Idorsia – Reaching out for more

The following information contains certain “forward-looking statements”, relating to the company’s business, which can be identified by the use of forward-looking terminology such as “estimates”, “believes”, “expects”, “may”, “are expected to”, “will”, “will continue”, “should”, “would be”, “seeks”, “pending” or “anticipates” or similar expressions, or by discussions of strategy, plans or intentions. Such statements include descriptions of the company’s investment and research and development programs and anticipated expenditures in connection therewith, descriptions of new products expected to be introduced by the company and anticipated customer demand for such products and products in the company’s existing portfolio. Such statements reflect the current views of the company with respect to future events and are subject to certain risks, uncertainties and assumptions. Many factors could cause the actual results, performance or achievements of the company to be materially different from any future results, performances or achievements that may be expressed or implied by such forward-looking statements. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected.

The purpose of Idorsia is to discover, develop, and commercialize innovative medicines to help more patients.

We have more ideas, we see more Opportunities, and we want to transform the horizon of therapeutic options.

Our company history and leadership

Actelion, founded in 1997 by four researchers, changed the lives of thousands of patients living with pulmonary arterial hypertension

1997

2017

Jean-Paul Clozel, MD (CEO) and Martine Clozel, MD (CSO) bring with them not only drug discovery pedigree as researchers but experience working as doctors to continue their philosophy of building a biopharma company focused on patients

Unique amongst biopharma start-ups, our discovery and clinical development teams have been working together for more than 25 years

Idorsia was created from the demerger of Actelion's drug discovery engine and early-stage clinical pipeline as part of the acquisition by Johnson & Johnson in 2017

A start-up like no other

Idorsia has the ideal constellation for bringing successful medicines to patient

>25-year

Heritage of drug discovery

>10

Idorsia and partner-led assets in our portfolio

>750

Highly qualified professionals

Global

Commercial operations in Europe and North America

TRYVIO™ (aprocitentan) 12.5 mg approved by the US FDA in March 2024

TRYVIO™

(aprocitentan) **12.5mg tablets**

Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

JERAYGO™ (aprocitentan) 12.5 mg & 25 mg positive CHMP opinion for EU in April 2024

JERAYGO™

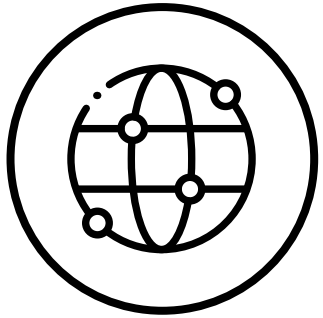
aprocitentan

Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

Collaboration and license agreement with Viatris for selatogrel and cenerimod

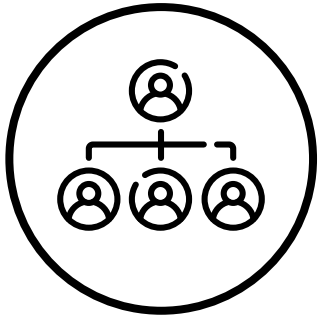
- Combines Viatris' financial strength and worldwide operational infrastructure with Idorsia's proven, highly productive drug development team and innovative engine.
- Idorsia received an upfront payment of USD 350 million, potential development and regulatory milestone payments, and certain contingent payments of additional sales milestone payments and tiered royalties from mid-single- to low double-digit percentage on annual net sales.
- A joint development committee oversees the development of the ongoing Phase 3 programs for selatogrel and cenerimod through regulatory approval.
- Idorsia transferred to Viatris both clinical programs for selatogrel and cenerimod and all key personnel involved in the development programs.
- The development costs for both programs are shared between Idorsia and Viatris, Idorsia will contribute up to USD 200 million in the next 3 years.
- Viatris will have worldwide commercialization rights for both selatogrel and cenerimod (excluding, for cenerimod only, Japan, South Korea and certain countries in the Asia-Pacific region).
- Includes future optionality to expand collaboration with additional pipeline assets.

Adapting the company to create sustainable value



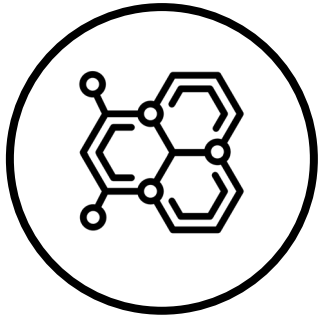
Adapting global presence

Sale of Idorsia Japan and South Korea



Adapting workforce

Reduction at all levels of the company



Adapting portfolio

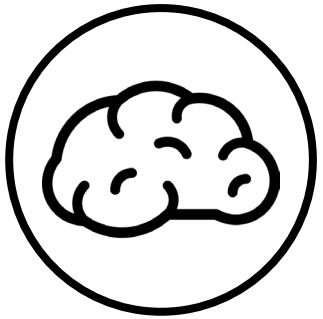
Stopping or partnering R&D assets

Raise cash

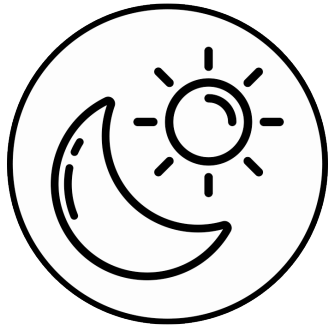
Extending cash runway beyond Q1 2024

CHF 400 million deal with Sosei Heptares

SALE of Idorsia's affiliates in Japan and Korea



PIVLAZ (clazosentan) assignment of Roche's license in the Territory



Daridorexant co-exclusive license in the Territory and assignment of all potential milestones from Mochida

Option to exclusive license lucerastat and cenerimod in the Territory

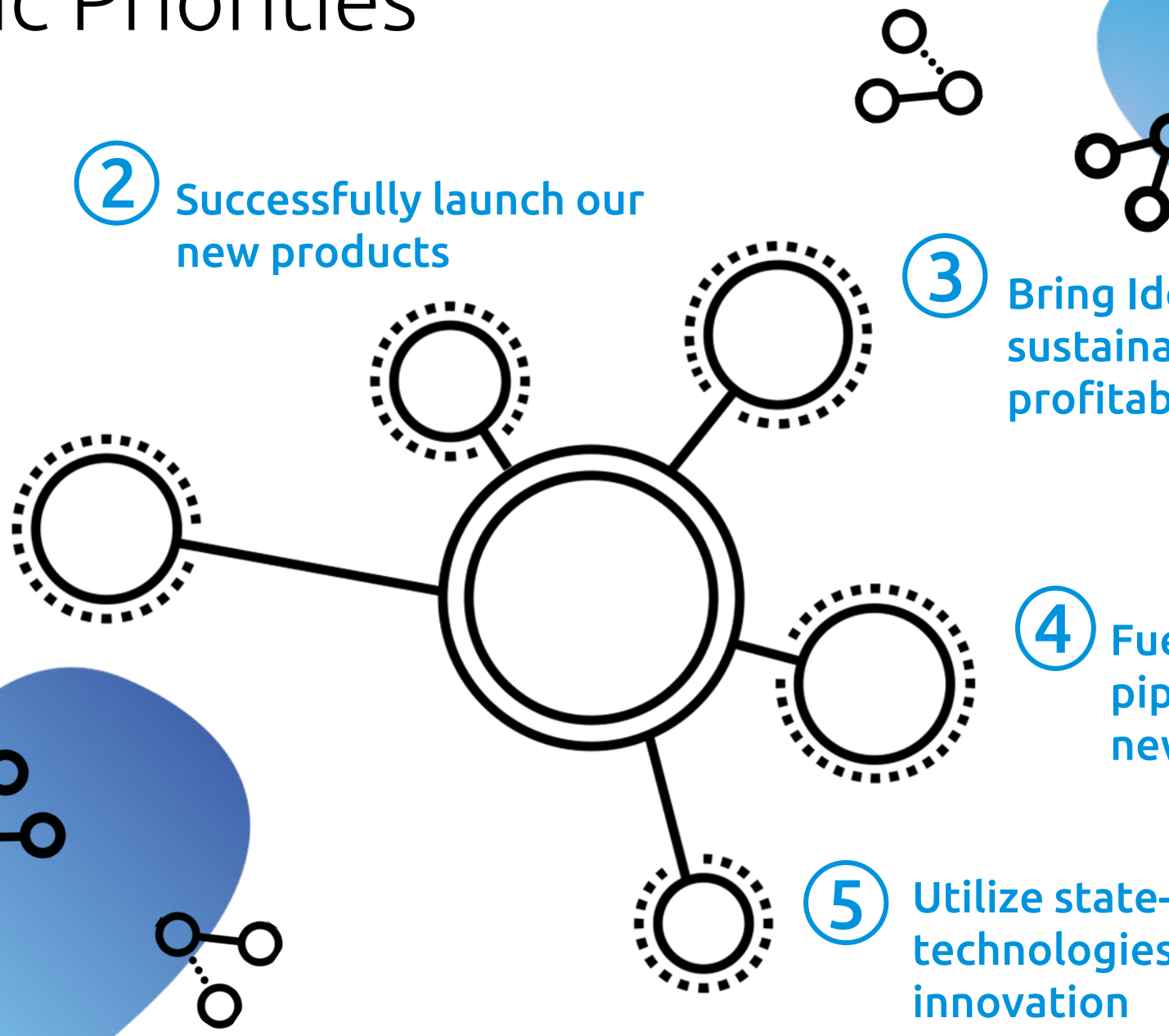
Territory: Australia, Brunei, Cambodia, Indonesia, Japan, Laos, Malaysia, Myanmar, New Zealand, Philippines, Singapore, South Korea, Thailand, Taiwan, and Vietnam.

Clazosentan is only marketed in Japan under the tradename PIVLAZ®

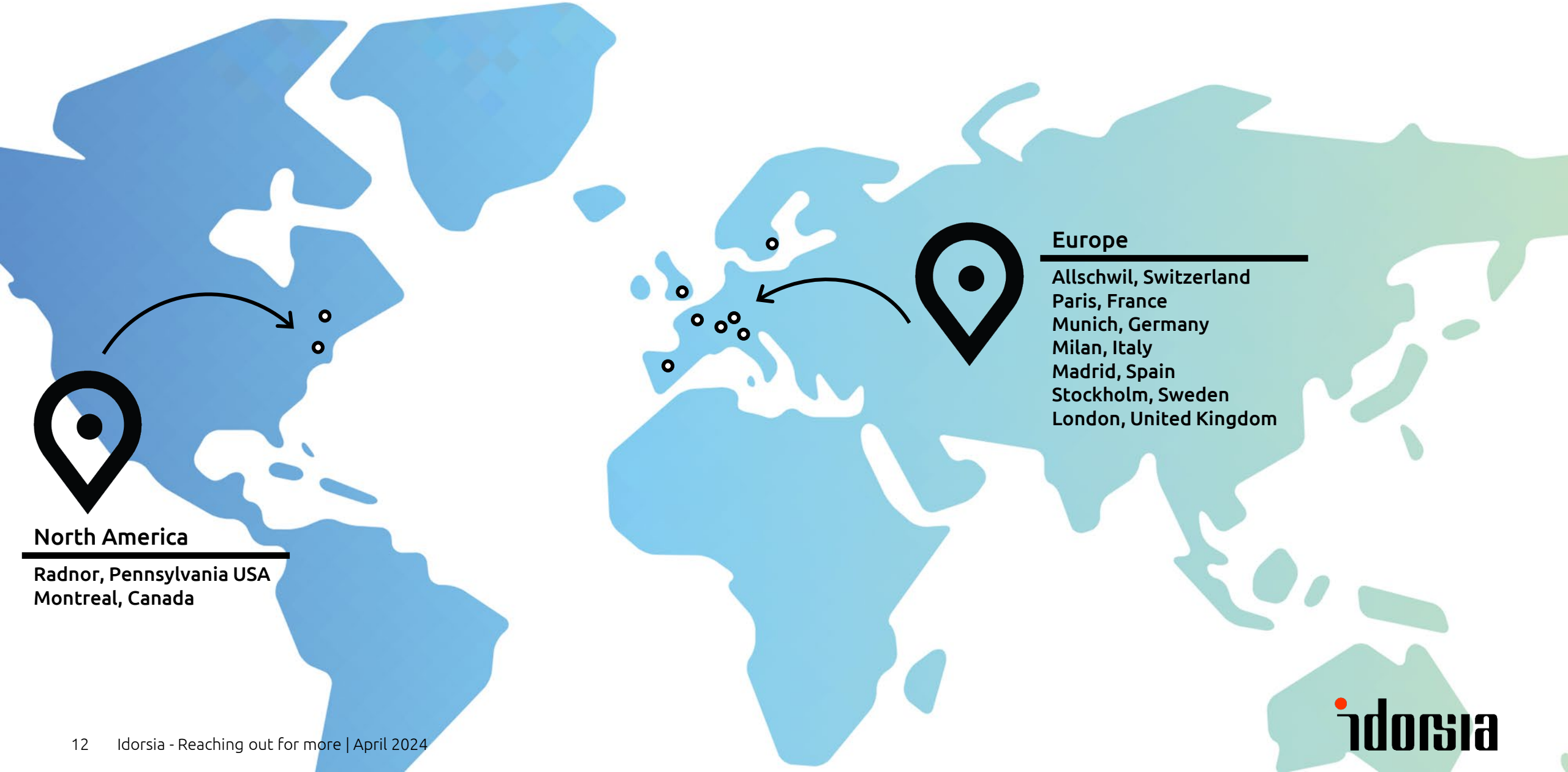
Our Strategic Priorities

Our mid-term key priorities to achieve long-term success:

1. Advance late-stage pipeline
2. Successfully launch our new products
3. Bring Idorsia to sustainable profitability
4. Fuel our pipeline with new discoveries
5. Utilize state-of-the-art technologies to drive innovation



Our commercial reach



North America

Radnor, Pennsylvania USA
Montreal, Canada

Europe

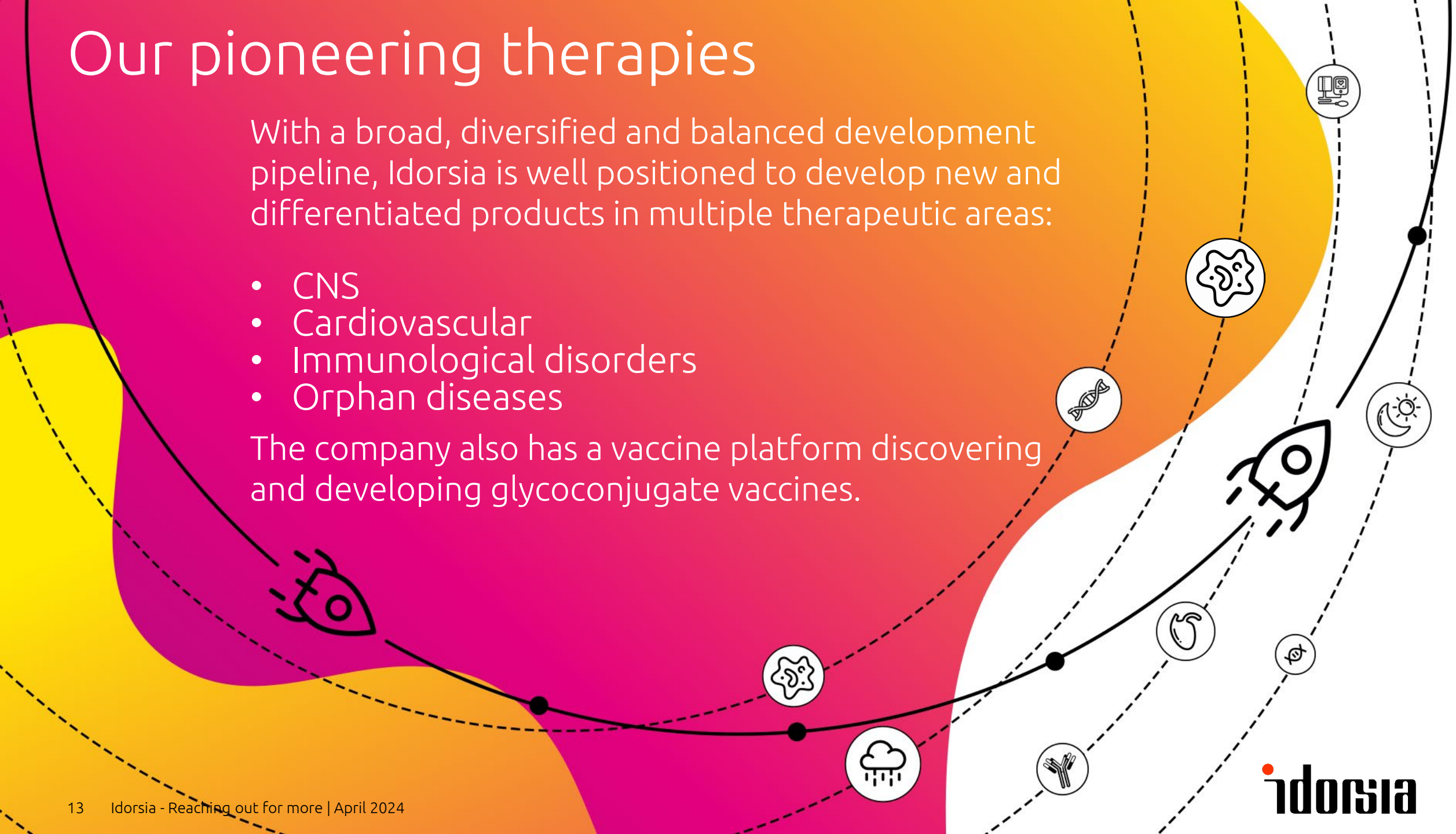
Allschwil, Switzerland
Paris, France
Munich, Germany
Milan, Italy
Madrid, Spain
Stockholm, Sweden
London, United Kingdom

Our pioneering therapies

With a broad, diversified and balanced development pipeline, Idorsia is well positioned to develop new and differentiated products in multiple therapeutic areas:

- CNS
- Cardiovascular
- Immunological disorders
- Orphan diseases

The company also has a vaccine platform discovering and developing glycoconjugate vaccines.

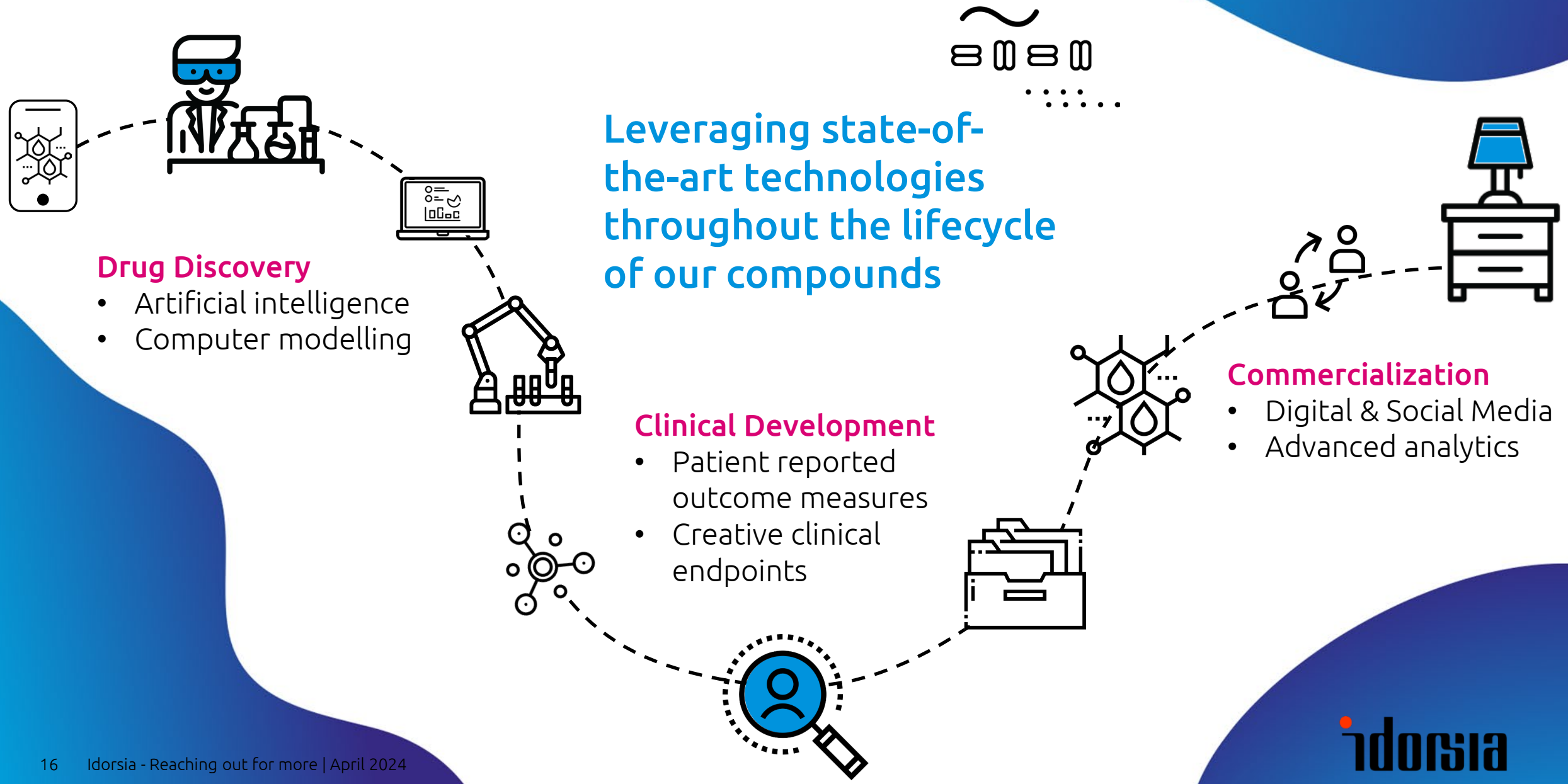


Idorsia-led portfolio

Partner-led portfolio

Compound / Mechanism of action / **Target indication**	**Partner**	Phase 1 / Phase 2 / Phase 3 / Registration / Commercially available
Daridorexant Dual orexin receptor antagonist **Insomnia**	Nxera	**Nxera Pharma** License to develop and commercialize for Asia Pacific (ex-China) NDA submitted in Japan.
Daridorexant Dual orexin receptor antagonist **Insomnia**	Simcere	**Simcere** License to develop and commercialize for Greater China region Phase 3 ongoing.
Selatogrel $P2Y_{12}$ inhibitor **Acute myocardial infarction**	VIATRIS	**Viatris** Worldwide development and commercialization rights. Phase 3 "SOS-AMI" program ongoing.
Cenerimod $S1P_1$ receptor modulator **Systemic lupus erythematosus**	VIATRIS	**Viatris** Worldwide development and commercialization rights (excluding Japan, South Korea and certain countries in the Asia-Pacific region). Phase 3 "OPUS" program ongoing.
Daridorexant Dual orexin receptor antagonist **PTSD**	US Department of Defense (DOD)	Idorsia supports a clinical study sponsored by the US DOD to develop new therapies to treat posttraumatic stress disorder (PTSD).
ACT-709478 (NBI-827104) T-type calcium channel blocker **Epileptic Encephalopathy with Continuous Spike-and-Wave During Sleep (CSCW)**	Neurocrine Biosciences	**Neurocrine Biosciences** Global license to develop and commercialize.

