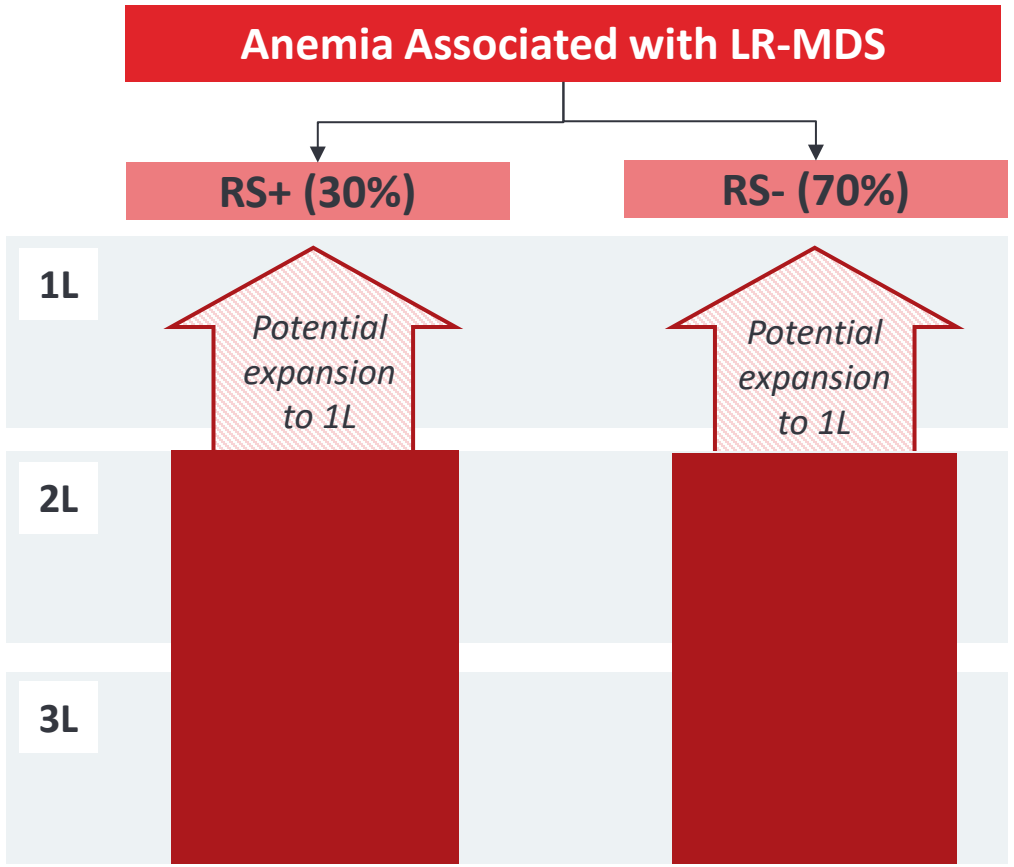
ESA: Erythropoiesis-Stimulating Agents

Elritercept profile has the potential to be best-in-class based on Ph2 data

Key Unmet Needs	Emerging Elritercept Profile[1]
Transfusion independence and time to response	✓ Nearly half of patients achieved TI ≥8 weeks ✓ Faster onset of action
Broad activity across patient segments	✓ Strong efficacy and eligibility across RS+ / RS- and HTB / LTB
Improved tolerability	✓ Generally well tolerated safety profile with a majority TEAEs being mild or moderate
Convenient dosing and administration	✓ Subcutaneous; once every 4 weeks

1. Target profile based on Ph2 data

Elritercept is a potential best-in-class treatment for AA LR-MDS targeting an initial indication in 2L+ with the aim to expand quickly into 1L



Elritercept target indications

Initial indication 2L+

LCM indication

Elritercept peak revenue potential $2 – 3B

Please refer to the Important Notice at the start of this presentation for more information about peak revenue estimates.

Please refer to the Important Notice at the start of this presentation for more information about the Elritercept license agreement

Elritercept: Potential to benefit a wide range of patients with MDS and MF

Strong strategic fit with existing hematology-oncology disease area focus

Differentiated mechanism of action impacting early and late haematopoiesis

Ph3 ready asset with lead indication in 2L+ AA LR-MDS and potential **expansion opportunities** in earlier lines, MF and other hematologic indications

Potential **best-in-class profile**, including prolonged and sustained efficacy across a broad set of patients and a generally well tolerated safety profile

Global peak revenue potential: $2-3B

Please refer to the Important Notice at the start of this presentation for more information about peak revenue estimates.

Please refer to the Important Notice at the start of this presentation for more information about the Elritercept license agreement

Late-stage programs have significant value potential; oveporexton, zasocitinib, rusfertide phase 3 data expected in 2025

Three Phase 3 Data Readouts Over the Next 12 Months

- Oveporexton in Narcolepsy Type 1
- Zasocitinib in Psoriasis
- Rusfertide in Polycythemia Vera[1]

>70% PTRS[2] to approval

Late-Stage Peak Revenue Potential

$10 - 20B

Target Filing Dates by Indication

FY25 / FY26

Oveporexton
Narcolepsy Type 1

Zasocitinib
Psoriasis

Rusfertide
Polycythemia Vera

FY27 - FY29

Zasocitinib
Psoriatic Arthritis

Mezagitamab
IgA Nephropathy
Immune Thrombocytopenia

Fazirsiran
AATD Liver Disease

Elritercept
Myelodysplastic Syndromes

1. Our partner Protagonist Therapeutics is responsible for Phase 3 development of Rusfertide and has stated Phase 3 data may be available as soon as March 2025 which is our Q4 FY24
2. Please refer to the Important Notice at the start of this presentation for more information about PTRS and peak revenue estimates

Please refer to the Important Notice at the start of this presentation for more information about the Elritercept license agreement

Q&A SESSION

CHRISTOPHE WEBER
Representative Director;
President & CEO

MILANO FURUTA
Director;
Chief Financial Officer

ANDY PLUMP
Director; President,
Research & Development

RAMONA SEQUEIRA
President,
Global Portfolio Division

TERESA BITETTI
President, Global
Oncology Business Unit

CHINWE UKOMADU
Head of GI&I Therapeutic
Area Unit

SARAH SHEIKH
Head of Neuroscience
Therapeutic Area Unit &
Global Development

P.K. MORROW
Head of Oncology
Therapeutic Area Unit

APPENDIX

Consolidated Development Pipeline by Phase

	PHASE 1 (5 NMEs)	PHASE 2 (11 NMEs + 2 LCM)
GASTROINTESTINAL AND INFLAMMATION	TAK-004 Nausea & Vomiting	zasocitinib Crohn's Disease; zasocitinib Ulcerative Colitis; TAK-101 Celiac Disease; zamaglutenase Celiac Disease; TAK-227 Celiac Disease; TAK-007 Autoimmune Disease[1]; ADZYNMA® iTTP ★
NEUROSCIENCE	TAK-360 NT2 / IH	danavorexton Respiratory[2]; TAK-653 Inadequate resp. in MDD; TAK-341 MSA ★; TAK-594 Frontotemporal dementia ★
ONCOLOGY	TAK-012 Acute myeloid leukemia[3]; TAK-280 B7-H3 Solid Tumor[3]; TAK-500 Solid Tumors[3]	dazostinag Solid Tumors[4]; TAK-186 EGFR Solid Tumor[4]; mirvetuximab PROC (JP)[4]
SELECT OPTIONS[5]		ACI-24.060[6] Alzheimer's Disease

NME | LCM | ★ Orphan Drug Designation potential (in any region / indication for a given asset)

1. TAK-007 Phase 1 trial in autoimmune disease is planned
2. Danavorexton trials in respiratory conditions under development
3. Currently in phase 1 of a phase 1/2 trial
4. Currently in phase 2 of a phase 1/2 trial
5. Select options: Other selected assets that Takeda holds contractual rights to potentially clinically develop and/or commercialize in the future.
6. ACI-24.060 is included for reference only. AC Immune retains ownership of this asset and is solely responsible for its clinical development prior to Takeda's potential exercise of its option to exclusively license certain rights, which is subject to customary conditions including regulatory approval.

All timelines are approximate estimates as of December 13th, 2024, are subject to change and are subject to clinical and regulatory success. Table is not comprehensive. For full glossary of abbreviations please refer to appendix.