Innovation from bench to bedside



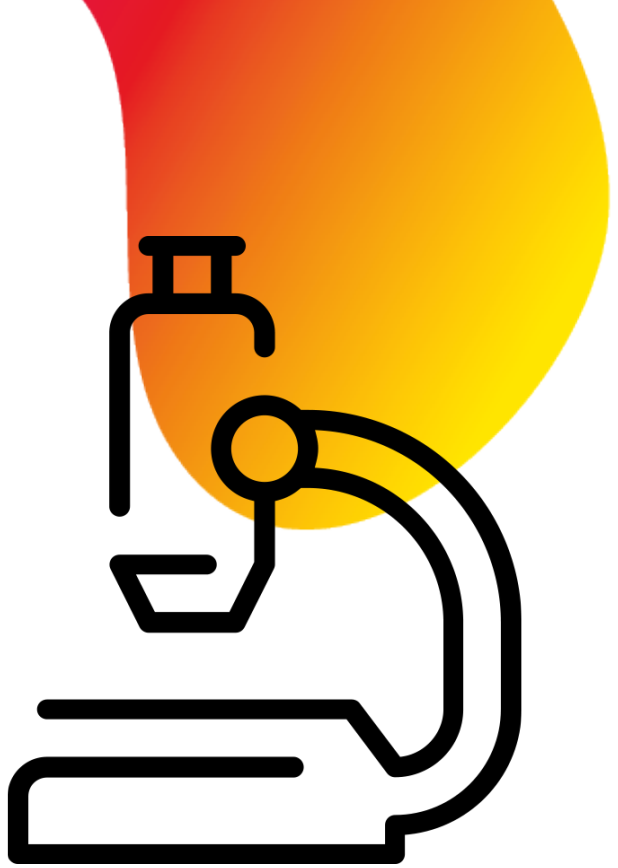
Leveraging state-of-the-art technologies throughout the lifecycle of our compounds

Drug Discovery
- Artificial intelligence
- Computer modelling

Clinical Development
- Patient reported outcome measures
- Creative clinical endpoints

Commercialization
- Digital & Social Media
- Advanced analytics

Find a comprehensive description of our pipeline assets as follows:

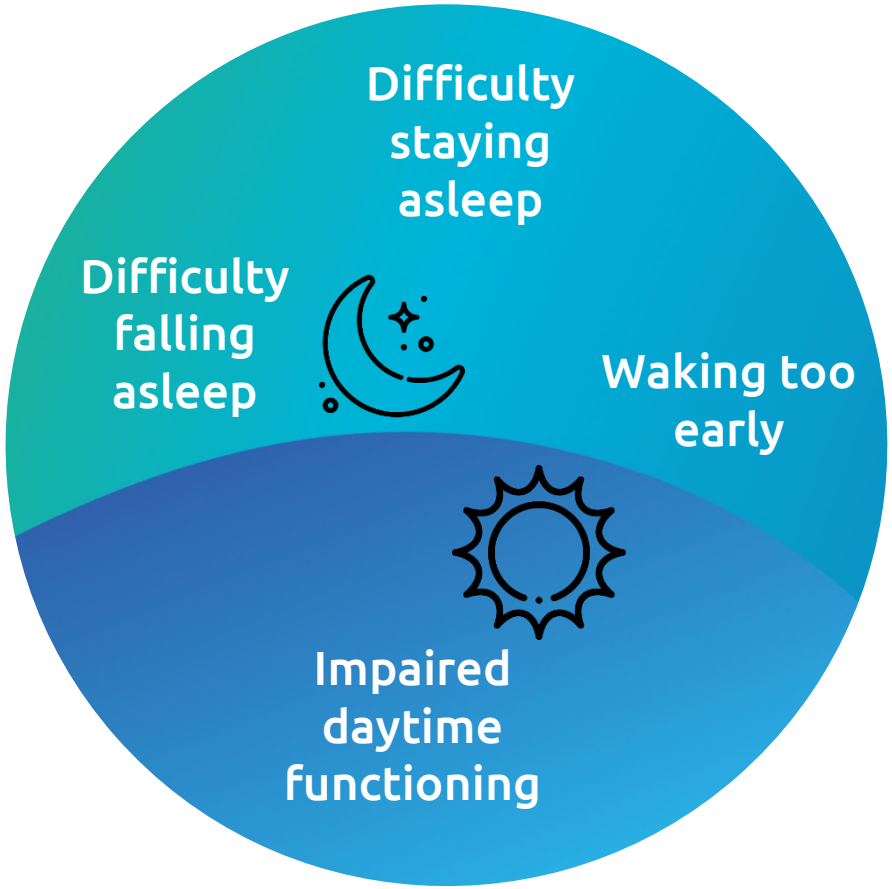


Daridorexant in insomnia

Daridorexant is available in the US, Germany, Italy, Spain, Switzerland, and the UK under the tradename QUVIVIQ. In addition, daridorexant is approved throughout the European Union, and Canada.

Insomnia: A disease of the night and the day

High unmet need for effective, safe medications to treat insomnia



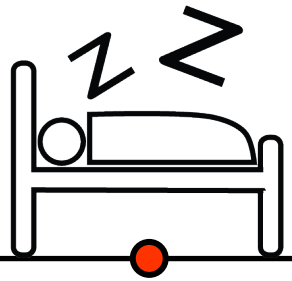
- Combination of difficulty obtaining sufficient sleep and dissatisfaction with sleep **combined with a significant negative impact on daytime functioning**

  Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5®)

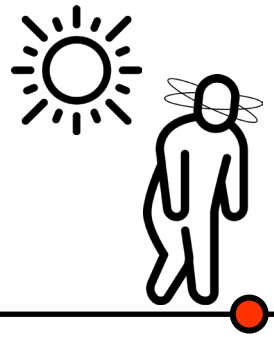
- Estimated approximately 25 million (10%[1]) adults in the US suffer from chronic insomnia

1 Morin CM, et al. Insomnia disorder. Nat Rev Dis Primers 2015;1:15026

Insomnia and the importance of sleep

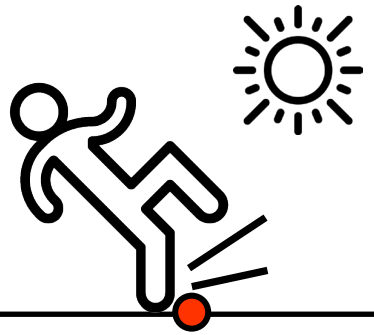


Sleep is an essential pillar for good physical and mental health to ensure optimal functioning throughout the day.

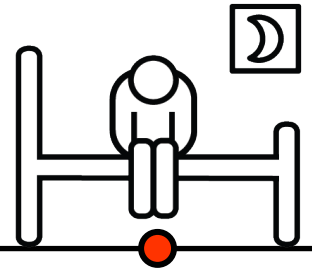


A key symptom of insomnia disorder is the **impairment of daytime functioning**, which is **linked to significant decrements in health status**, such as fatigue, reduced energy, mood alteration and cognitive difficulties.

Therefore, **without adequate, quality sleep**, one can face many issues that will impact day-to-day life.



Poor management of insomnia is associated with **increased risk of motor vehicle accidents, falls, and costly workplace errors**.



Insomnia disorder, the most common sleep-wake disorder, is **defined by difficulties in initiating or maintaining sleep, and early-morning awakening** with the inability to return to sleep, for **at least 3 months or longer.**

Improving daytime functioning is a critical unmet need that has not been addressed in a rigorous manner.

How is insomnia treated, what are the limitations?

Sleep hygiene

- Active patient participation required

Cognitive behavioral therapy

- Recommended first-line therapy but inconsistently practiced
- Not easily accessible
- Often not reimbursed
- Active patient participation required

Pharmacological therapy

- Many have significant limitations
- Insufficient acute effect:
  lack of sustained effect through the night
- Insufficient long-term effect:
  lack of continued benefit over time
- Next morning residual effect
- Abuse potential, withdrawal effect, and rebound
- May have significant adverse effects

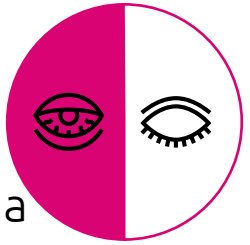
Prevalence and impact of insomnia across Europe

With respect to global burden, insomnia is ranked by the World Health Organization as the

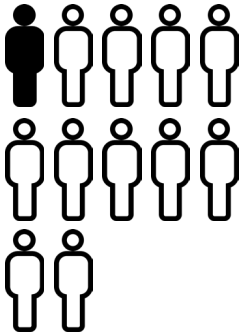
11th

most important brain disorder*

Across Europe, approximately half of all adults are expected to experience some insomnia symptoms, and



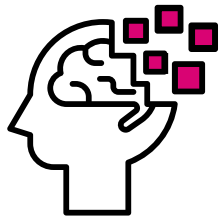
1 in 12 (8.2%) of adults live with chronic insomnia disorder (CID)



CID is associated to **11/18 days of absenteeism** and

39-45 days of presenteeism (showing up at work but less productive) leading to an overall, yearly

45-54 days of loss of productivity*



* Source: Roth, Thomas; Insomnia: Definition, Prevalence, Etiology, and Consequences; Journal of Sleep Medicine; Published Online: November 14, 2019; https://jcsm.aasm.org/doi/10.5664/jcsm.26929

** *Hafner M., Romanelli R.J., Yerushalmi E. & Troxel W.M. *The Societal and Economic Burden of Insomnia in Adults: An International Study*. Santa Monica, CA: RAND Corporation, 2023.

Hidden economic burden of CID (working-age adults)

	Who's affected?		Estimated "hidden" annual financial burden across working-age population suffering from CID
	% of adults suffering from CID	Number of adults	
	7.6%	18.6 million	€92bn
	8.8%	2.2 million	Can$ 10.7bn
	7.7%	16.6 million	$127.1bn

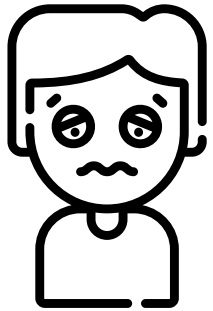
The US insomnia market is large, highly dissatisfied, and ripe for disruption

Who's affected?

~25M

Total insomnia patients

(~10% of US adults)



12M

Treated insomnia patients

Dissatisfaction

In a recent poll of 1001 Americans who struggle with sleep

70%

say they are desperate to find a solution to get quality sleep and fully function the next day

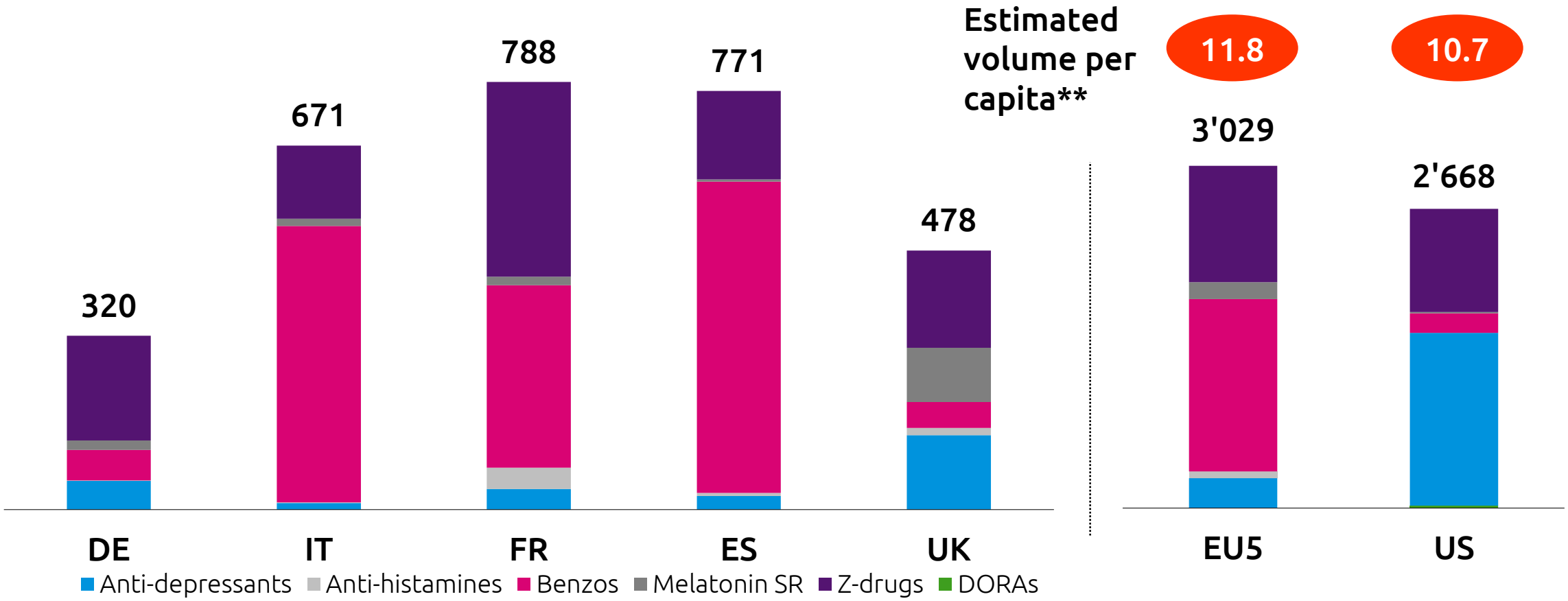
What are the costs?

$100B+

Insomnia related costs per year alone in the US

High unmet need in EU insomnia market

Estimated insomnia market volume*, standard units, millions

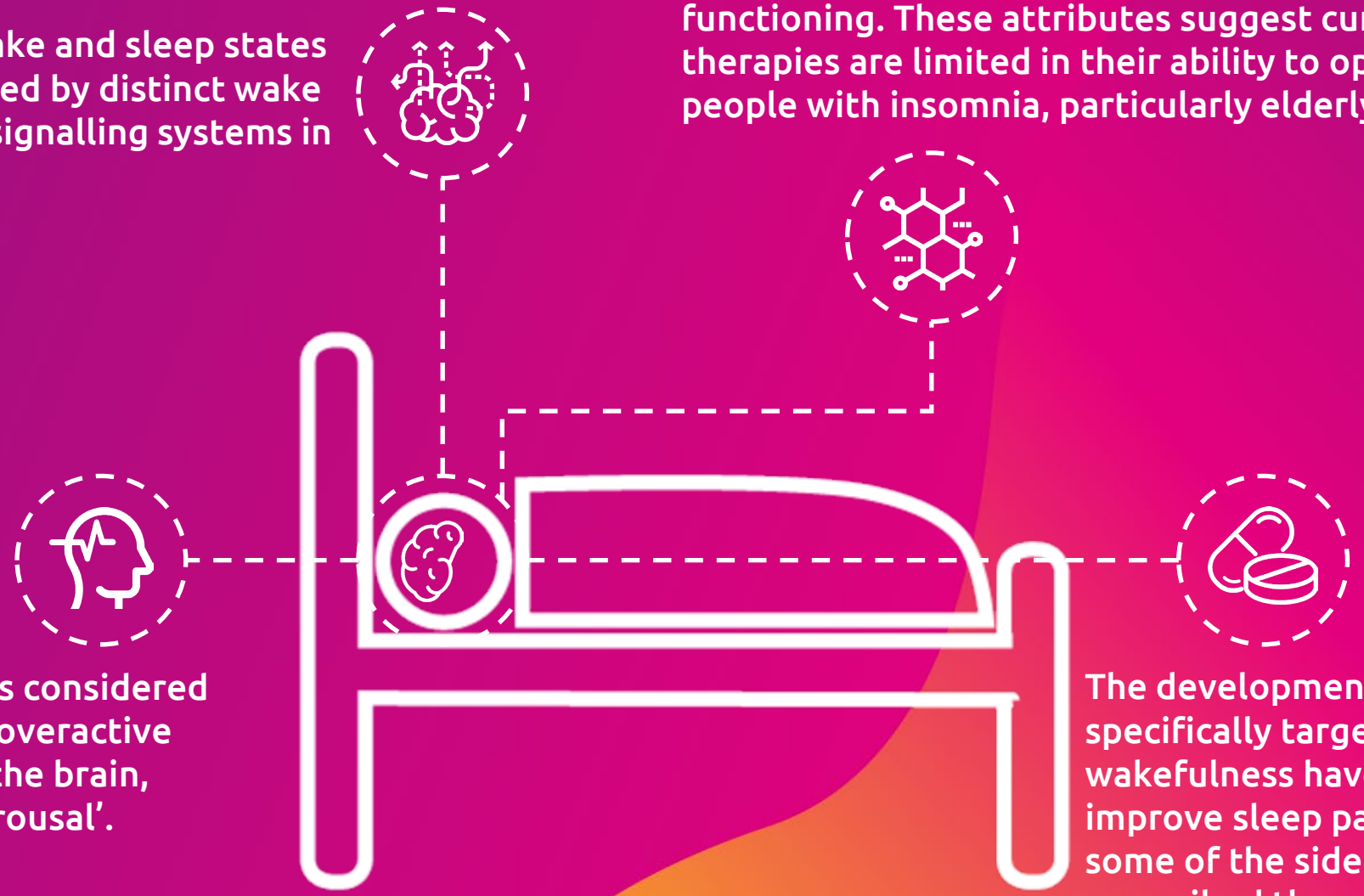


Source: IQVIA MIDAS EU5 – MAT/July 2022; IQVIA US Edition – MAT/August 2022; United Nations population division
* Includes estimated off-label usage of anti-depressants, anti-histamines and benzos to treat insomnia
** Based on adult population

The science of sleep

Healthy wake and sleep states are governed by distinct wake and sleep signalling systems in the brain.

Some therapies may increase somnolence and impair functioning. These attributes suggest current therapies are limited in their ability to optimally treat people with insomnia, particularly elderly patients.



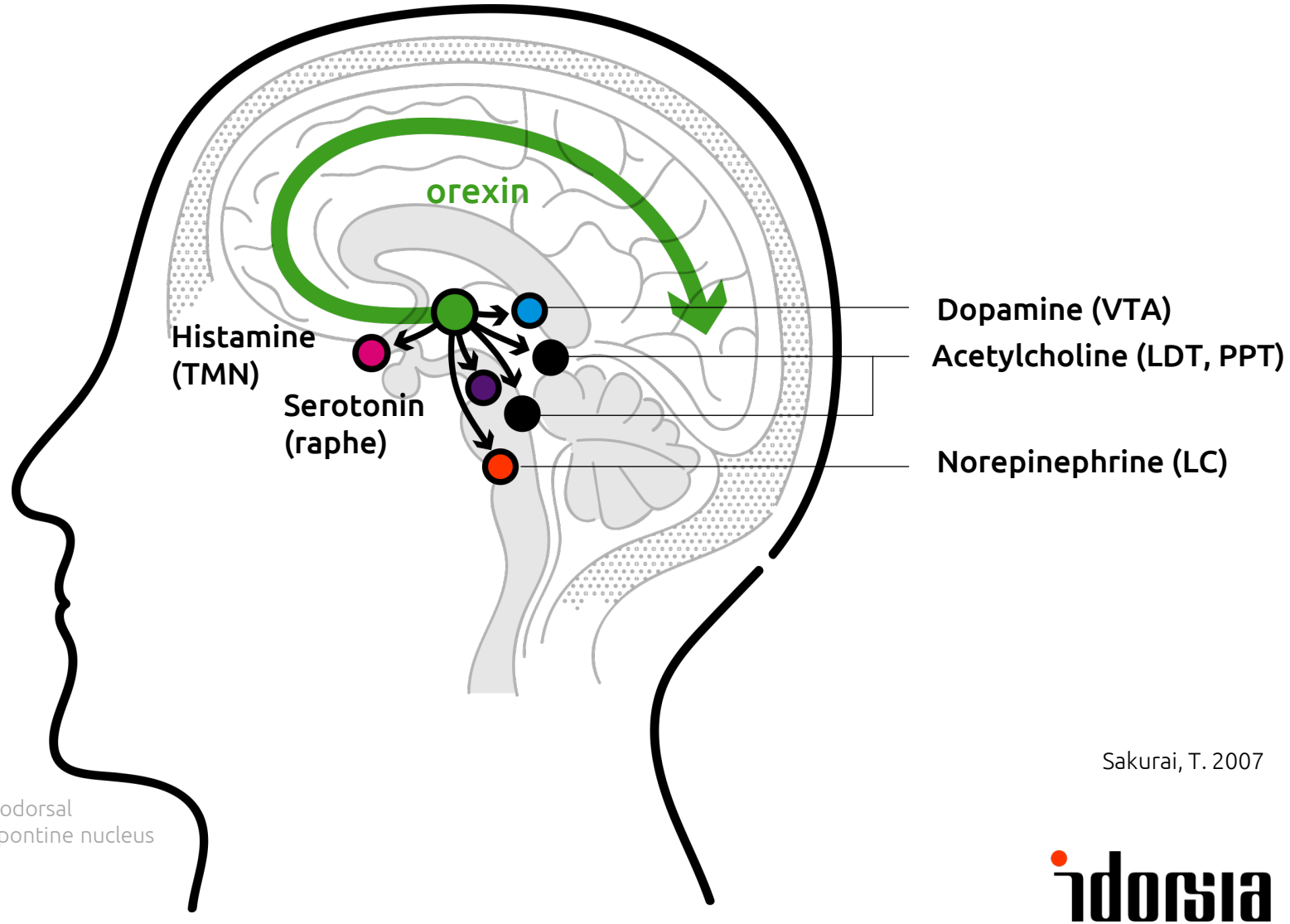
The underlying pathophysiological cause of insomnia is considered to be the result of overactive wake signalling in the brain, also called ‘hyperarousal’.

The development of medications that specifically target excessive wakefulness have been shown to improve sleep parameters without some of the side effects of commonly prescribed therapies for insomnia.

The orexin system is crucial for the regulation of wakefulness

Orexin stimulates many wake-promoting pathways

●	**LHA / PH**	**Orexin**
●	**LC**	OX_1R
●	**TMN**	OX_2R
●	**Raphe**	OX_1R and OX_2R
●	**LTD / PPT**	OX_1R and OX_2R
●	**VTA**	OX_1R and OX_2R



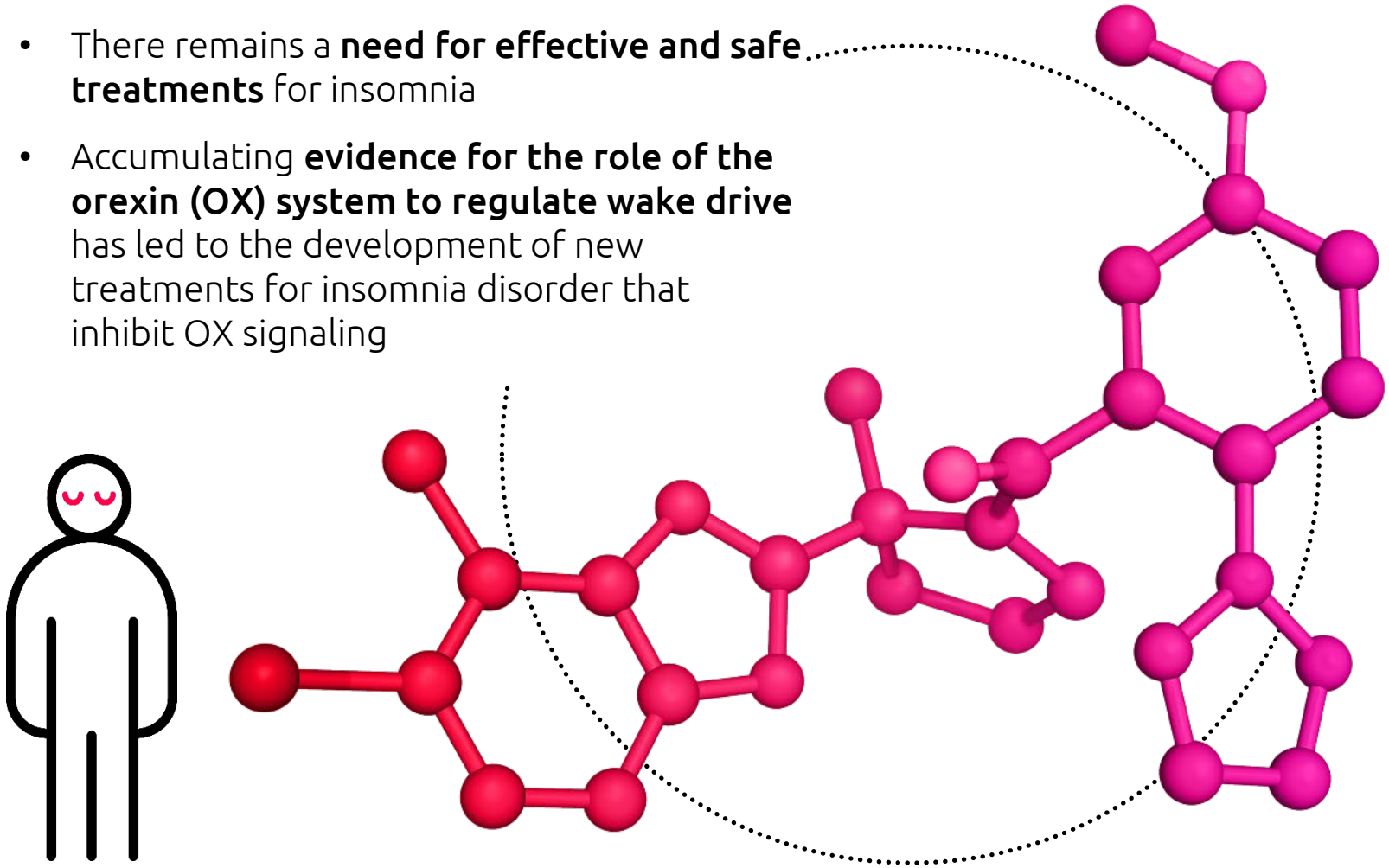
Sakurai, T. 2007

LHA = lateral hypothalamic area; PH = posterior hypothalamus
LC = locus coeruleus; TMN = tuberomammillary nucleus; LDT = laterodorsal tegmental nucleus; VTA = ventral tegmental area; PPT = pedunculopontine nucleus

Daridorexant in insomnia

Rationale

- There remains a **need for effective and safe treatments** for insomnia
- Accumulating **evidence for the role of the orexin (OX) system to regulate wake drive** has led to the development of new treatments for insomnia disorder that inhibit OX signaling



Daridorexant

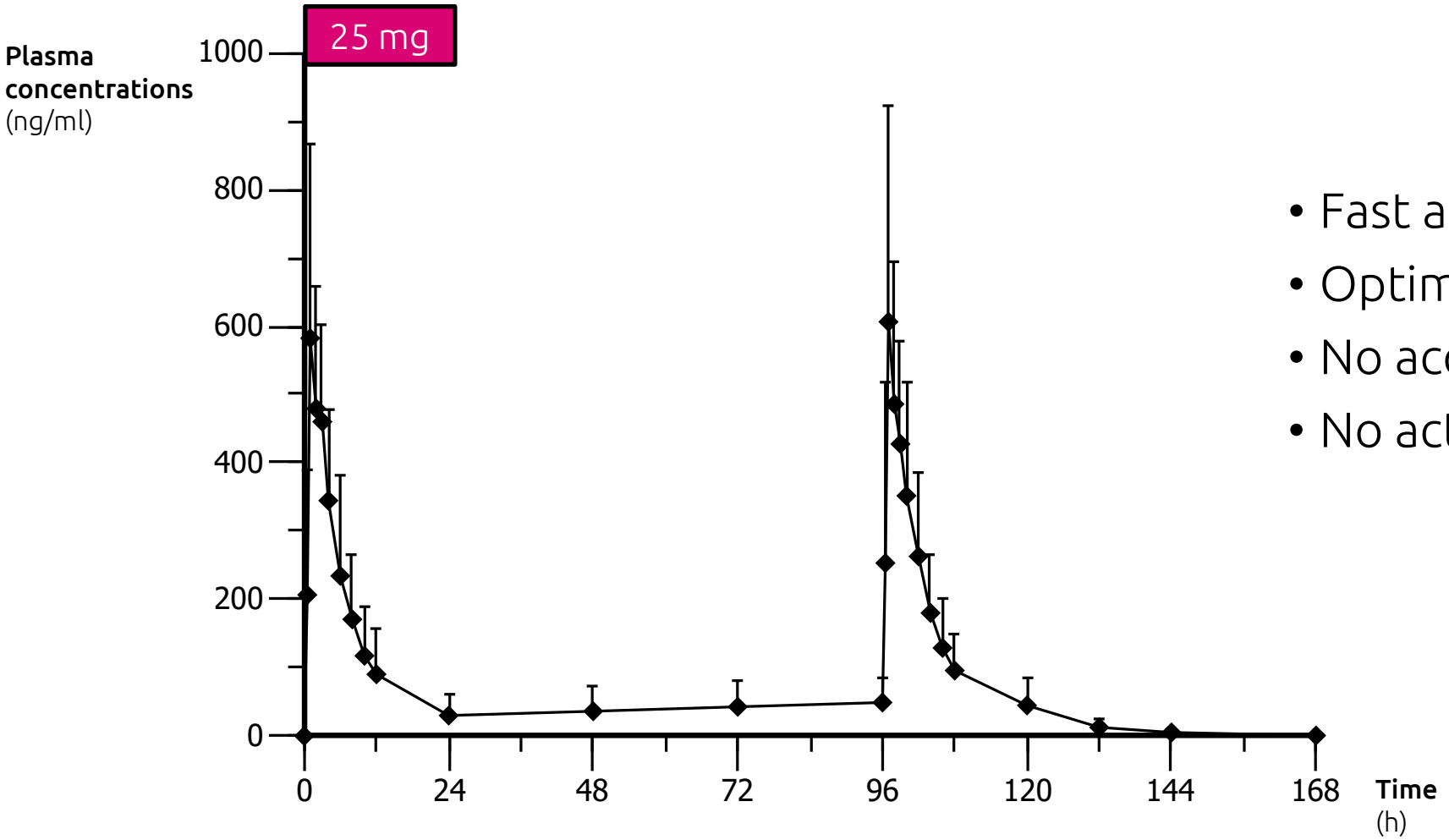
- a **potent and selective** dual orexin receptor antagonist (DORA)
- selected to **promote sleep onset and sleep maintenance, without impairing the next day**

Daridorexant is available in the US, Germany, Italy, Spain, Switzerland, the UK and Canada under the tradename QUVIVIQ.
In addition, daridorexant is approved throughout the European Union.

Different by design – next generation DORA

Optimized pharmacokinetic profile

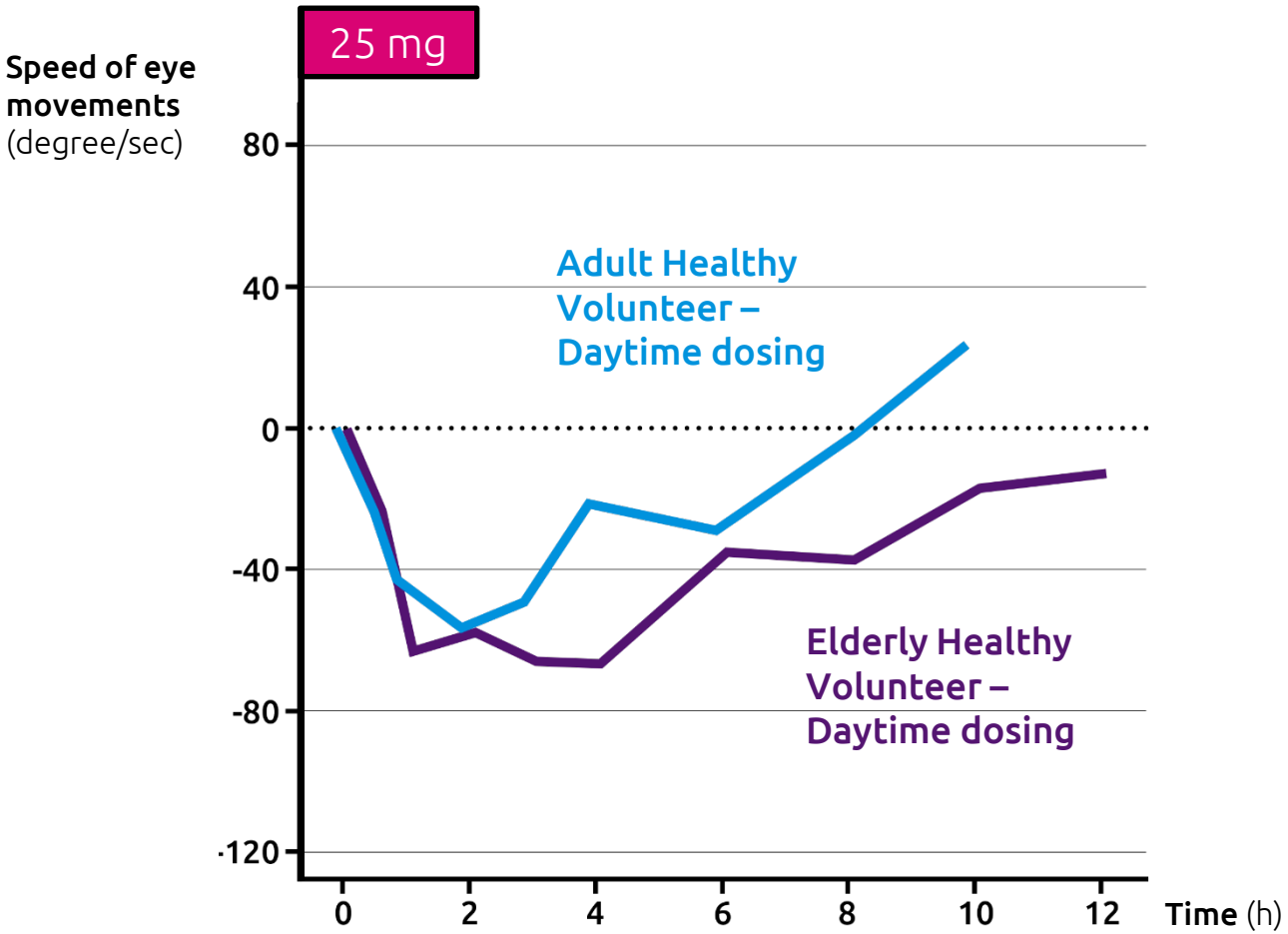
Entry into man studies

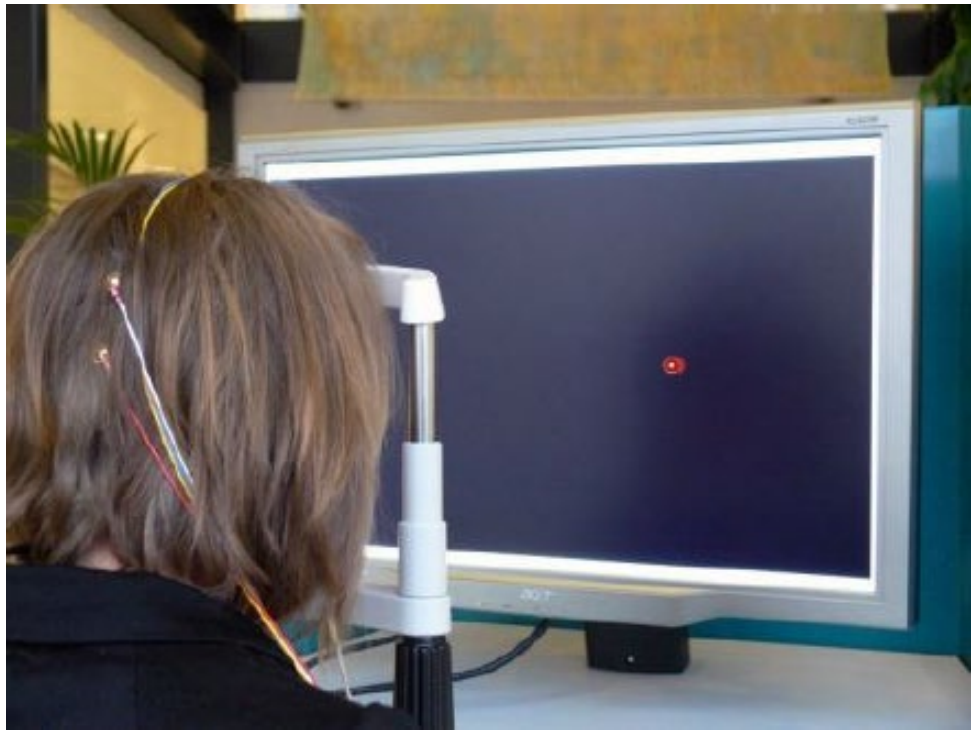


- Fast absorption
- Optimal half-life (8 h)
- No accumulation over time
- No active metabolites

Daridorexant is available in the US, Germany, Italy, Spain, Switzerland, the UK and Canada under the tradename QUVIVIQ.
In addition, daridorexant is approved throughout the European Union.

Fast and time limited pharmacodynamic effect





Person performing eye movement test

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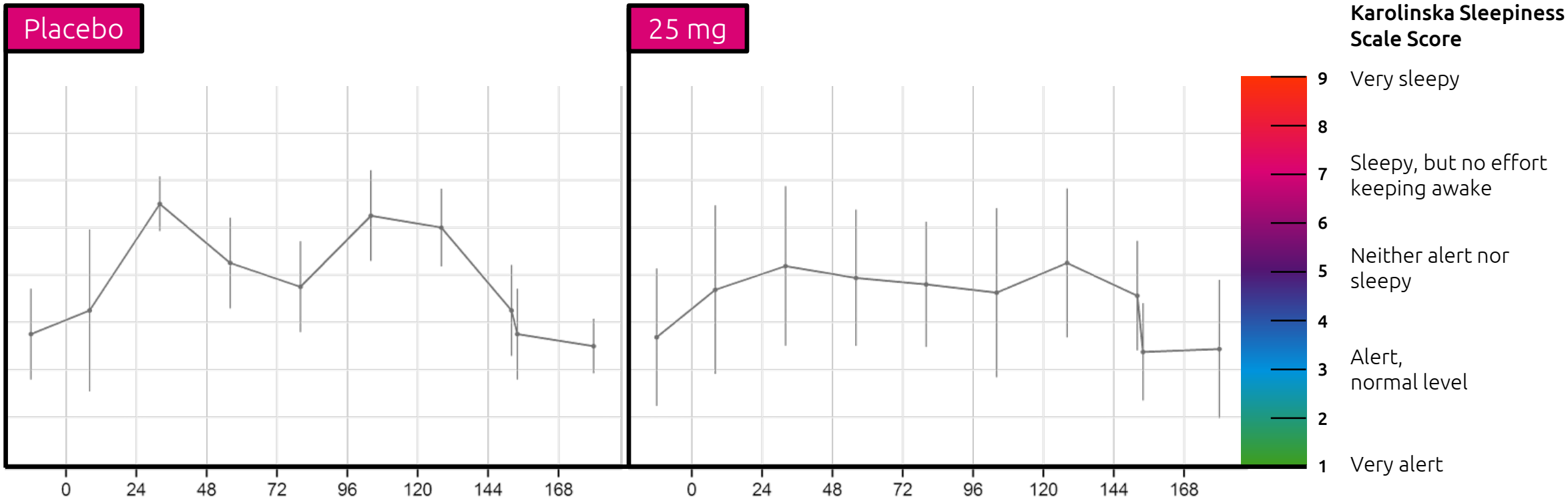
No pharmacodynamic effect on next morning

Entry into man studies



Time after first dose (h) – measures 8 hours after dosing

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In addition, daridorexant is approved throughout the European Union.

Daridorexant registration program

Robust program in adult and elderly insomnia patients

Following completion of Phase 2 studies, two similar pivotal studies of 3-month duration in moderate and severe insomnia

Efficacy

- Objective and subject sleep parameters (onset and maintenance) by polysomnography (PSG) and sleep diary questionnaire (SDQ)
- Daytime functioning assessed by insomnia daytime symptoms and impact questionnaire (IDSIQ)
- Replicated in two confirmatory studies

Safety

- Adverse events, vital signs, biochemistry and hematology
- Next morning residual “hang-over” effect
- Withdrawal/physical dependence, and rebound insomnia

Comprehensive clinical pharmacology program including:

- Driving performance, interaction (medicines, alcohol), Safety in specific population (COPD, obstructive sleep apnea, liver and renal impairment), drug abuse potential

Daridorexant is available in the US, Germany, Italy, Spain, Switzerland, the UK and Canada under the tradename QUVIVIQ.
In addition, daridorexant is approved throughout the European Union.

Study objectives

1st study, 50, 25 mg; 2nd study, 25, 10 mg

Primary objective

- To evaluate the efficacy of daridorexant on objective sleep parameters in patients with insomnia.

Secondary objective

- To evaluate the efficacy of daridorexant on subjective sleep parameters and daytime functioning in patients with insomnia.

Safety objective

- To assess the safety and tolerability of daridorexant in patients with insomnia during treatment and upon treatment discontinuation.

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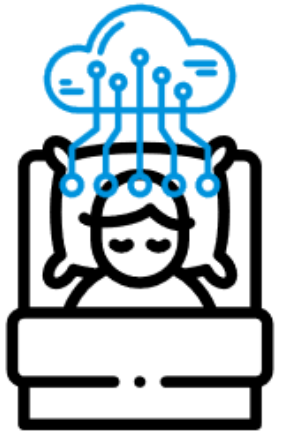
In addition, daridorexant is approved throughout the European Union.

Objective sleep assessments

Repeated polysomnography recordings in a sleep lab in all patients

Phase 3 program

- Assess insomnia objectively
- Ensure well-characterized insomnia patients are randomized
- Establish solid baseline during placebo run-in
- Measure primary endpoint at Month 1 and Month 3
  - **Latency to persistent sleep**
  - **Wakening after sleep onset**
- Asses the potential for rebound
- Collect comprehensive information on total sleep time and sleep architecture



Sensors measure brain activity, eye movements, muscle tone, respiratory, and heart parameters.

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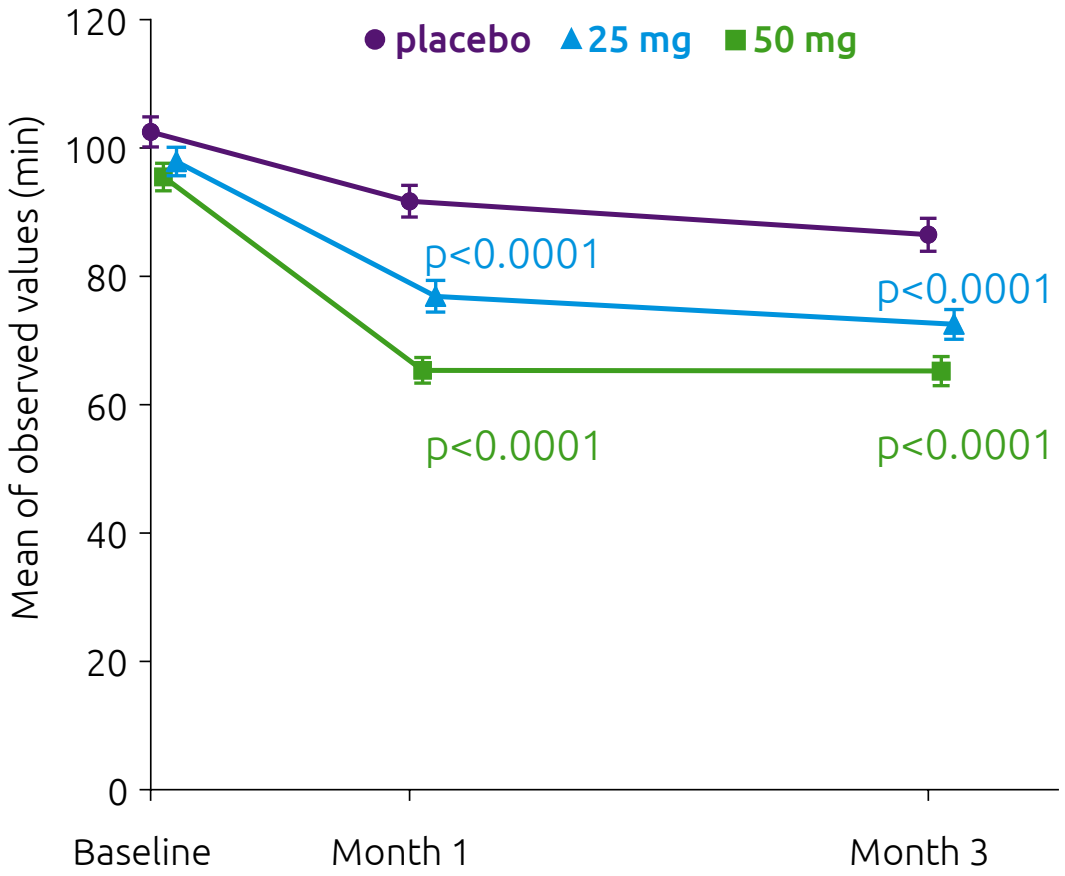
In addition, daridorexant is approved throughout the European Union.