Consolidated Development Pipeline by Phase

	PHASE 3 (6 NMEs + 13 LCMs)	FILED (2 NME + 11 LCMs)
GASTROINTESTINAL AND INFLAMMATION	zasocitinib – Psoriasis zasocitinib – Psoriatic Arthritis[1] rusfertide – Polycythemia Vera ★ mezagitamab – ITP[1] ★ mezagitamab – IgAN[1] ★ fazirsiran – AATD Liver Disease ★ ENTYVIO® – Pediatric UC/Crohn's ADZYNMA® – cTTP (CN) ★ ALOFISEL® – Pediatric Perianal Fistulas in Crohn's ★	ADZYNMA® – cTTP (EU) ★ maralixibat – ALGS (JP) ★ maralixibat – PFIC (JP) ★
NEUROSCIENCE	TAK-861 – NT1 ★ soticlestat – DS[2] ★	
ONCOLOGY	CABOMETYX® – mCRPC combo w/atezolizumab (JP) mirvetuximab – PSOC[3] (JP)	FRUZAQLA™ – mCRC (EU) FRUZAQLA™ – mCRC (JP) ADCETRIS® – FL HL BrECADD (EU)
Other Rare Diseases	LIVTENCITY® – Pediatric Post-transplant CMV infection ★ VONVENDI® – vWD Pediatric On-demand & Surgery ★ ADYNOVATE® – recombinant Factor VIII Pediatric HemA (EU) ADYNOVATE® – recombinant Factor VIII HemA (CN)	LIVTENCITY® – Post-transplant CMV infection (JP) ★ VONVENDI® – vWD On-demand & Surgery (CN) ★
PLASMA-DERIVED THERAPIES	TAK-881 – PID Prothromplex – DOAC Reversal (US) Glovenin-I 5% – Autoimmune Encephalitis (JP) ★	HYQVIA® – PID, SID (JP) HYQVIA® – CIDP, MMN (JP) TAK-880 – IgG – Low IgA (EU) TAK-880 – IgG – Low IgA (US) HyHub™ – AVA Device
VACCINES	QDENGA® – Dengue Vaccine Booster	Nuvaxovid® – COVID-19 Variant Vaccine (JP)
SELECT OPTIONS[4]	olverembatinib[5] HQP1351 – CP-CML ★	

1. Trials for zasocitinib PsA is active and not yet recruiting. Mezagitamab ITP and IgAN are planned.
2. Soticlestat DS totality of Phase 3 data suggests potential clinically meaningful benefit despite missing primary endpoint.
3. Mirvetuximab PSOC trial actively recruiting.
4. Select options: Other selected assets that Takeda holds contractual rights to potentially clinically develop and/or commercialize in the future.
5. Olverembatinib/HQP1351 is included for reference only. Ascentage Pharma retains ownership of this asset and is solely responsible for its clinical development prior to Takeda's potential exercise of its option to exclusively license certain rights, which is subject to customary conditions including regulatory approval.

APPROVED | NME | LCM

★ Orphan Drug Designation potential (in any region / indication for a given asset)

All timelines are approximate estimates as of December 13th, 2024, are subject to change and are subject to clinical and regulatory success. Table is not comprehensive. For full glossary of abbreviations please refer to appendix.

Glossary of Abbreviations - 1

Regional Abbreviations:
CN: China; EU: Europe; JP: Japan; U.S.: United States of America

AA	anemia-associated
AATD	α1-antitrypsin deficiency
AATD LD	α1-antitrypsin deficiency associated liver disease
ACE/ARB	angiotensin converting enzyme / angiotensin receptor blockers
ACR	American College of Rheumatology
ADAMTS13	a disintegrin-like and metalloproteinase with a thrombospondin type 1 motifs 13
ADC	antibody–drug conjugate
ADHD	attention deficit hyperactivity disorder
AE	adverse event
ALGS	Alagille syndrome
ALL	acute lymphocytic leukemia
AML	acute myeloid leukemia
APRIL	A PRoliferation-Inducing Ligand
AT	advanced therapy
ATP	adenosine triphosphate
BBB	blood brain barrier
BID	bis in die, twice a day
BLA	biologics license application
BLyS	B lymphocyte stimulator
BSC	best supportive care
BTD	breakthrough therapy designation
CAR NK	chimeric antigen receptor natural killer cell
CDAI	Crohn's Disease Activity Index
CGI-C	Clinical Global Impression of Change
CHMP	Committee for Medicinal Products for Human Use
CI	confidence interval
CIDP	chronic inflammatory demyelinating polyradiculoneuropathy
CML	chronic myeloid leukemia
CMV	cytomegalovirus
CP-CML	chronic-phase chronic myeloid leukemia
CRC	colorectal cancer
CRPC	castrate-resistant prostate cancer
CSF	cerebrospinal fluid
cTTP	congenital thrombotic thrombocytopenic purpura
CV	cardiovascular
DOAC	direct oral anti-coagulation
DS	Dravet syndrome
Dx	diagnosis
EDS	excessive daytime sleepiness
EGFR	epidermal growth factor receptor
eGFR	estimated glomerular filtration rate
EMA	European Medicines Agency
EPO	erythropoietin
ER	endoplasmic reticulum
ESA	erythropoiesis-stimulating agents
ESRS	European Sleep Research Society
ESS	Epworth Sleepiness Scale
ETA(AT1)	endothelin A - angiotensin II (1) receptor
F1-F4	liver fibrosis stages 1 to 4
FDA	U.S. Food & Drug Administration
FIH	first in human
FINI	Functional Impacts of Narcolepsy Instrument
FL	front line
fSCIG	facilitated Subcutaneous Immunoglobulin
FSI	first subject in
FY	fiscal year
Gd-IgA	galactose-deficient IgA
GI	gastrointestinal
GI&I	Gastrointestinal and Inflammation
H2H	head-to-head
HCC	hepatocellular carcinoma
HCP	healthcare professional
HCT	hematocrit
HemA	hemophilia A
HI-E	hematologic improvement–erythroid
HL	Hodgkin lymphoma
HR	high risk
HTB	high transfusion burden
HU	hydroxyurea
IBD	inflammatory bowel disease
IC50	50% inhibitory concentration
IFN-α/β	interferon alpha/beta
IgA	immunoglobulin A
IgAN	immunoglobulin A nephropathy
IgG	immunoglobulin G
IH	idiopathic hypersomnia
IL-12/17/23	interleukin 12/17/23
IND	investigational new drug
INN	international non-proprietary name
IQR	Interquartile Range
ISTH	International Society on Thrombosis and Haemostasis
ITP	immune thrombocytopenia
iTTP	immune thrombotic thrombocytopenic purpura
IV	intravenous
IWG	International Working Group
JAK	Janus kinase
KOL	key opinion leader
LCM	lifecycle management
LFT	liver function test
LR	low risk