1º endpoint: Wake after sleep onset (WASO)

A measure of sleep maintenance



Daridorexant 25 mg and 50 mg significantly improved WASO compared to placebo at months 1 and 3

LSM change from baseline (95% CI)

	Month 1	Month 3
Placebo	**–6.2** (–9.9 to –2.5)	**–11.1** (–15.1 to –7.1)
Daridorexant 25 mg	**–18.4** (–22.1 to –14.7)	**–23.0** (–27.0 to –19.0)
LSM difference compared with placebo (95% CI)	**–12.2** (–17.4 to –7.0)	**–11.9** (–17.5 to –6.2)
Daridorexant 50 mg	**–29.0** (–32.7 to –25.3)	**–29.4** (–33.4 to –25.4)
LSM difference compared with placebo (95% CI)	**–22.8** (–28.0 to –17.6)	**–18.3** (–23.9 to –12.7)

CI = confidence interval; LSM = least squares mean

Mignot E, et al. *Lancet Neurol* 2022; 21: 125–39

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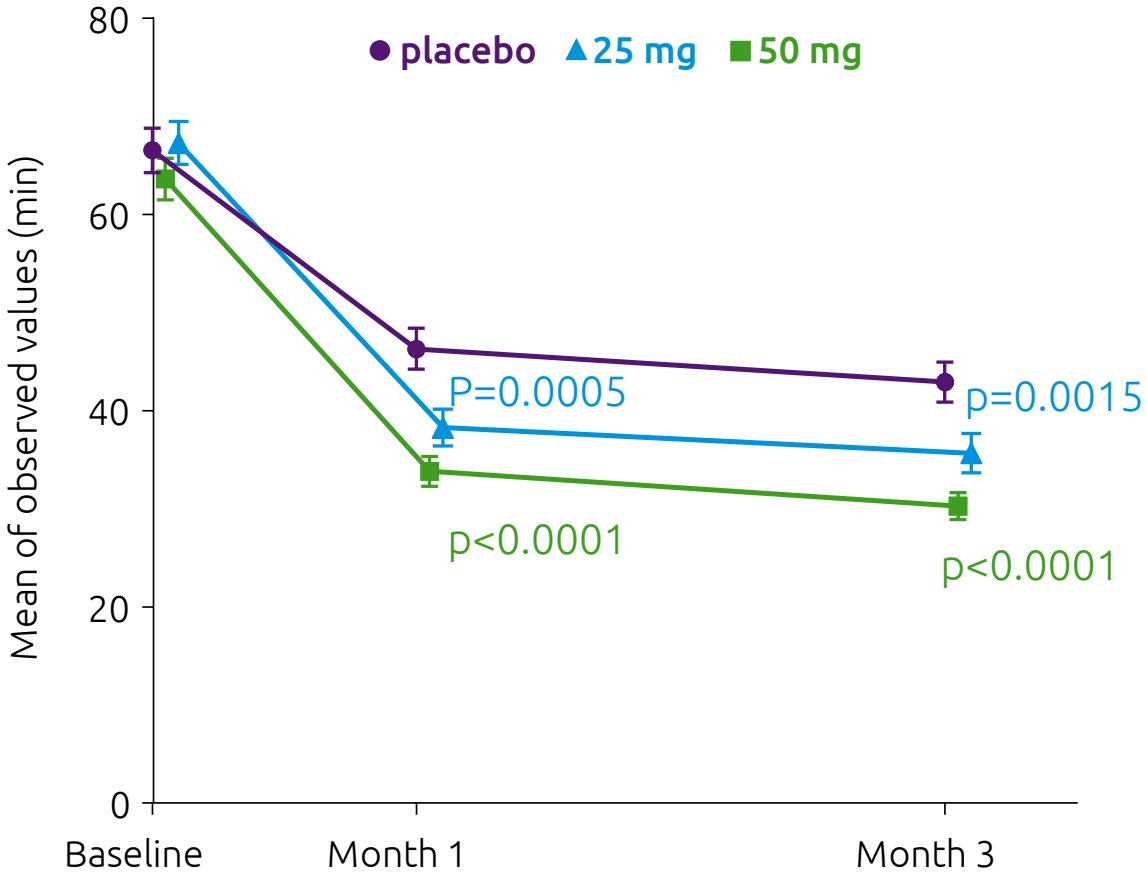
1º endpoint: Latency to persistent sleep (LPS)

A measure of sleep onset



Daridorexant 25 mg and 50 mg **significantly improved LPS** compared to placebo at months 1 and 3

LSM change from baseline (95% CI)

	Month 1	Month 3
Placebo	**–19.9** (–23.2 to –16.5)	**–23.1** (–26.5 to –19.8)
Daridorexant 25 mg	**–28.2** (–31.5 to –24.8)	**–30.7** (–34.0 to –27.4)
LSM difference compared with placebo (95% CI)	**–8.3** (–13.0 to –3.6)	**–7.6** (–12.3 to –2.9)
Daridorexant 50 mg	**–31.2** (–34.5 to –27.9)	**–34.8** (–38.1 to –31.5)
LSM difference compared with placebo (95% CI)	**–11.4** (–16.0 to –6.7)	**–11.7** (–16.3 to –7.0)

CI = confidence interval; LSM = least squares mean

Mignot E, et al. *Lancet Neurol* 2022; 21: 125–39

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Sleep diary questionnaire (SDQ)

Daily recording

Morning questionnaire

- 10 questions related to medication, quantification of sleep, awakenings
- 3 visual analog scales related to quality and deepness of sleep and sleepiness in the morning

→ **Total sleep time**
Secondary endpoint

Evening questionnaire

- 2 questions related to napping
- 2 visual analog scales related to alertness and ability to perform

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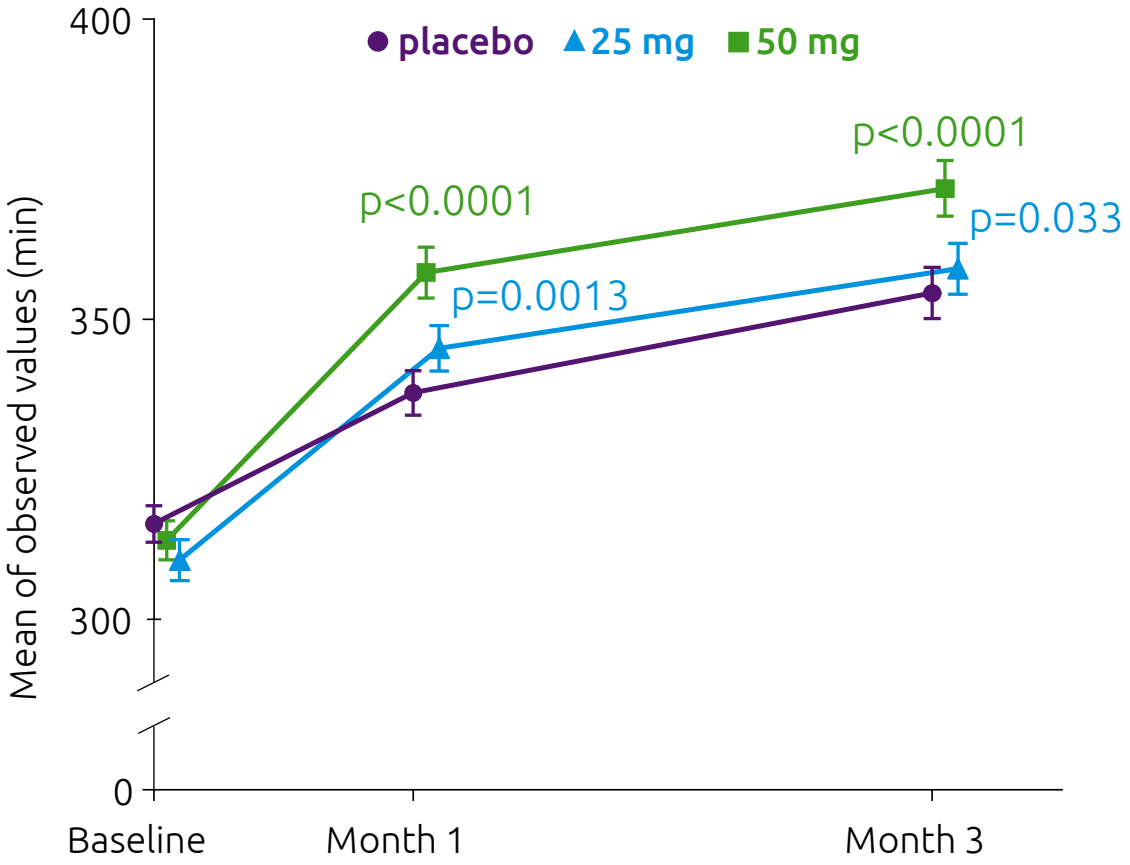
2º endpoint: Subjective Total Sleep Time (sTST)

A measure of how the patient think they slept



Daridorexant 25 mg and 50 mg **significantly improved sTST** compared to placebo at months 1 and 3

LSM change from baseline (95% CI)

	Month 1	Month 3
Placebo	**21.6** (16.1 to 27.0)	**37.9** (31.4 to 44.4)
Daridorexant 25 mg	**34.2** (28.7 to 39.6)	**47.8** (41.3 to 54.3)
LSM difference compared with placebo (95% CI)	**12.6** (5.0 to 20.3)	**9.9** (0.8 to 19.1)
Daridorexant 50 mg	**43.6** (38.2 to 49.1)	**57.7** (51.2 to 64.2)
LSM difference compared with placebo (95% CI)	**22.1** (14.4 to 29.7)	**19.8** (10.6 to 28.9)

CI = confidence interval; LSM = least squares mean

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Subjective assessment of daytime functioning

Insomnia Daytime Symptoms and Impacts Questionnaire (IDSIQ)

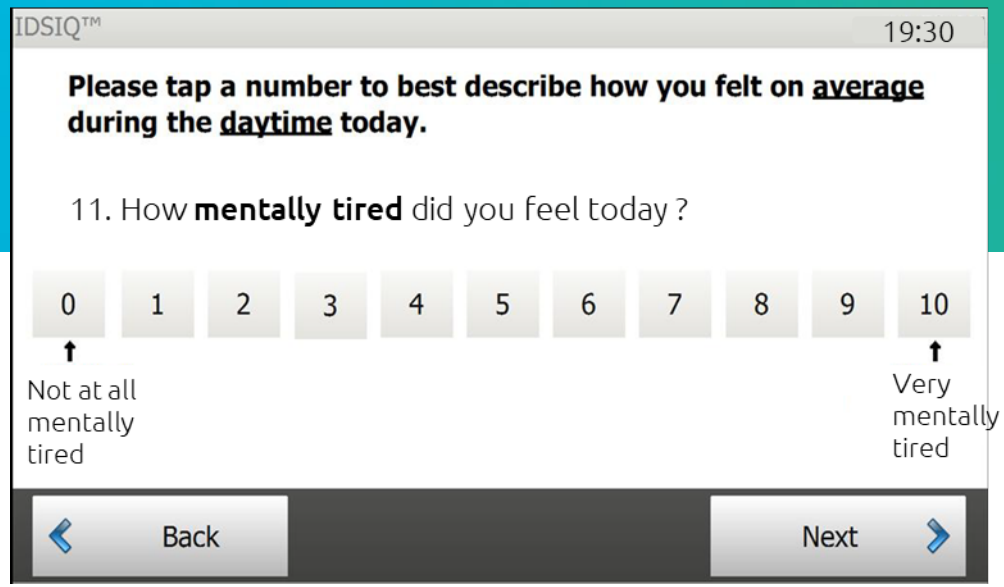
Measures
Item 1. How **clear-headed** did you feel today?
Item 2. How well were you able to **concentrate** today?
Item 3. How **forgetful** did you feel today?
Item 4. How **worried** did you feel today?
Item 5. How **frustrated** by your lack of sleep did you feel today?
Item 6. How **irritable** did you feel today?
Item 7. How **stressed** did you feel today?
Item 8. How **energetic** did you feel today?
Item 9. How **much of an effort** was it to perform daily activities (i.e. reading, cleaning, work, school) today?
Item 10. How **refreshed** did you feel today?
Item 11. How **mentally tired** did you feel today?
Item 12. How **physically tired** did you feel today?
Item 13. How **sleepy** did you feel today?
Item 14. How **awake** did you feel today?

"Alert/cognition" domain score (0-60)

"Mood" domain score (0-40)

"Sleepiness" domain score (0-40)

Items are ranked on a numeric rating scale from 0-10



Daytime functioning measured by sleepiness domain score
Secondary endpoint

Daridorexant is available in the US, Germany, Italy, Spain, Switzerland, the UK and Canada under the tradename QUVIVIQ.
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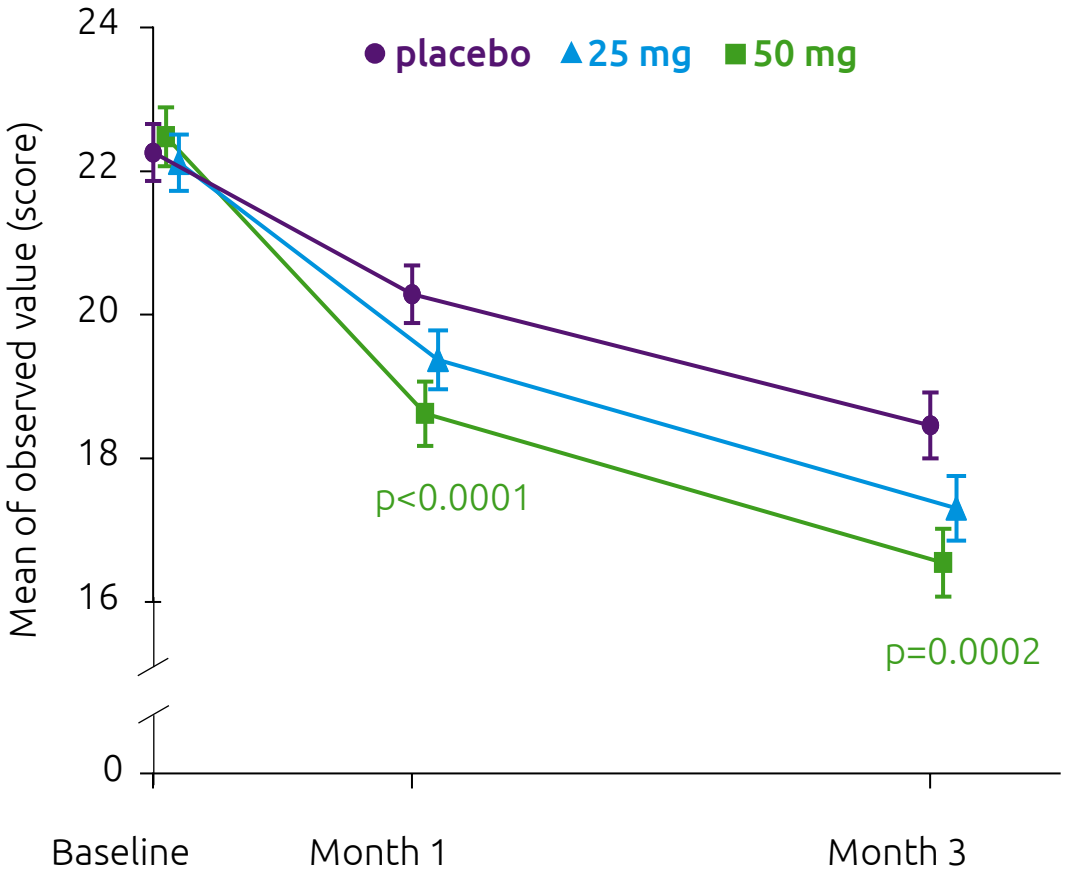
2º endpoint: IDSIQ sleepiness domain

A measure of daytime functioning

How **energetic** did you feel today?
How **mentally tired** did you feel today?
How **physically tired** did you feel today?
How **sleepy** did you feel today?



Daridorexant 50 mg significantly improved IDSIQ sleepiness domain score compared to placebo at months 1 and 3

LSM change from baseline (95% CI)

	Month 1	Month 3
Placebo	**–2.0** (–2.6 to –1.5)	**–3.8** (–4.5 to –3.1)
Daridorexant 25 mg	**–2.8** (–3.3 to –2.2)	**–4.8** (–5.5 to –4.1)
LSM difference compared with placebo (95% CI)	**–0.8** (–1.5 to 0.01)	**–1.0** (–2.0 to 0.01)
Daridorexant 50 mg	**–3.8** (–4.3 to –3.2)	**–5.7** (–6.4 to –5.0)
LSM difference compared with placebo (95% CI)	**–1.8** (–2.5 to –1.0)	**–1.9** (–2.9 to –0.9)

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Exploratory endpoints: IDSIQ other scores

A measure of daytime functioning

IDSIQ mood domain, alert/cognition domain, and total scores at both timepoints were reduced (improved) (all nominal p-values for daridorexant 50 mg versus placebo ≤0.0005; not adjusted for multiplicity)

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Adverse events

In the safety analysis population (n=1847)

	Study 1			Study 2		
	Dari 50 mg (n = 308)	Dari 25 mg (n = 310)	Placebo (n = 309)	Dari 25 mg (n = 308)	Dari 10 mg (n = 306)	Placebo (n = 306)
Participants with ≥1 adverse event*	116 (38%)	117 (38%)	105 (34%)	121 (39%)	117 (38%)	100 (33%)
Adverse events* leading to treatment discontinuation	3 (1%)	7 (2%)	10 (3%)	4 (1%)	6 (2%)	7 (2%)
Participants with ≥1 serious adverse event	3 (1%)	2 (1%)	7 (2%)	3 (1%)	3 (1%)	4 (1%)
Participants with adverse event* (≥2% in any group)						
Nasopharyngitis	20 (6%)	21 (7%)	20 (6%)	13 (4%)	32 (10%)	16 (5%)
Headache	19 (6%)	16 (5%)	12 (4%)	15 (5%)	12 (4%)	11 (4%)
Accidental overdose	8 (3%)	4 (1%)	5 (2%)	4 (1%)	4 (1%)	1 (<1%)
Fatigue	7 (2%)	7 (2%)	2 (1%)	11 (4%)	7 (2%)	2 (1%)
Dizziness	7 (2%)	6 (2%)	2 (1%)	6 (2%)	4 (1%)	4 (1%)
Nausea	7 (2%)	1 (<1%)	3 (1%)	2 (1%)	3 (1%)	3 (1%)
Somnolence	5 (2%)	11 (4%)	6 (2%)	10 (3%)	6 (2%)	4 (1%)
Fall	1 (<1%)	1 (<1%)	8 (3%)	3 (1%)	4 (1%)	3 (1%)
Upper respiratory tract infection	1 (<1%)	1 (<1%)	3 (1%)	3 (1%)	5 (2%)	6 (2%)

Data are n (%). The safety analysis population included all participants who received at least one dose of double-blind treatment. *Adverse events that occurred during the double-blind treatment period in the safety population are included in the table and presented with their preferred terms.

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Adjudicated adverse events

In the safety analysis population (n=1847)

	Study 1			Study 2		
	Dari 50 mg (n = 308)	Dari 25 mg (n = 310)	Placebo (n = 309)	Dari 25 mg (n = 308)	Dari 10 mg (n = 306)	Placebo (n = 306)
Adjudicated adverse events†						
Excessive daytime sleepiness	1 (<1%)	2 (1%)	1 (<1%)	4 (1%)	1 (<1%)	1 (<1%)
Sleep paralysis	1 (<1%)	1 (<1%)	0	2 (1%)	0	0
Hallucinations	0	1 (<1%)	0	1 (<1%)	0	0
Suicidal ideation or self-injury‡	0	0	0	1 (<1%)	1 (<1%)	0

Data are n (%). The safety analysis population included all participants who received at least one dose of double-blind treatment. †Adjudicated adverse events were reported during the double-blind treatment up to 30 days after the end of treatment or date of enrolment into the extension trial and were adjudicated blindly by an independent safety board. ‡Adjudicated adverse events belonging to the category suicidal ideation or self-injury (preferred term: suicidal ideation) were reported in two participants, one in each daridorexant group in study 2; both patients had pre-existing medical conditions (paranoid schizophrenia or depression) and the independent safety board adjudicated both adverse events as potentially related to trial treatment.

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Further safety observations

No adverse events suggested that **drug misuse** might have occurred

No withdrawal symptoms were observed during the placebo run-out period, as assessed by adverse events or the Benzodiazepine Withdrawal Symptom Questionnaire (BWSQ)

During the placebo run-out period, WASO and LPS were numerically lower, and mean self-reported total sleep time was higher than respective baseline values, indicating **absence of rebound insomnia**

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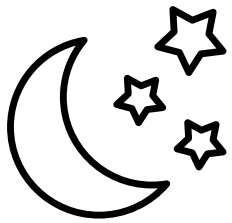
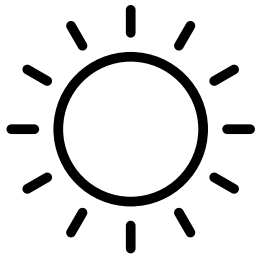
The daridorexant clinical program provides a wealth of evidence



Comprehensive sleep efficacy perceived by patients (25 mg & 50 mg)

- Fall asleep faster
- Stay asleep longer
- Time in each sleep stage preserved

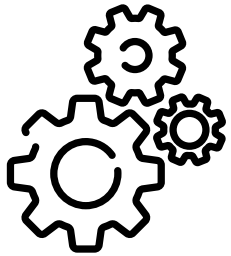


Daytime functioning perceived by patients (50 mg)

- Improved sleepiness
- Consistent effect on mood and alertness / cognition on exploratory endpoints
- Progressive improvement over time

Documented safety

- A low overall incidence of adverse events (AE), comparable between treatment groups
- Most common AEs (>5%): nasopharyngitis and headache
- No evidence of tolerance or dependence
- No rebound insomnia or withdrawal effects



Precision MOA & intrinsic properties of daridorexant

- Targets only the part of the brain that keeps you awake, without broad sedation
- Ideal pharmacological profile

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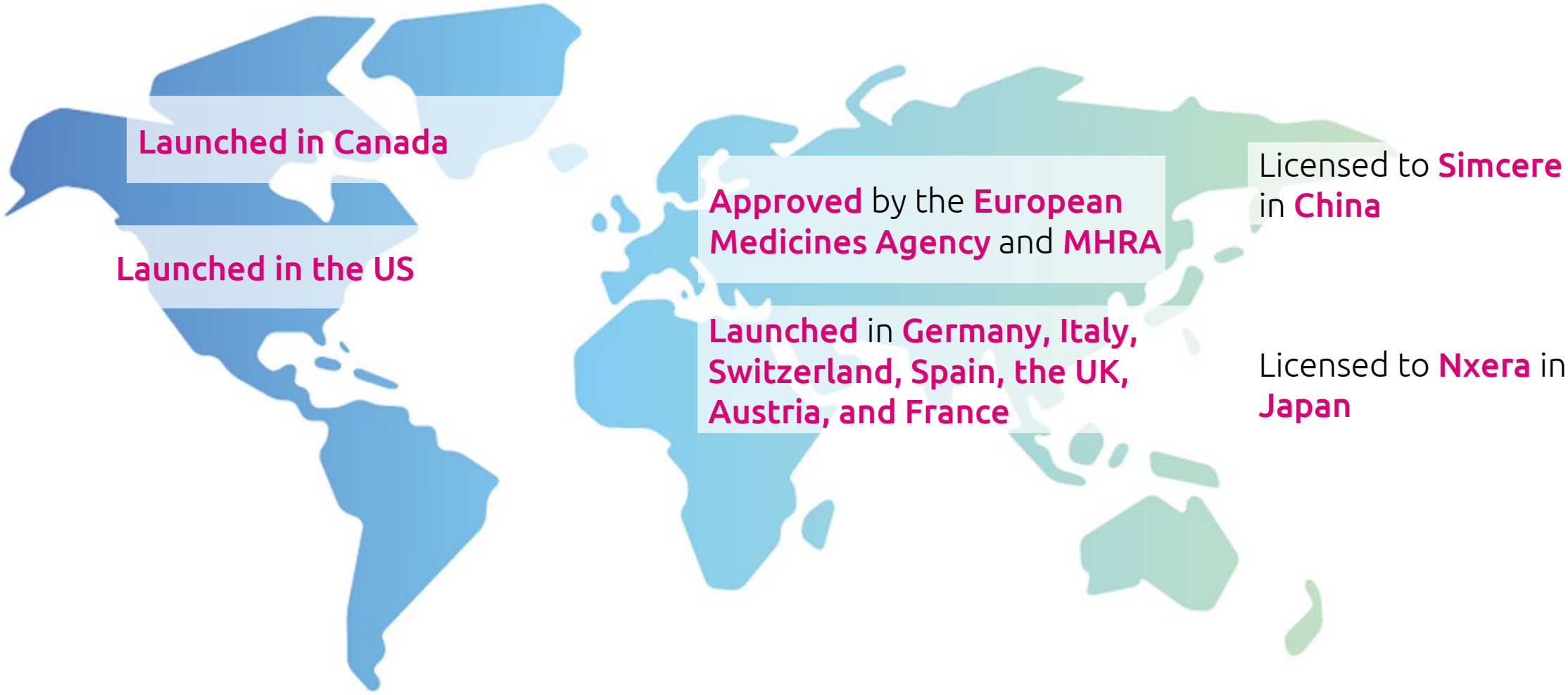
On track to become a global brand

QUVIVIQ daridorexant 25mg, 50mg tablets



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Collaboration with Syneos Health

Commercialization partner to launch daridorexant in the US, Europe, and Canada

- Syneos Health selected as commercialization partner in order to effectively reach the primary care market, which accounts for a large volume of insomnia prescriptions, in the US, Europe, and Canada
- Syneos Health brings a robust customer-facing sales expertise and proven track record in launching new products in these regions
- An innovative, revenue-driven agreement to accelerate and maximize reach to patients
- Together we will lead the transformation and modernization of the insomnia market

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License agreements with Nxera & Mochida

Nxera Pharma

Co-exclusive license granted to Nxera (previously known as Sosei Heptares) for daridorexant in Australia, Brunei, Cambodia, Indonesia, Japan, Laos, Malaysia, Myanmar, New Zealand, Philippines, Singapore, South Korea, Thailand, Taiwan, and Vietnam

Mochida

Supply, co-development and co-marketing of daridorexant in Japan

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License agreement with Simcere

Development and commercialization of daridorexant in the Greater China region

- Simcere has an exclusive right to develop and commercialize daridorexant in the Greater China region (Mainland China, Hong Kong, and Macau), one of the world's largest pharmaceutical markets
- Simcere is responsible for the local development program with Chinese patients
- Idorsia receives a US$ 30 million upfront payment and will be eligible to receive an additional milestone payment of US$ 20 million upon regulatory approval by the National Medical Products Administration, as well as commercial milestone payments and low double-digit tiered royalties based upon future sales.

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QUVIVIQ® (daridorexant) launched in the US in May 2022

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Educational campaigns to prime the US market

The Alliance for Sleep

Top sleep experts drive education, awareness and research to medical community and consumers

Seize the Night & Day

Partnering with **Jennifer Aniston** to drive awareness and education

Wake up America Sleep Survey

Consumer and HCP survey to reveal views and patient unmet needs

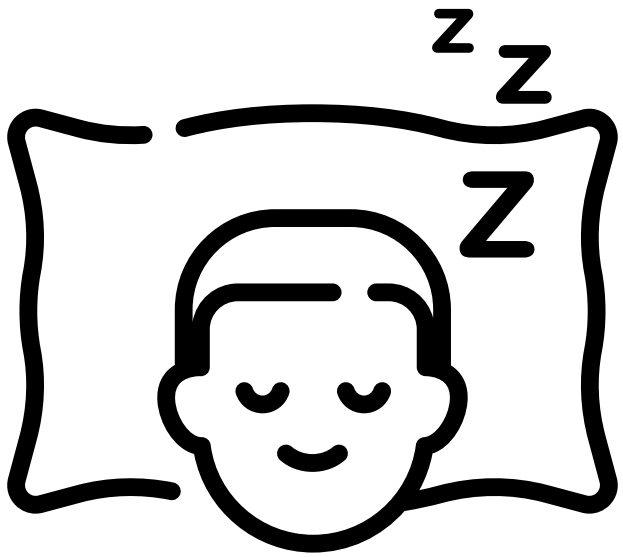
The Quest for Sleep

Documentary Film using storytelling to raise awareness of insomnia, and bring the science of sleep to life

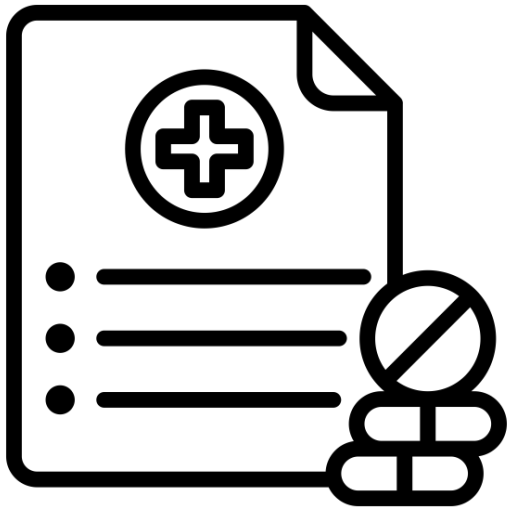
QUVIVIQ US launch

QUVIVIQ (daridorexant) IV 25mg, 50mg tablets

>125K
patients treated



>300K
prescriptions dispensed



>35K
prescribers

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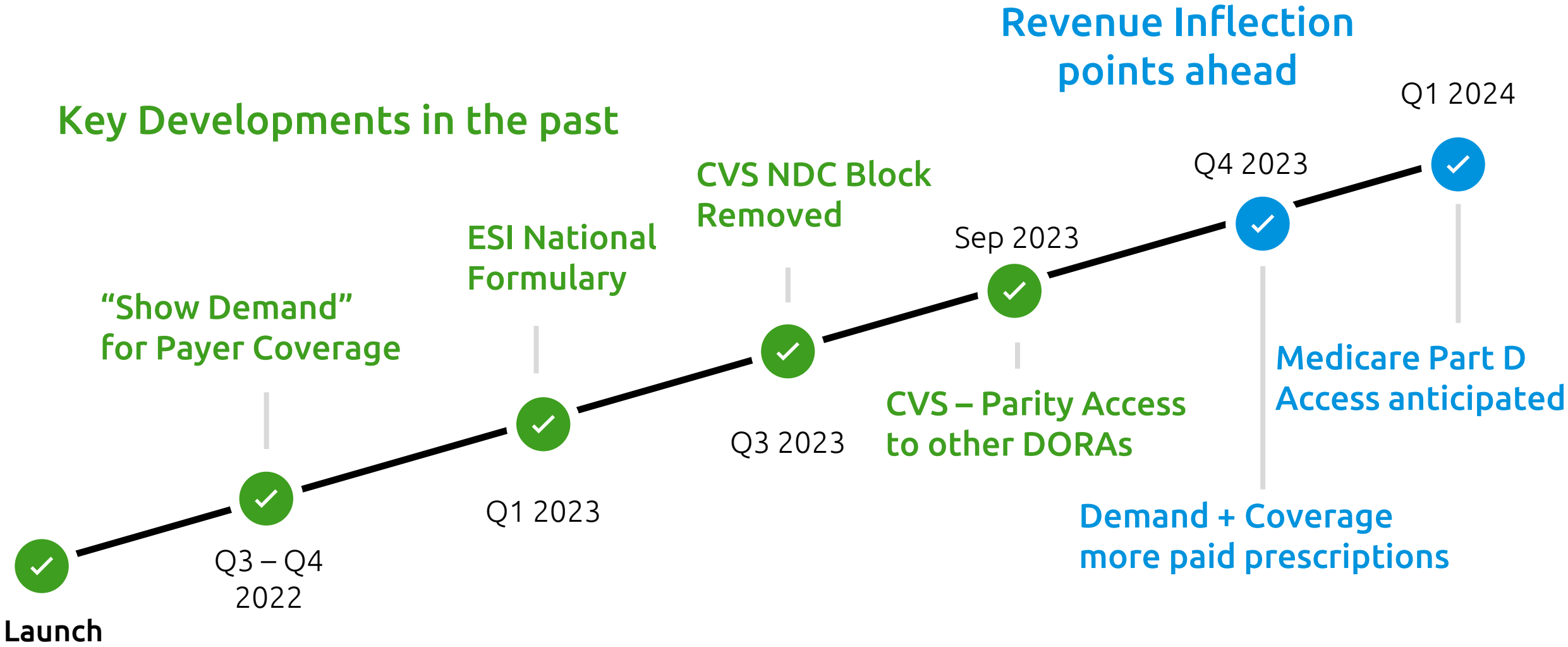
Demand and payer coverage enable conversion to paid scripts



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Supporting patient access and generating demand

QUVIVIQ (daridorexant) 25mg, 50mg tablets

CHF

15 million

net sales in 9M 2023*

*net sales do not reflect the volume of prescriptions dispensed due to patient assistance and coupon programs

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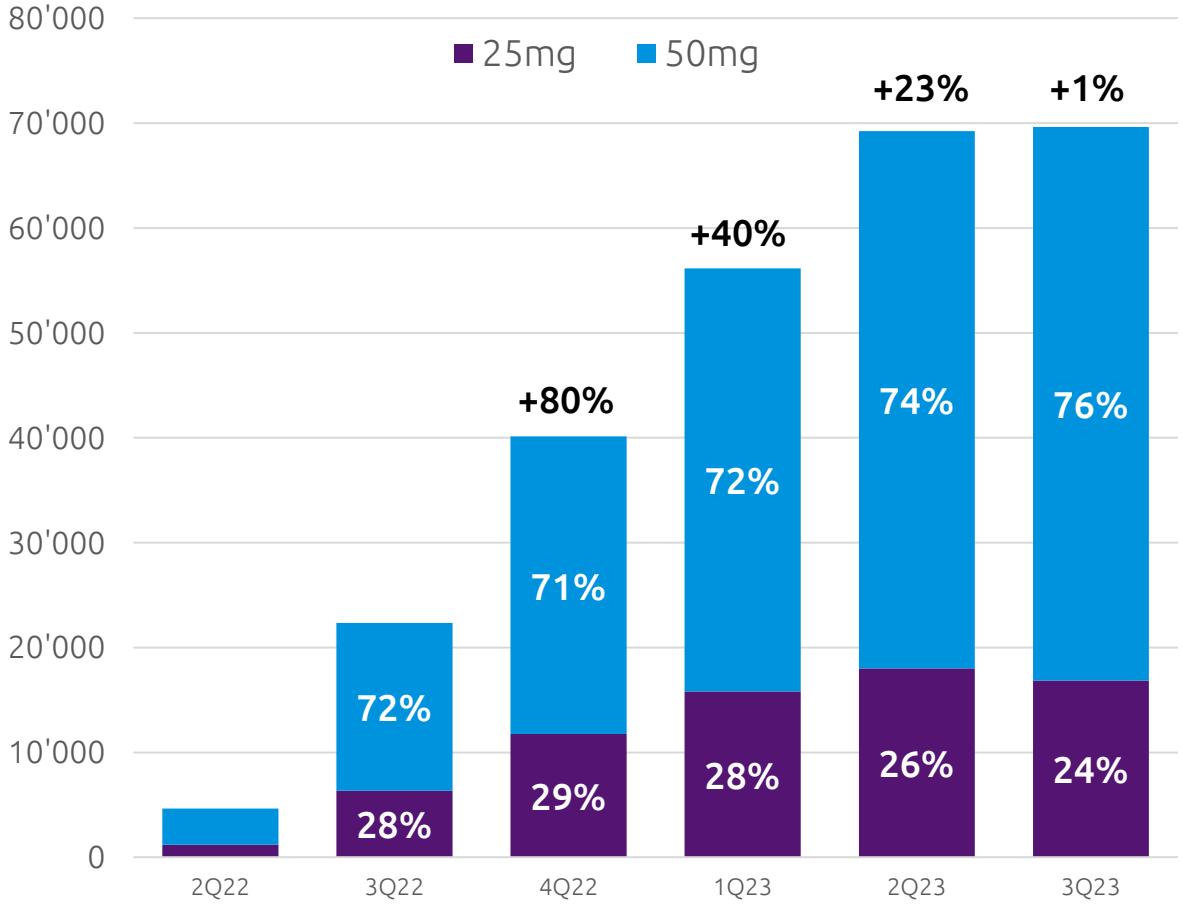
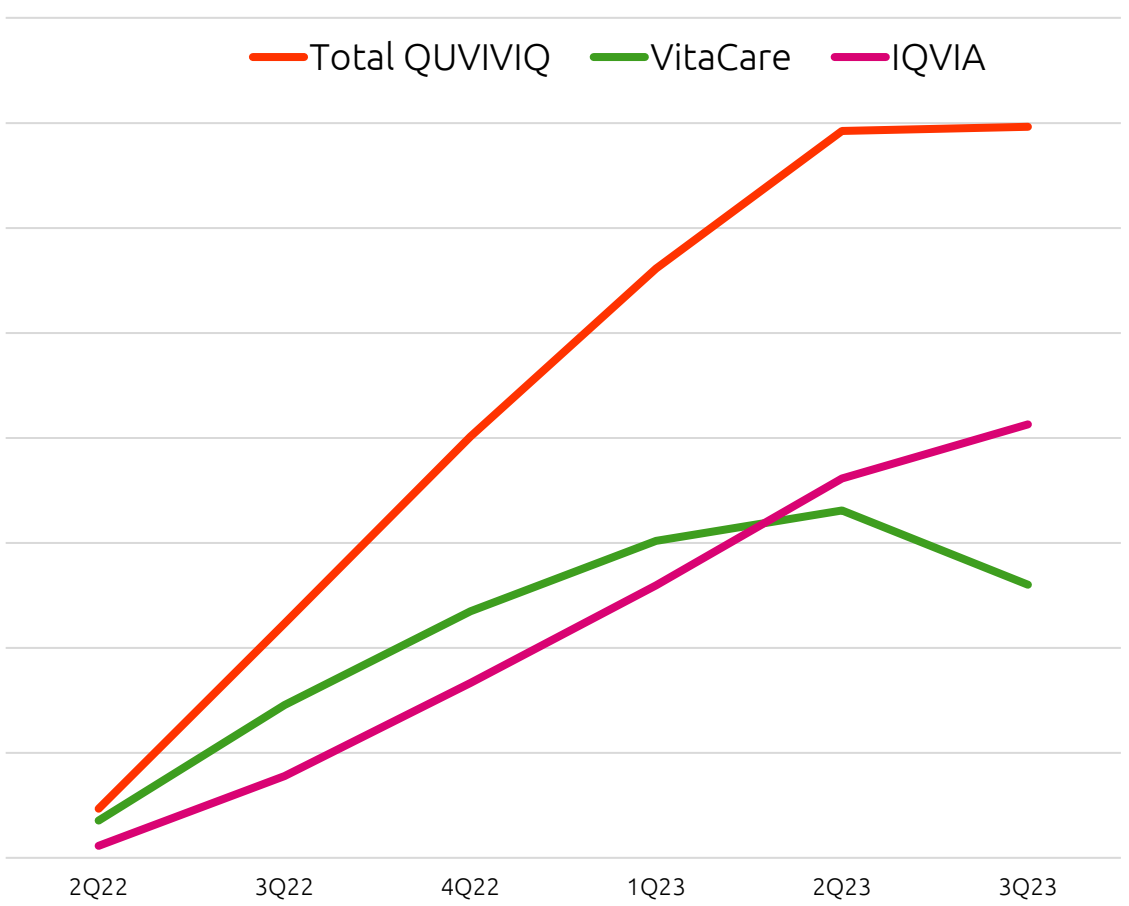
QUVIVIQ demand with increasing volume coming from retail

QUVIVIQ Quarterly TRxs by Strength



QUVIVIQ Quarterly TRxs by Source



Source: IQVIA + VitaCare + KnippeRx Pharmacy Services

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Payer wins accelerate conversion to paid scripts

Key payer wins for QUVIVIQ

- CVS caremark — Commercial Preferred 23.1M lives[1]
- EXPRESS SCRIPTS® — Commercial Covered 22.2 MM Lives [1]
- AARP | Medicare Plans from UnitedHealthcare — Medicare Part D Non-Preferred 10.3 MM Lives [1]
- TRICARE® — Commercial Preferred 8.8 MM Lives [1]
- VA | U.S. Department of Veterans Affairs — Commercial Preferred 5.0 MM Lives [1]

Source: MMIT January 2, 2024

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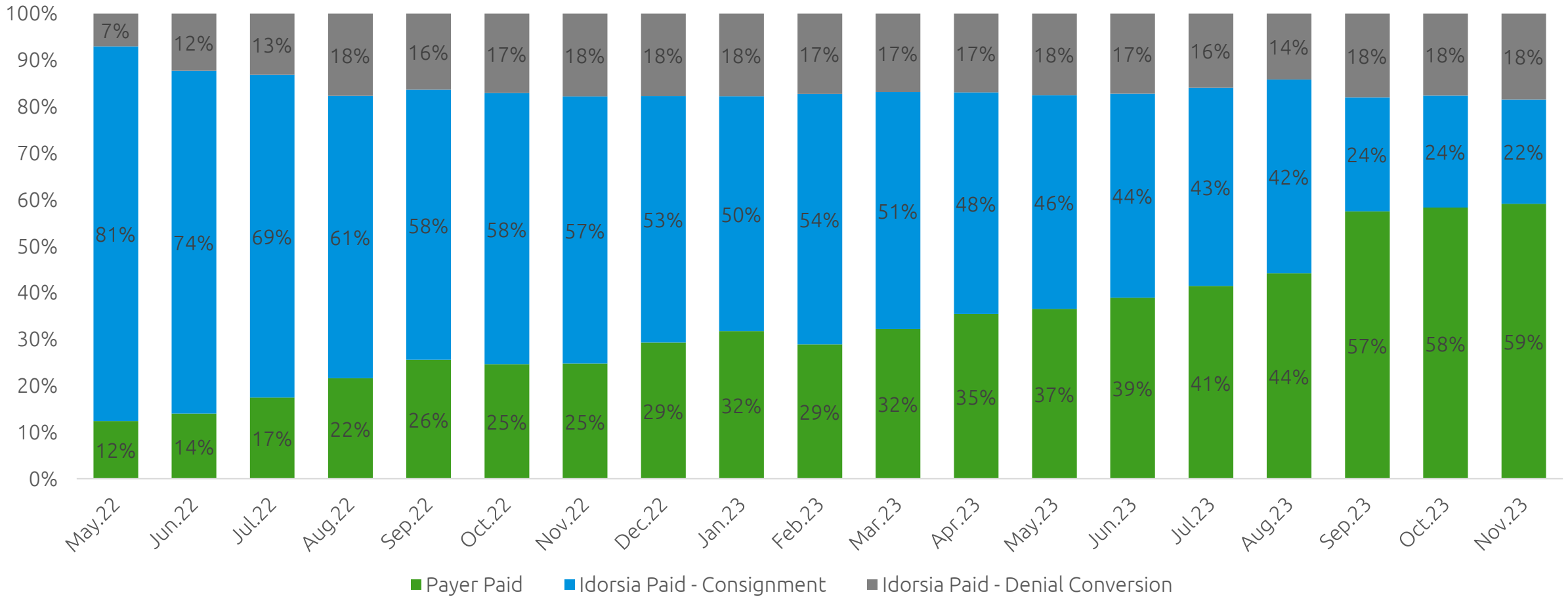
Payer coverage and percentage of paid claims

Idorsia Paid vs Payer Paid prescription Mix



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Scheduling under discussion

Citizen's Petition

The FDA and DEA have acknowledged our Citizen Petition requesting de-scheduling the DORA class of medicines, and the process to analyze and examine the request seems to be moving forward

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“We have streamlined the US operations for 2024 with the mindset **‘Achieving more with less’**. For example, our dynamic digital marketing campaign is the #1 driver of traffic to the QUVIVIQ website so it will replace DTC TV commercials realizing substantial cost savings.”