Glossary of Abbreviations - 2

Regional Abbreviations:
CN: China; EU: Europe; JP: Japan; U.S.: United States of America

LS	least square
LTB	low transfusion burden
LTE	long-term extension
MASH	Metabolic dysfunction-associated steatohepatitis
mCRC	metastatic colorectal cancer
mCRPC	metastatic castrate-resistant prostate cancer
MDA	minimal disease activity
MDD	major depressive disorder
MDS	myelodysplastic syndrome
MELD	Model for End-Stage Liver Disease
MF	myelofibrosis
MG	myasthenia gravis
$mITT_{24}$	modified intent to treat 0-24 weeks
MMN	multifocal motor neuropathy
mMS	modified Mayo Score
MOA	mechanism of action
MPN-SAF	Myeloproliferative Neoplasms Symptom Assessment Form
MSA	multiple system atrophy
MWT	maintenance of wakefulness test
ND	newly diagnosed
NDA	new drug application
NK	natural killer
nM	nano molar
NME	new molecular entity
NMPA	(China's) National Medical Products Administration
NSCLC	non-small cell lung cancer
NSS-CT	Narcolepsy Severity Scale
NT1 or 2	narcolepsy type 1 or 2
OX2R	orexin 2 receptor
OX-A	orexin A
PASI	psoriasis area and severity index
PC	platelet count
PDT	plasma derived therapies
PFIC	progressive familial intrahepatic cholestasis
PGI-C	Patient Clinical Global Impression of Change
PHL	phlebotomy
PID	primary immunodeficiency
PK	pharmacokinetics
PMDA	Japan's Pharmaceuticals and Medical Devices Agency
POC	proof of concept
PR	platelet response
PRO	patient reported outcomes
PROC	platinum-resistant ovarian cancer
PSG	polysomnography
PSOC	platinum-sensitive ovarian cancer
PTRS	probability of technical and regultory success
PV	polycythemia vera
PVT	Psychomotor Vigilance Task
QD	quaque die, every day
QOL	quality of life
RBC	red blood cells
RS +/-	ringed sideroblast positive/negative
RTU	ready to use
SAE	serious adverse event
SC	subcutaneous formulation
SCCHN	squamous cell carcinoma of head and neck
SCLC	small-cell lung cancer
SEM	standard error of the mean
SES-CD	simple endoscopic score for Crohn's disease
SGLT2	sodium-glucose transport protein 2
SID	secondary immunodeficiency
SOC	standard of care
sPGA	static Physician's Global Assessment
TE	Thromboembolic events
TEAE	treatment emergent adverse event
TGF-β	transforming growth factor beta
TI	transfusion independence
TKI	tyrosine kinase inhibitor
TNFα	tumor necosis factor alpha
TTP	thrombotic thrombocytopenic purpura
Tx	therapy
TYK2	tyrosine kinase 2
UC	ulcerative colitis
UPCR	urine protein-creatinine ratio
VEGFR	vascular endothelial growth factor receptors
vWD	von Willebrand disease
WCR	weekly cataplexy rate
WW	worldwide
Z-AAT	mutant Z-form of α1-antitrypsin

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Better Health, Brighter Future