Tosh Butt
President Idorsia US

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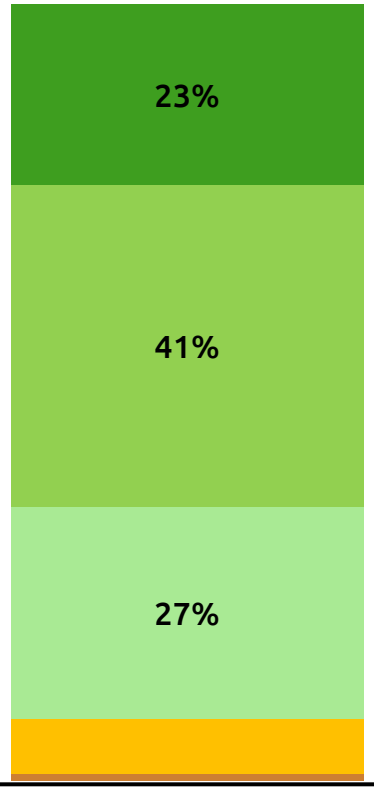
Excitement about QUVIVIQ in Europe

How likely would you be to prescribe QUVIVIQ to your insomnia patients?

HCPs

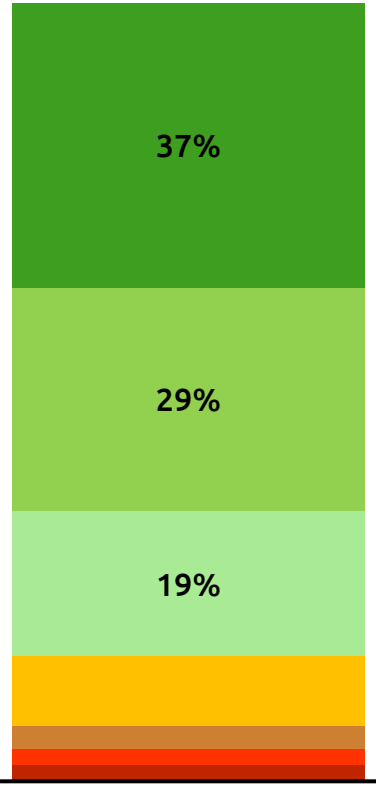
HCPs likely to prescribe **91%**



How likely would you be to ask your HCP about QUVIVIQ?

Patients

Patients likely to ask about **85%**



Extremely Likely (7) | 6 | 5 | Neutral (4) | 3 | 2 | Not at all Likely (1)

Source: Idorsia market research in EU5 (n=1200); 2021

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QUVIVIQ: first DORA in Europe

QUVIVIQ daridorexant 25mg, 50mg tablets

Launched in Nov 2022

- 4-week limitation (Anlage III exemption) lifted Nov 2023
- Negotiated price (AMNOG 1) effective Dec 2023
- AMNOG 2 negotiation to be initiated in 2024

Launched in Nov 2022

- Reimbursement submission under review
- Expansion of prescriber base requested

Launched in Oct 2023

- NICE positive recommendation
- Unrestricted reimbursed market
- Listing by health care boards underway

Launched in June 2023 (self-pay)

- Reimbursement targeted for mid-H1

Launched in Sep 2023 (self-pay)

"ASMR IV – SMR Moderate" recognizing the added value over available treatments

- Price agreement with CEPS
- Unrestricted reimbursed market
- Price publication & launch Q1 2024

Approved in April 2023

- Launched to private market
- 1 month after private market reimbursement submission >40% lives covered

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In addition, daridorexant is approved throughout the European Union.

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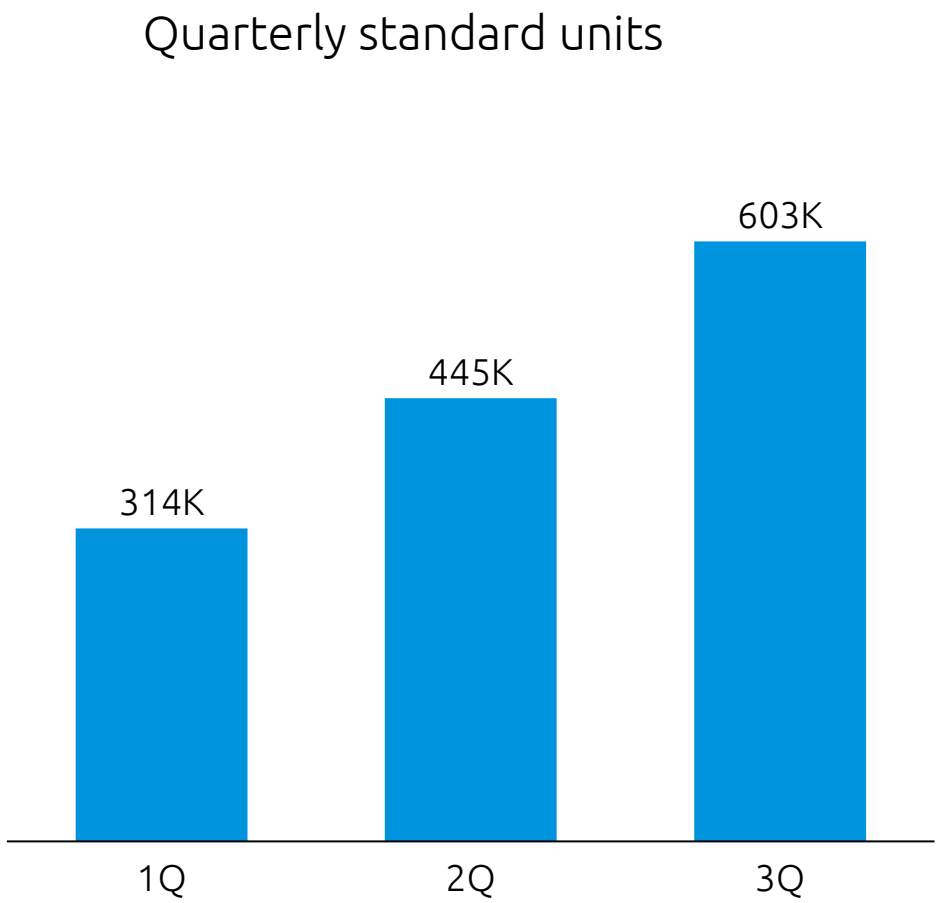
Demand is growing in Europe

QUVIVIQ daridorexant 25mg, 50mg tablets



>45'000
patient months of treatment since launch

Source: 100% sales record from wholesaler to pharmacy – IQVIA Midas Jan-Aug 2023, Sep estimated from internal sales

Daridorexant is available in the US, Germany, Italy, Spain, Switzerland, the UK and Canada under the tradename QUVIVIQ. In addition, daridorexant is approved throughout the European Union.

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QUVIVIQ™ (daridorexant)

CHF

20.2

million

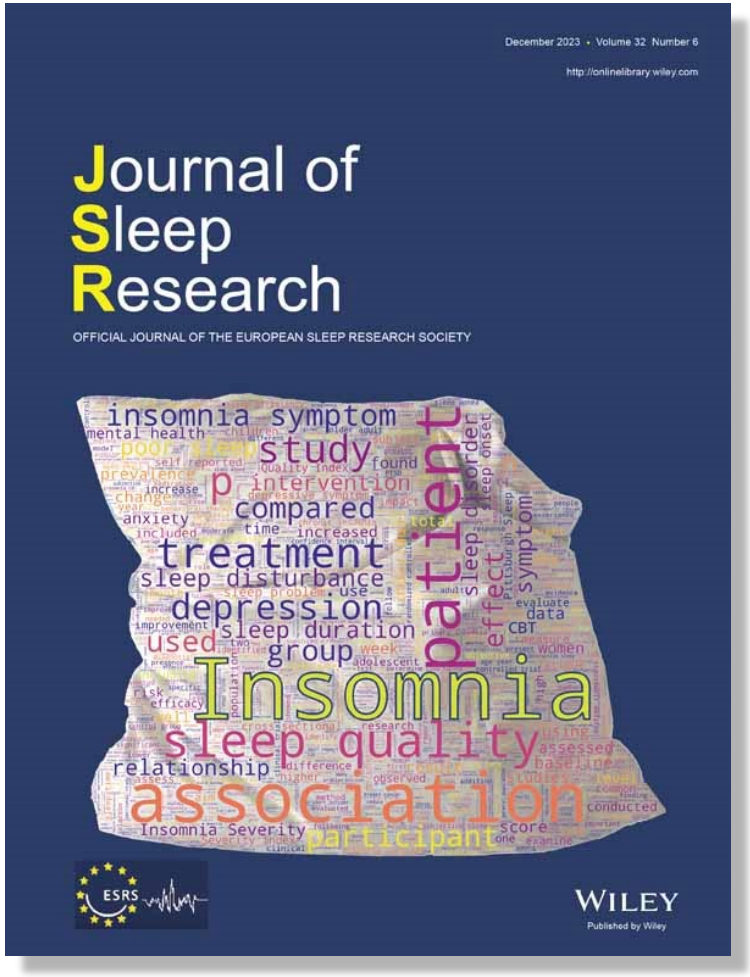
net sales in
9M 2023*

*in the US, Germany, Italy, Spain, and Switzerland;
US net sales do not reflect the volume of prescriptions dispensed due to patient assistance and coupon programs

Daridorexant is available in the US, Germany, Italy, Spain, Switzerland, the UK and Canada under the tradename QUVIVIQ.
In addition, daridorexant is approved throughout the European Union.

The European Insomnia Guideline: An update on the diagnosis and treatment of insomnia 2023

"The introduction of DORAs has probably been the most significant recent development in the pharmacological treatment of insomnia..."



Updates are being pulled through to local guidelines – already launched in Italy and Switzerland – Germany imminent

Daridorexant is available in the US, Germany, Italy, Spain, Switzerland, the UK and Canada under the tradename QUVIVIQ. In addition, daridorexant is approved throughout the European Union.

More sleep – over 11 million tablets dispensed to help better nights and days

QUVIVIQ™

daridorexant 25mg, 50mg tablets

Daridorexant is available in the US, Germany, Italy, Spain, Switzerland, the UK and Canada under the tradename QUVIVIQ. In addition, daridorexant is approved throughout the European Union.

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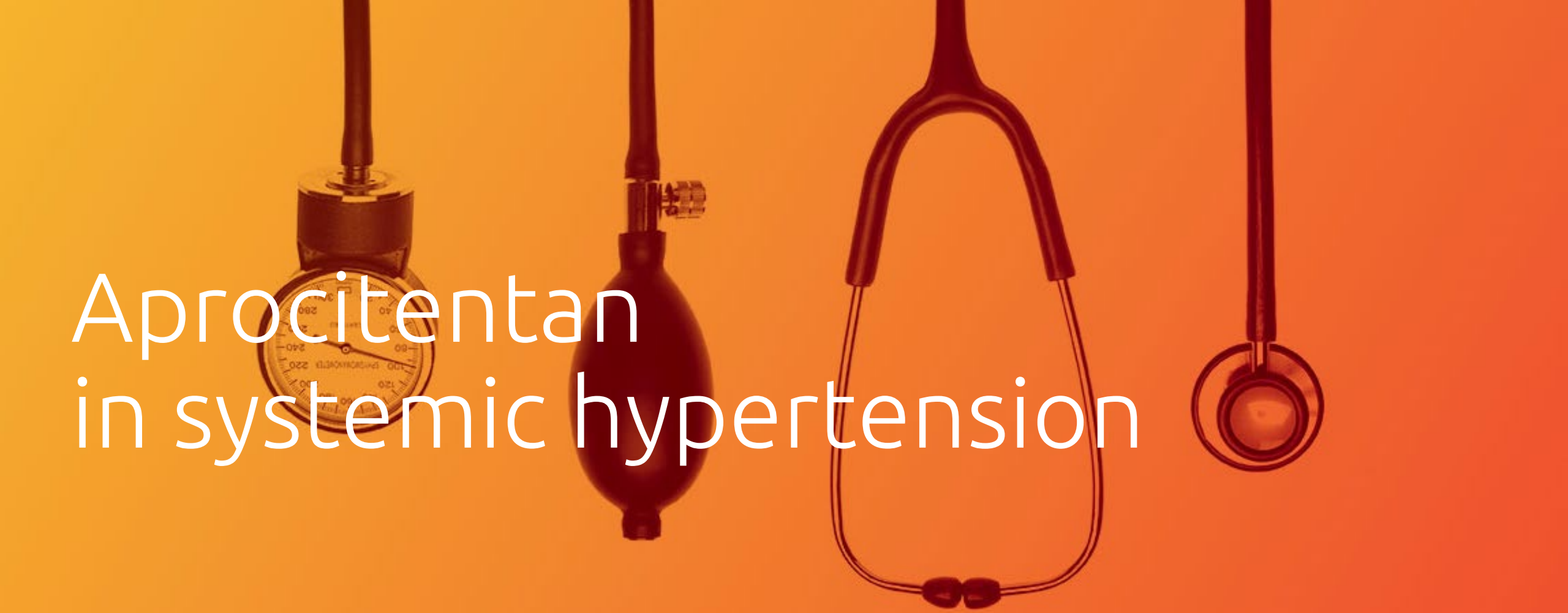


Aprocitentan in systemic hypertension

Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

"Today, there are millions of Americans whose blood pressure is not well-controlled despite existing therapy. This is a major public health issue leading to a high incidence of cardiovascular events."

Jean-Paul Clozel
Chief Executive Officer

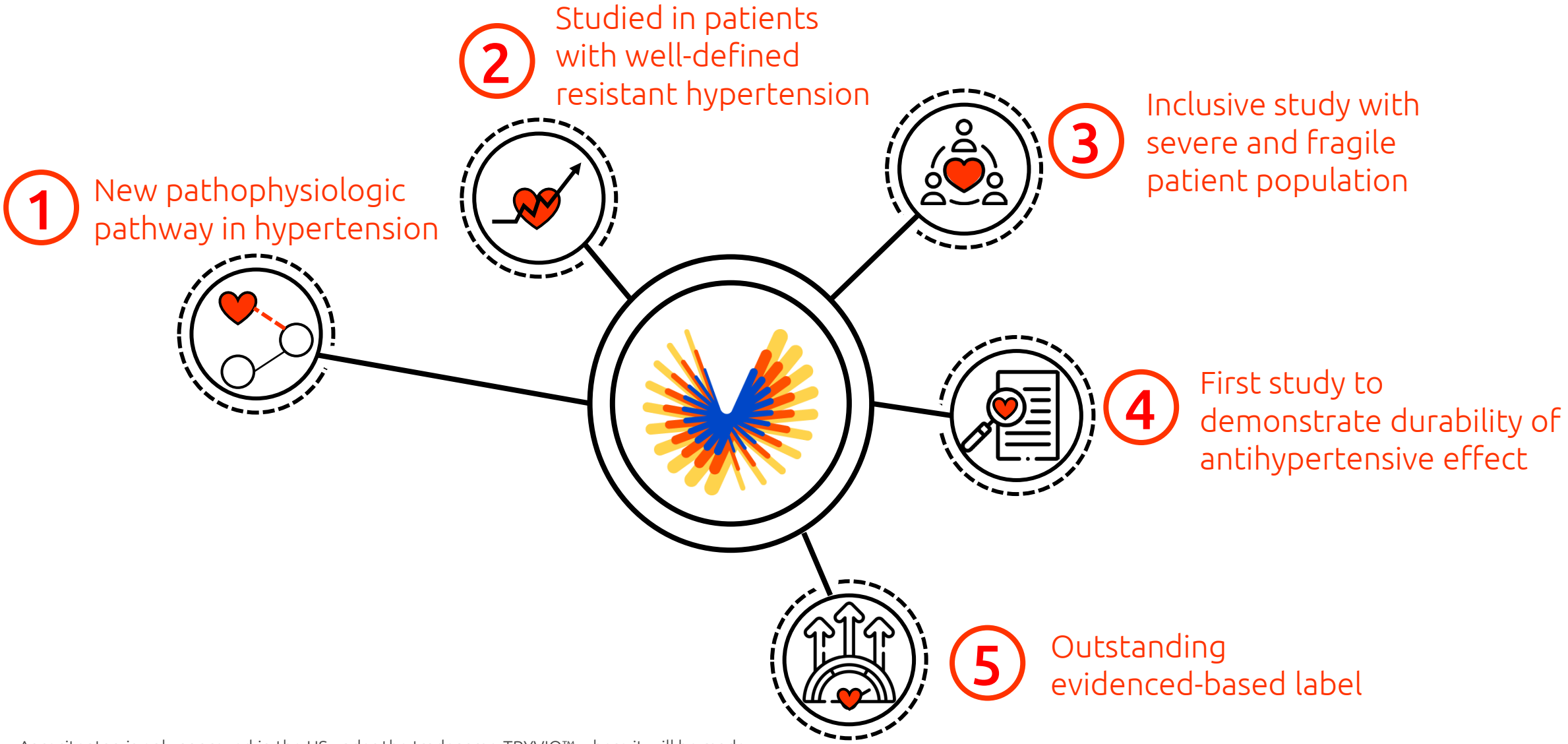
TRYVIO (aprocitentan) 12.5 mg approved by the US FDA

TRYVIO™

(aprocitentan) **12.5mg tablets**

Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

A unique compound with unique data



Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

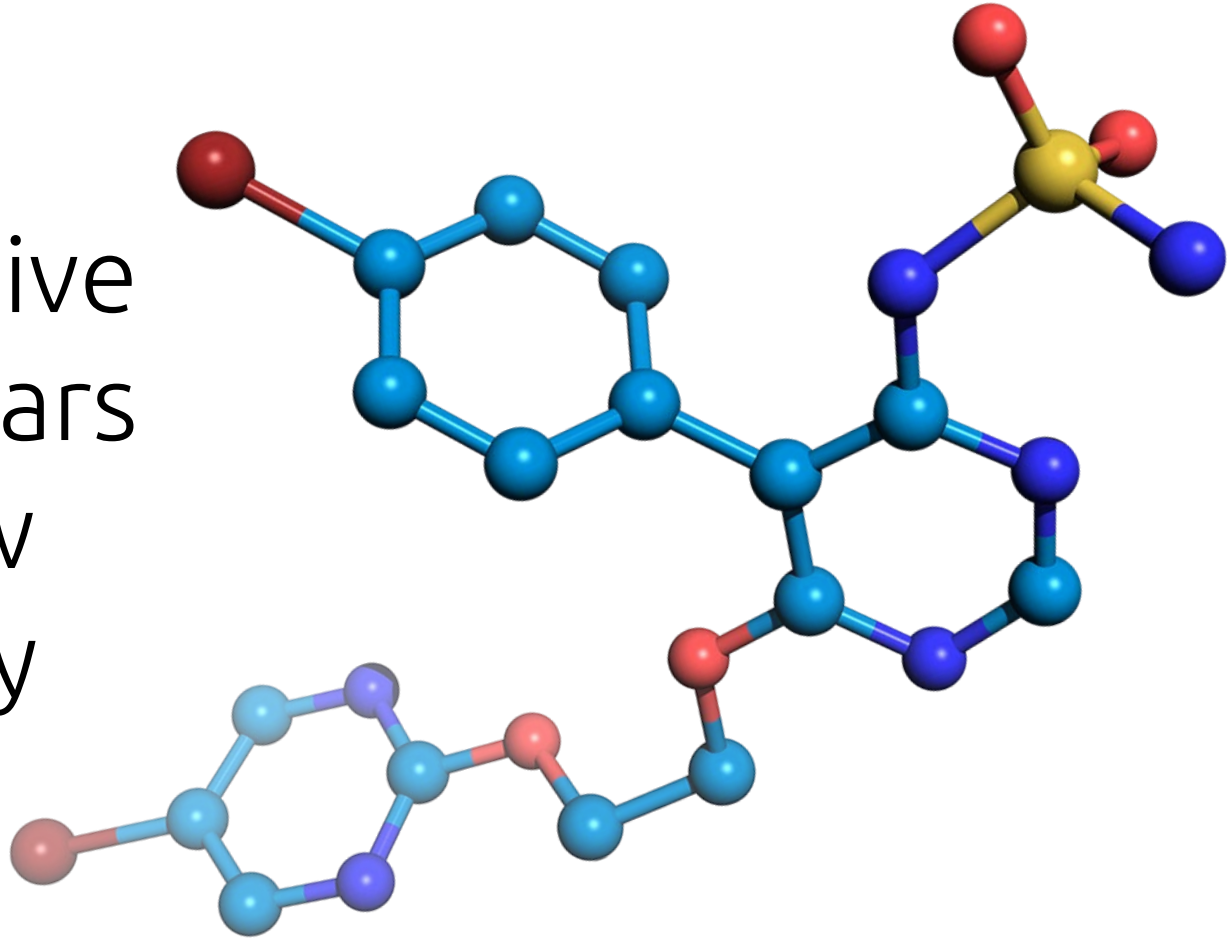
“Since the endothelin pathway was not yet tackled, we selected aprocitentan, an endothelin receptor antagonist with the ideal properties for use with patients whose hypertension is not adequately controlled with other antihypertensives.”

Martine Clozel
Chief Scientific Officer

Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

TRYVIO™
(aprocitentan) 12.5mg tablets

The first anti-hypertensive therapy in almost 40 years which works on a new physiological pathway



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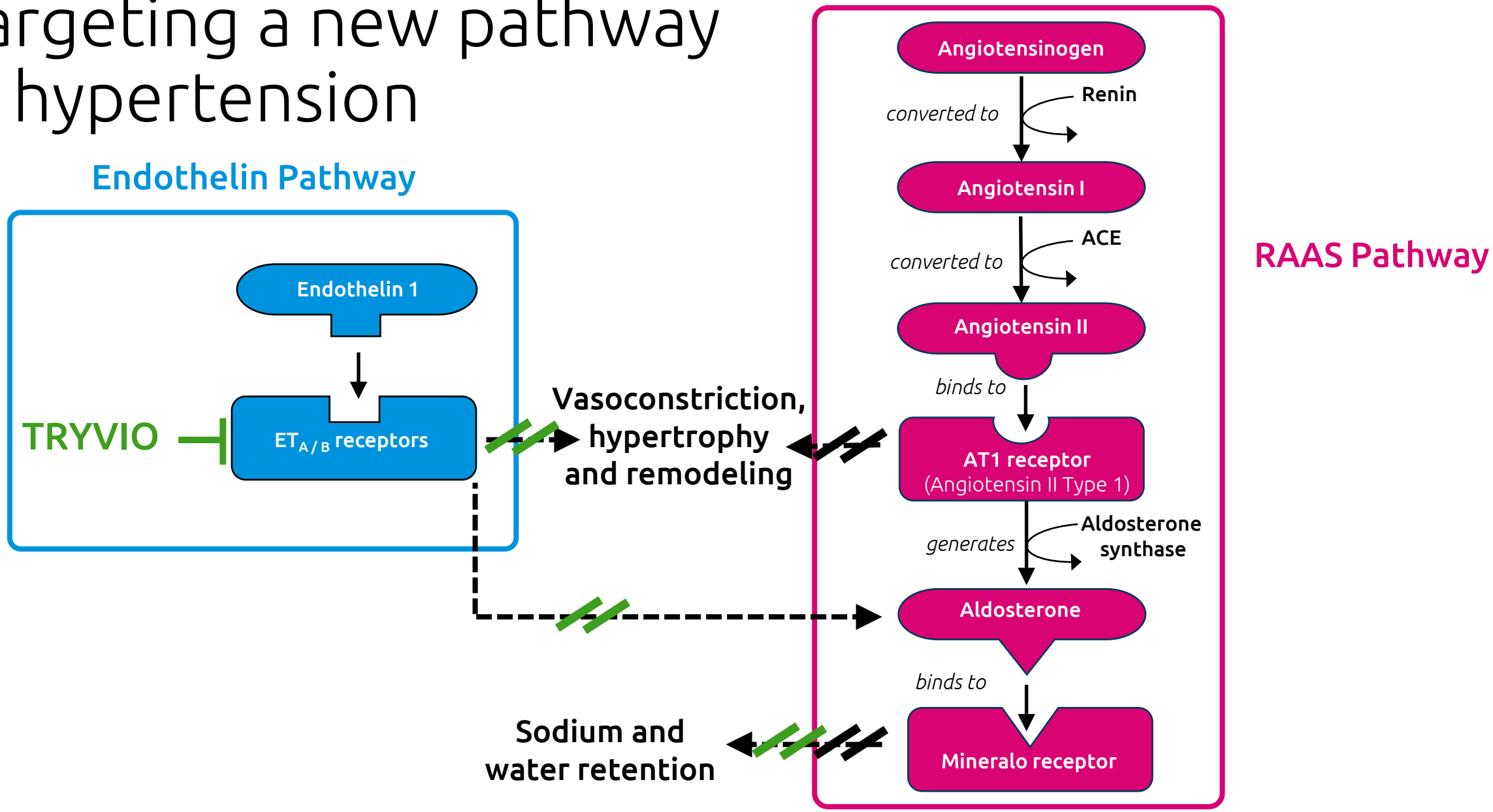
Targeting a new pathway in hypertension



Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

>30 years of researching the endothelin system

1988
Endothelin-1 identified

1990
ET_A and ET_B receptors identified

1993
First proof of the role of ERA published in *Nature*

1998
First evidence of dual ERA effect in hypertension published in *New England Journal of Medicine*

2007
Failed attempt by competition in resistant hypertension with selective ERA

2022
Aprocitentan – positive Phase 3 in resistant hypertension

2024
TRYVIO™ (aprocitentan) approved by US FDA

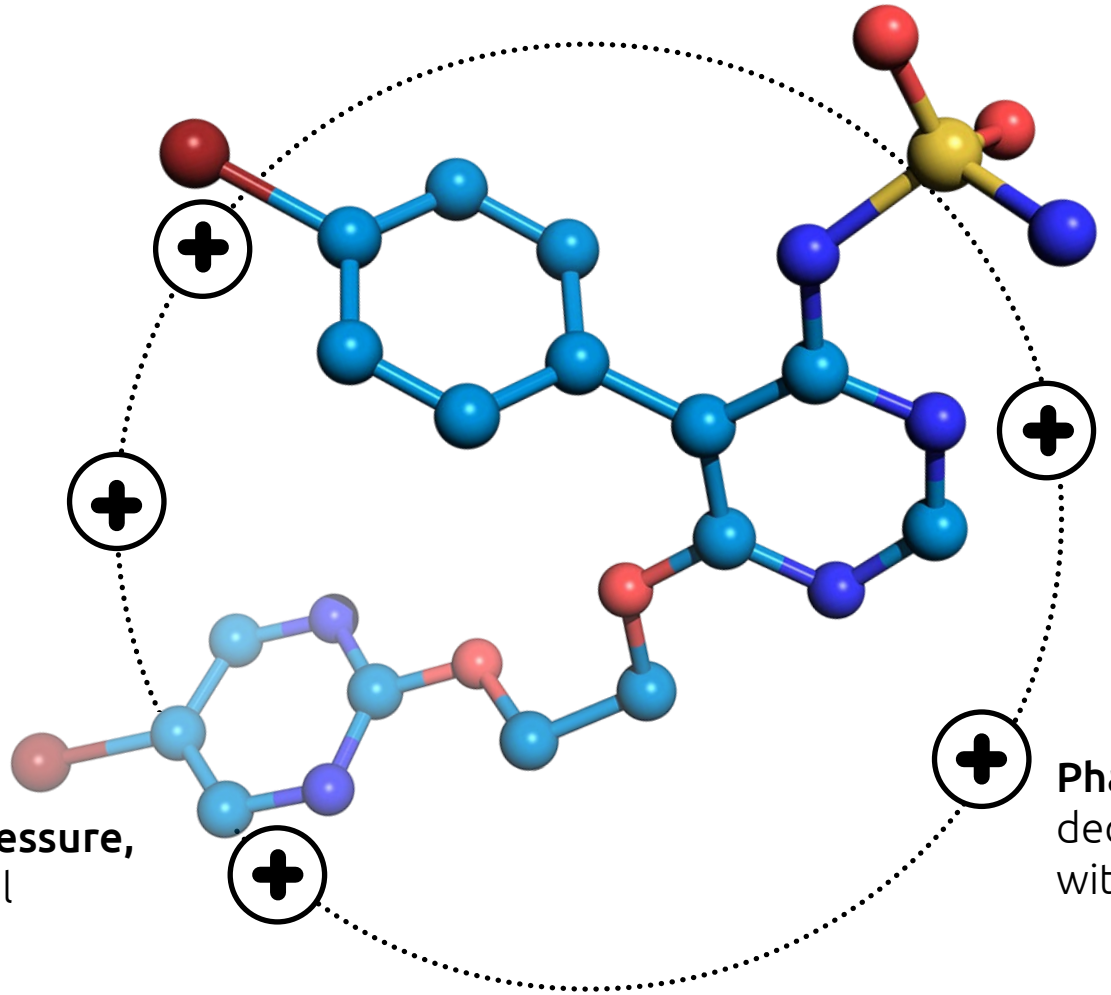
Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

Aprocitentan selected for its ideal properties

Orally-active, potent dual ET_A and ET_B receptor antagonist

Synergistic effect with other antihypertensive drugs (RAAS blockers) in animal models

Demonstrated efficacy on blood pressure, renal and cardiac protection in animal models



Low potential for drug-drug interaction

Phase 2 study shows blood pressure decrease as monotherapy in patients with hypertension

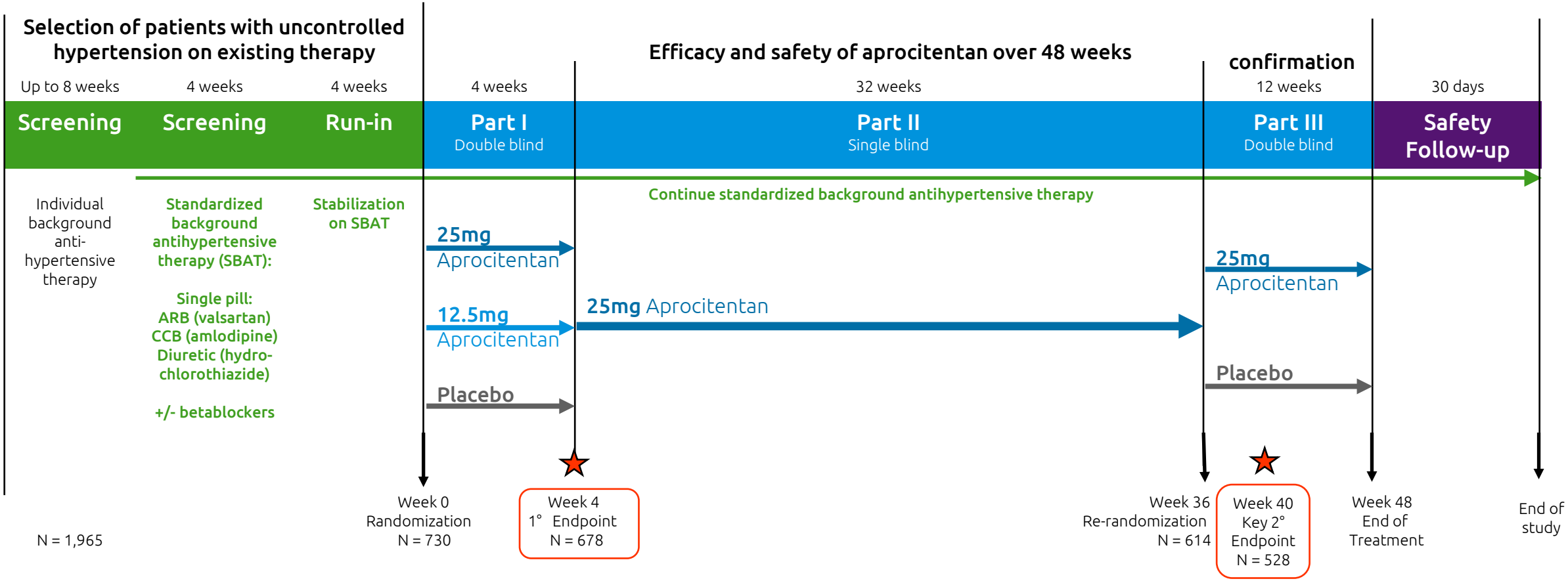
Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

“TRYVIO demonstrated a clear and consistent effect across all endpoints of blood pressure measurement and in key sub-populations.”

Alberto Gimona
Head of Global Clinical Development

Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

PRECISION investigated durability of BP reduction



Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

Frail population with multiple co-morbidities

Total: N = 730 [n (%)]

Age (years)		
Mean (SD)	61.7	(10.6)
18 to <65	409	(56.0)
65 - <75	**249**	**(34.1)**
≥75	**72**	**(9.9)**
Race		
White	605	(82.9)
Black or African American	**82**	**(11.2)**
Asian	38	(5.2)
Other	5	(0.7)
BMI# (kg/m^2)		
Mean (SD)	**33.7**	**(6.2)**
SiSBP / SiDBP (mmHg)*		
Mean (SD)	153.3 (8.9) / 87.6 (9.7)	

Antihypertensive therapies#		
3	269	(36.8)
4	337	(46.2)
≥ 5	123	(16.8)
UACR [mg/g]*		
< 30	453	(63.2)
30–300	**174**	**(24.3)**
> 300	**90**	**(12.6)**
missing	13	
eGFR [mL/min]*		
< 30	**21**	**(2.9)**
30 – < 45	**48**	**(6.6)**
45 – < 60	**93**	**(12.7)**
≥ 60	568	(77.8)

Medical history		
Diabetes mellitus	**395**	**(54.1)**
Congestive heart failure	**143**	**(19.6)**
Sleep apnea syndrome	103	(14.1)
Stroke	57	(7.8)
Myocardial infarction	51	(7.0)

BMI: *body mass index*
eGFR: *estimated glomerular filtration rate*
RHT: *resistant hypertension*
SD: *standard deviation*
SiDBP: *sitting diastolic blood pressure*
SiSBP: *sitting systolic blood pressure*
UACR: *urine albumin-to-creatinine ratio*

**** at baseline***
 # at screening

Danaietash P et al., *J Clin Hypertens* 2022 Jul; 24(7):804-813

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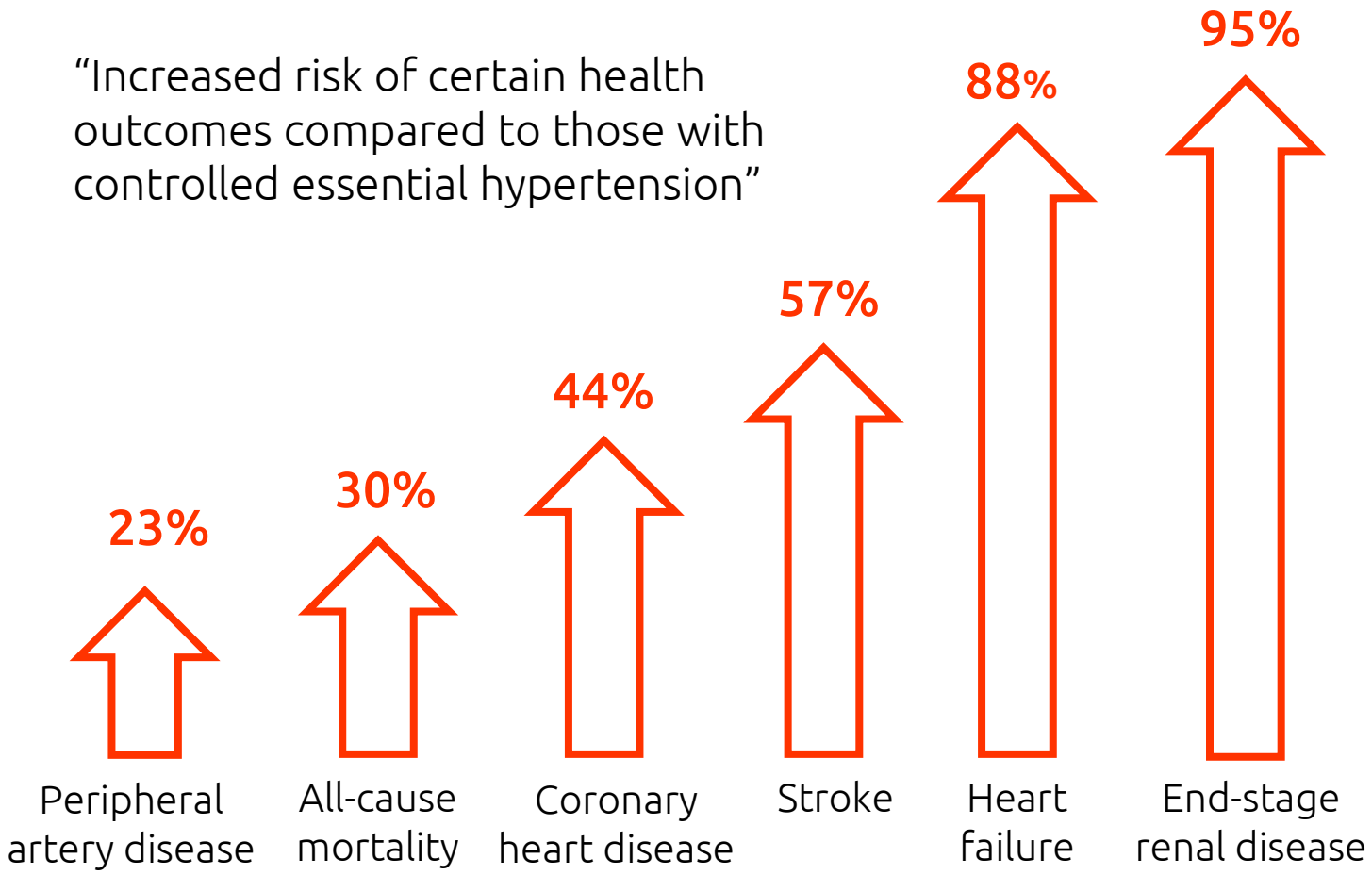
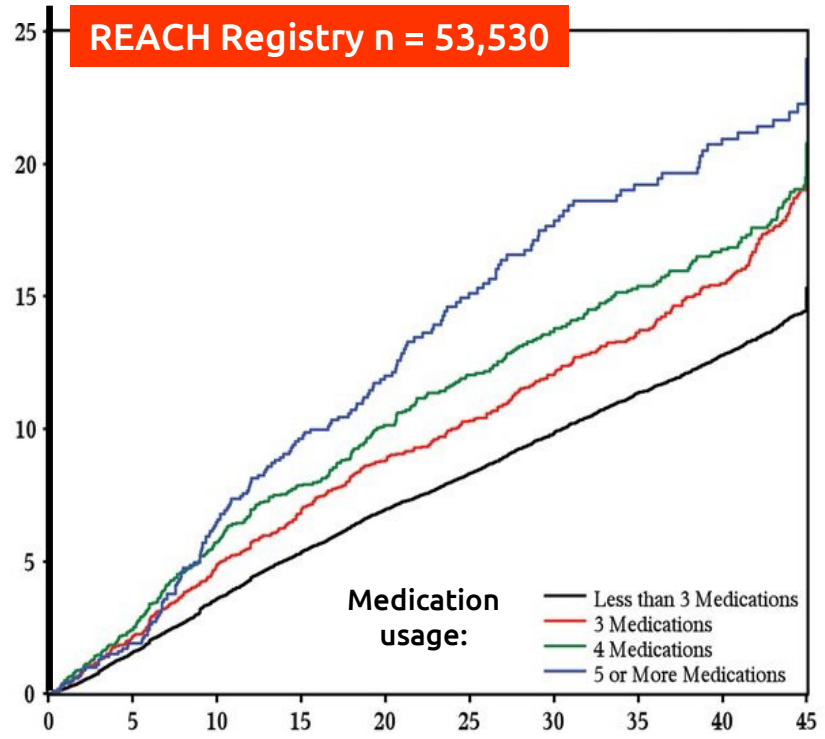
Disease burden when hypertension is uncontrolled

"Increased risk of certain health outcomes compared to those with controlled essential hypertension"



Muntner et al., 2014

Higher incidence of major cardiovascular events



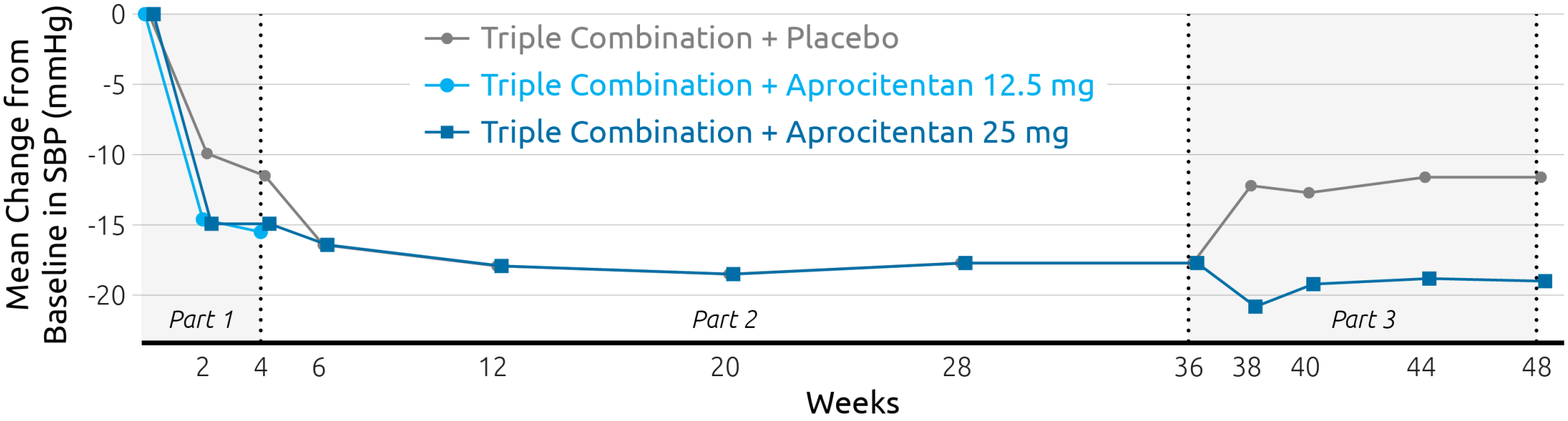
European Heart Journal, 2013

Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

Significant and sustained BP reduction

Absolute BP reduction of 15 mmHg

TRYVIO™ (aprocitentan) 12.5mg tablets



Primary endpoint
12.5 mg vs placebo: -3.8 mmHg, P=0.0042
25 mg vs placebo: - 3.7 mmHg, P=0.0046

Key secondary endpoint
25 mg vs placebo: - 5.8 mmHg P<0.0001

Triple combination: single pill ARB (valsartan), CCB (amlodipine) , diuretic (hydrochlorothiazide) +/- beta blockers

Schlaich MP, et al. The Lancet, 2022; Dec 3;400(10367):1927-1937.

Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

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USPI Highlights: Indication and Usage

TRYVIO™ (aprocitentan) 12.5mg tablets

----------INDICATIONS AND USAGE----------

TRYVIO is an endothelin receptor antagonist indicated for the treatment of hypertension in combination with other antihypertensive drugs, to lower blood pressure in adult patients who are not adequately controlled on other drugs. Lowering blood pressure reduces the risk of fatal and non-fatal cardiovascular events, primarily strokes and myocardial infarctions. (1)

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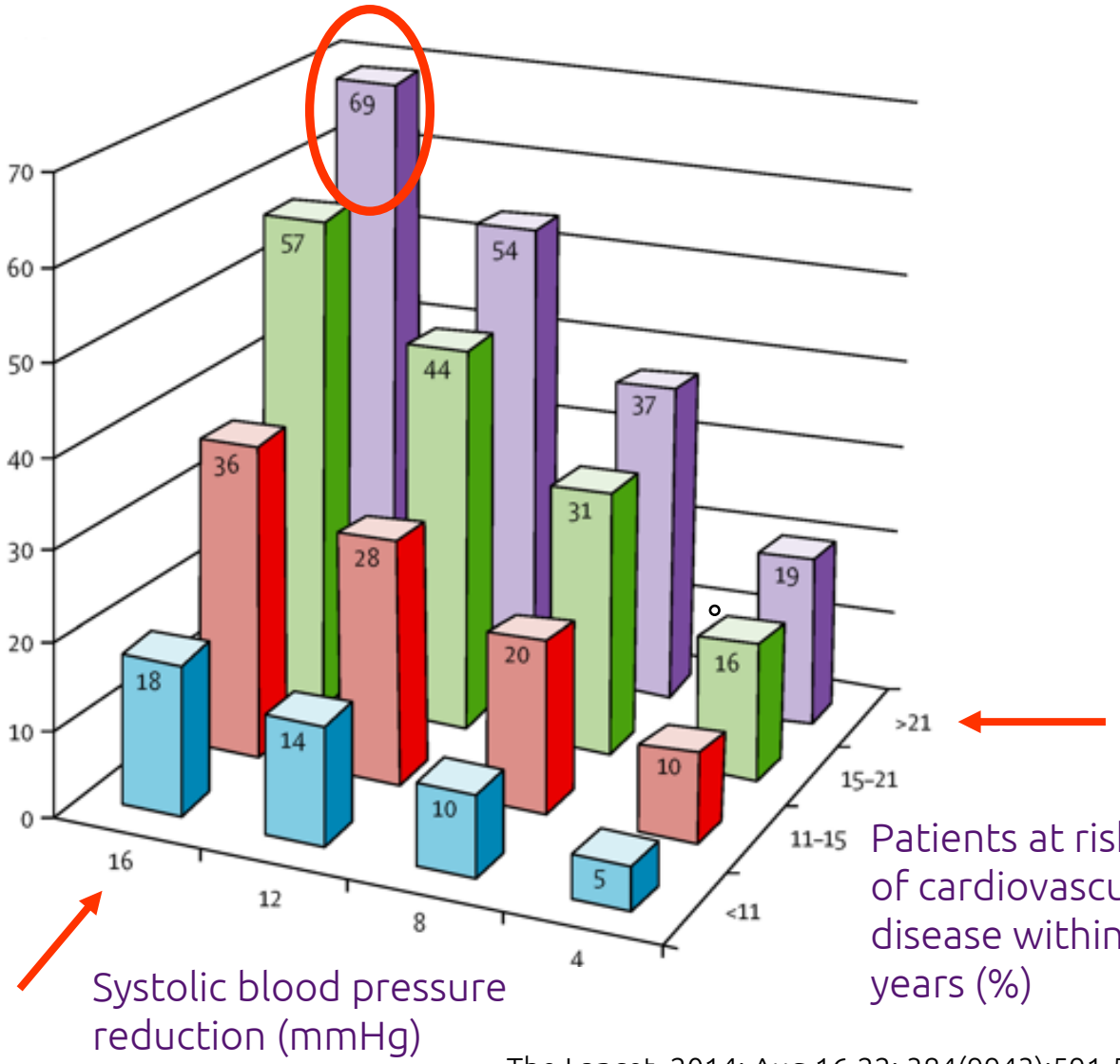
Reduction in BP will prevent CV events

16-mmHg (uAOBPM) reduction in SBP vs baseline would avoid approximately 70 CV events per 1000 patients over the following 5 years



NB: There are no controlled trials demonstrating reduction of risk of these events with TRYVIO

The Lancet, 2014; Aug 16-22; 384(9943):591-598.

Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

USPI Highlights: Dosage and Administration

TRYVIO™ (aprocitentan) 12.5mg tablets

----------DOSAGE AND ADMINISTRATION----------

- The recommended dosage of TRYVIO is 12.5 mg orally once daily, with or without food. (2.1)

USPI Section 14: Clinical Studies

TRYVIO **long-term sustained effect**

The persistence of the BP-lowering effect of TRYVIO was demonstrated in part 3 of the trial, in which patients on aprocitentan were re-randomized to placebo or 25 mg aprocitentan following a period during which all patients were treated with 25 mg. In patients re-randomized to placebo, the mean SiSBP increased, whereas in patients re-randomized to 25 mg aprocitentan the mean effect on SiSBP was maintained and was statistically superior to placebo at Week 40. The treatment effect was consistent for SiDBP.

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USPI Section 14: Clinical Studies

TRYVIO consistent **effect in subgroups** and across **measures**

TRYVIO™ (aprocitentan) 12.5mg tablets

Most of the BP-lowering effect occurred within the first two weeks of treatment with TRYVIO.

TRYVIO's BP-lowering effect appeared consistent among subgroups defined by age, sex, race, BMI, baseline eGFR, baseline UACR, medical history of diabetes, and between BP measurement methodologies (uAOBP and ambulatory BP measurements).

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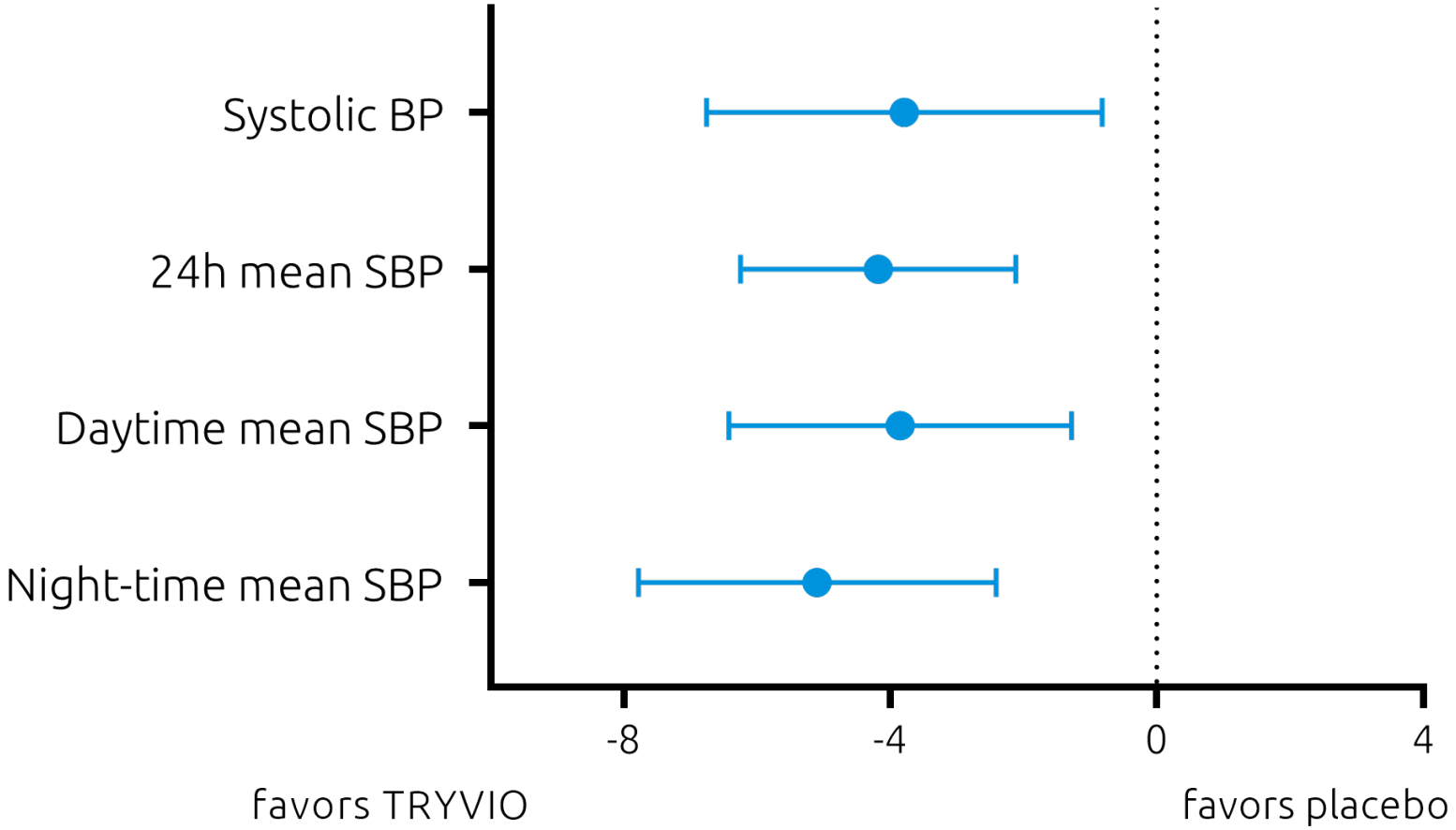
Consistent effect between BP measurement methodologies

TRYVIO™ (aprocitentan) 12.5mg tablets



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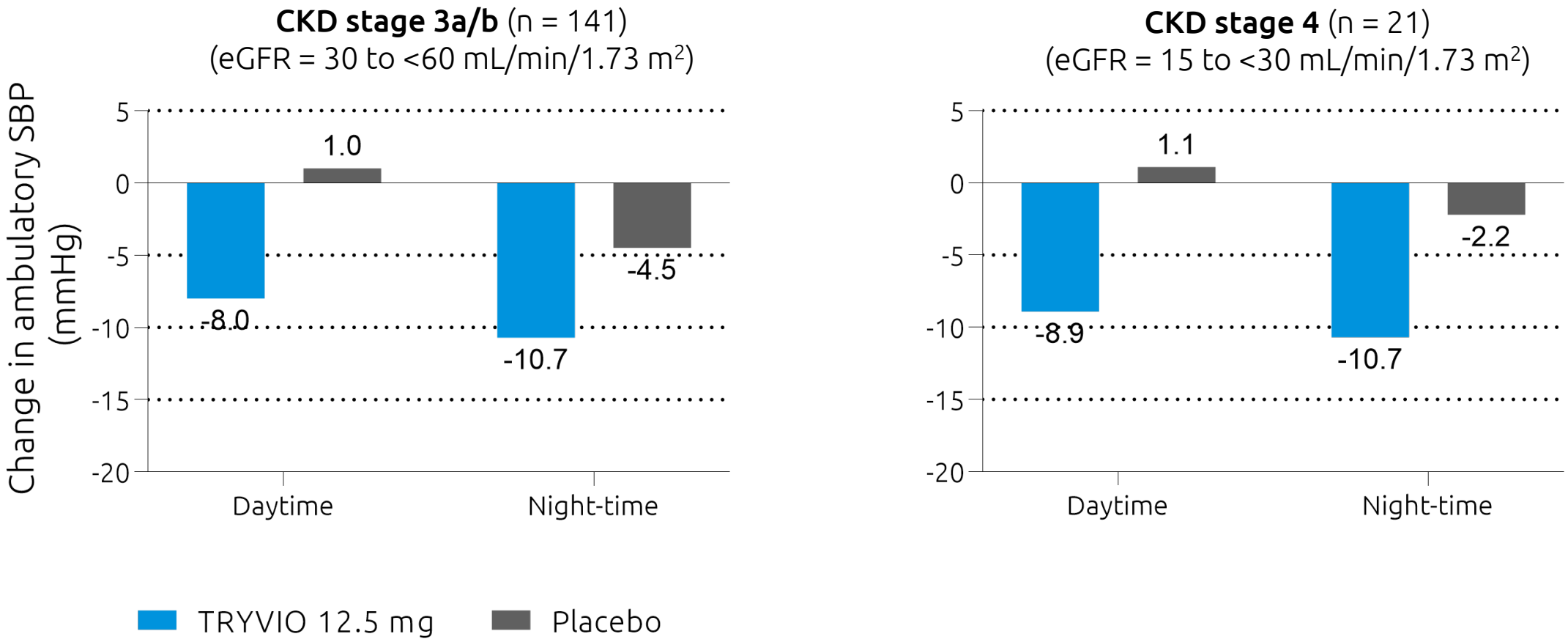
Consistent effect among subgroups: E.g., Patients with chronic kidney disease

TRYVIO™ (aprocitentan) 12.5mg tablets



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USPI Section 6: Adverse Reactions

TRYVIO™ (aprocitentan) 12.5mg tablets

Table 1 Adverse reactions reported with a frequency of ≥2% in TRYVIO-treated patients and greater (≥1%) than in placebo-treated patients during the initial 4-week double-blind placebo-controlled treatment (part 1)

Adverse Reaction	12.5 mg N = 243 %	Placebo N = 242 %
Edema/fluid retention	9.1	2.1
Anemia	3.7	0

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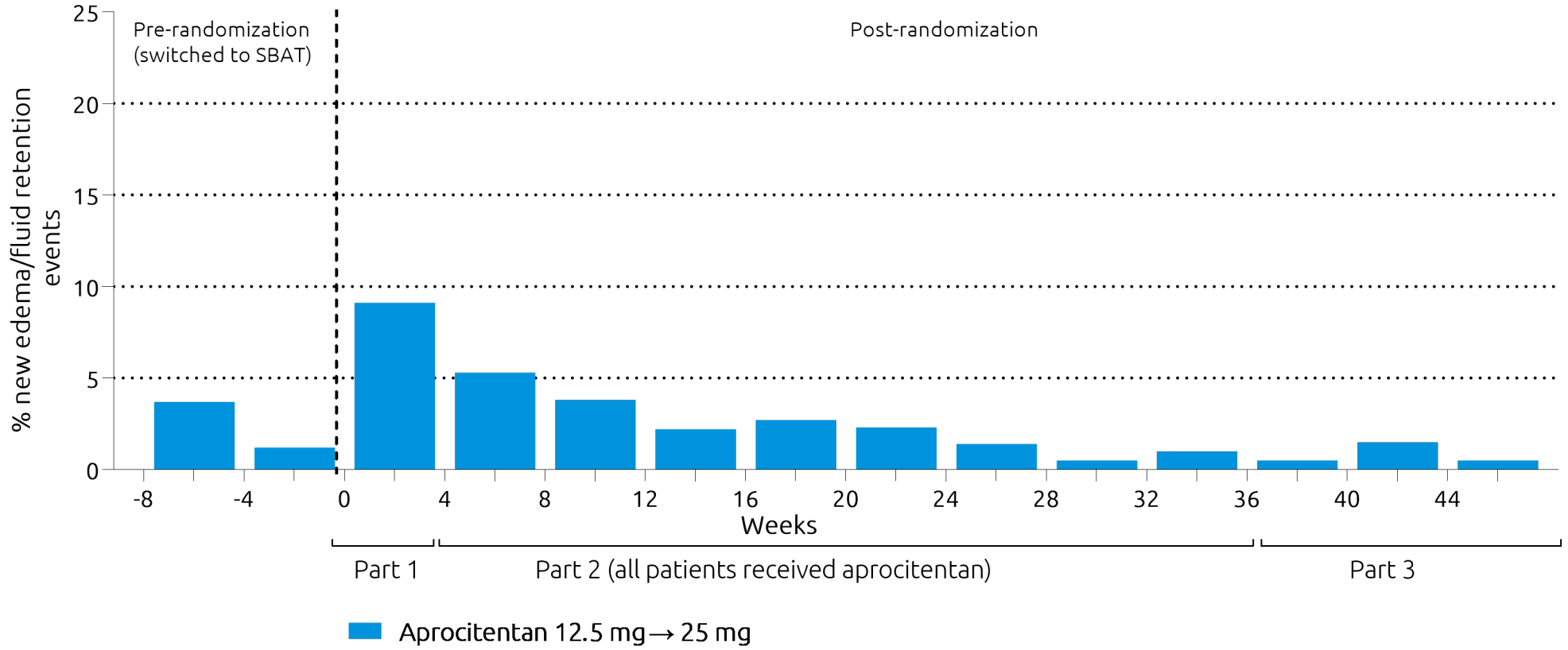
Incidence of edema

TRYVIO™ (aprocitentan) 12.5mg tablets

Returns to levels observed before randomization 8 weeks after treatment



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USPI Section 5.2: TRYVIO REMS

5.2 TRYVIO REMS

TRYVIO is available only through a restricted program under a REMS called the TRYVIO REMS because of the risk of embryo-fetal toxicity *[see Contraindications (4.1), Warnings and Precautions (5.1), Use in Specific Populations (8.1, 8.3)]*.

Important requirements of the TRYVIO REMS include the following:

- Prescribers must be certified with the TRYVIO REMS by enrolling and completing training.
- Pharmacies that dispense TRYVIO must be certified with the TRYVIO REMS.

Further information is available at www.TRYVIOREMS.com or 1-866-429-8964.

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“We are eager to provide physicians and patients with a novel medicine working in a new pathway in uncontrolled hypertension that can provide additional blood pressure control”

Tausif ‘Tosh’ Butt
President Idorsia US

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Hypertension is the leading modifiable risk factor for early death and disability

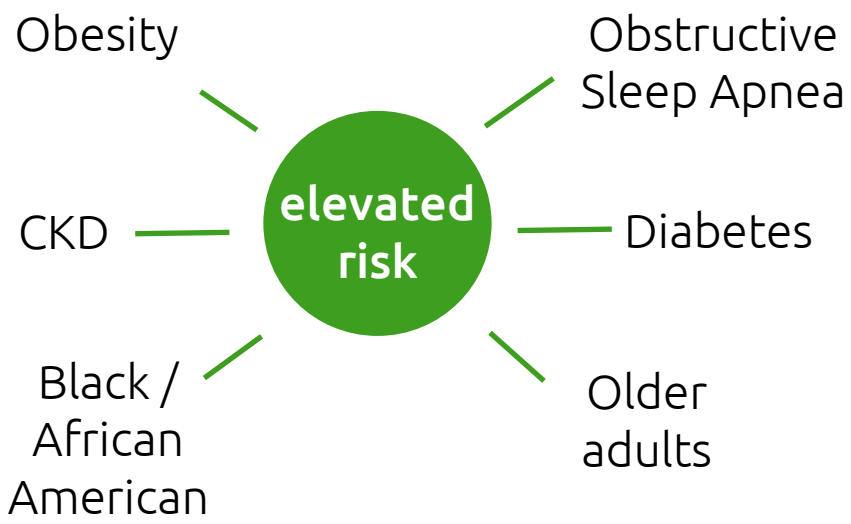
The importance of treating hypertension is well established

The risk of developing **uncontrolled hypertension is elevated in certain subgroups** of patients

2-6x
Greater Risk

especially for uncontrolled patients at high risk of cardio- and neurovascular events

5 mmHg reduction in SBP
= ~10% reduction in the risk of major cardiovascular events



Uncontrolled hypertension patients have a **greater risk** for CV events and end-stage renal disease

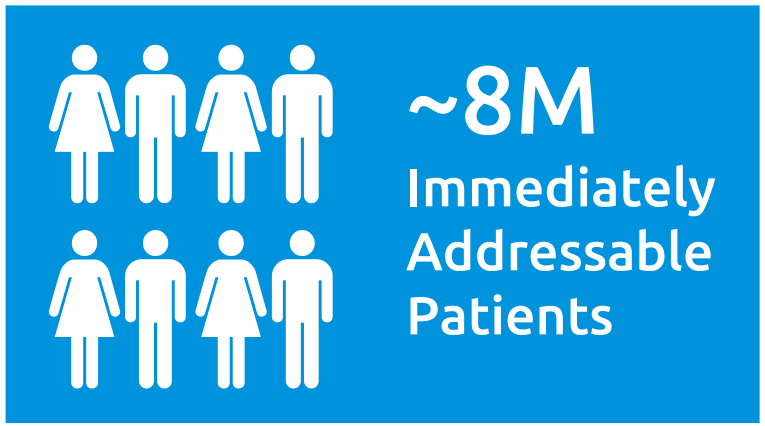
Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

~8M patients immediately addressable at launch* – most with multiple comorbidities

TRYVIO™ (aprocitentan) 12.5mg tablets

3.5M Patients
on **3 meds for hypertension are not controlled**

4.6M Patients
on 4+ meds for hypertension



90% of these patients have comorbidities and are taking branded meds

* in line with Phase 3 criteria

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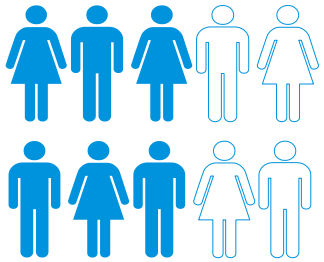
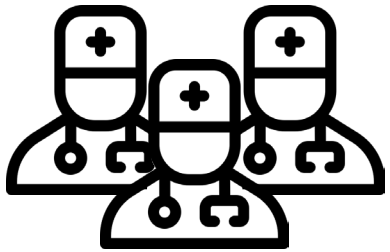
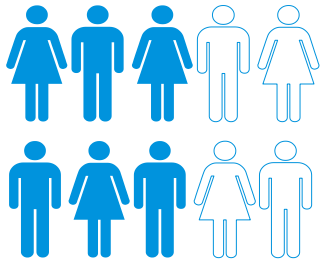
Prescribers span several specialties – often more than one HCP involved

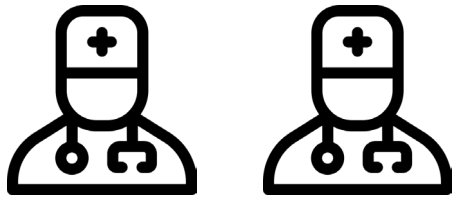


60% of Patients
on 3+ Meds were treated by 2 or more HCPs

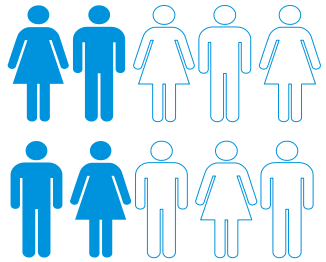




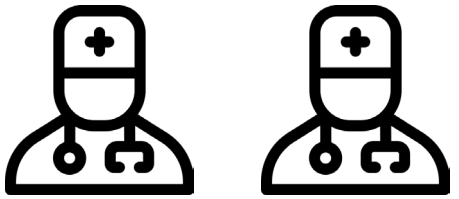
50-60% of patients
on 3+ Meds were treated by cardiologists and nephrologists



cardiologists nephrologist



30-40% of patients
on 3+ Meds were treated by primary care physicians (PCPs)/other



PCPs other

Source: Komodo claims; 3-Year Dx: Sep'20 - Aug'23; 1-Year Rx: Sep'22 - Aug'23

Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

Early dialogues with Payers suggest an overall favorable reaction to TRYVIO clinical profile

- Recognize the unmet patient need of uncontrolled hypertension
- Favorable reaction to Phase 3 trial design
- Perceive efficacy as favorable, highlighting BP differences vs placebo clinically meaningful
- Product available through med exception process until the NTM / NDC Blocks removed

NTM: New To Market; NDC: National Drug Code

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Important aspects of TRYVIO for US market

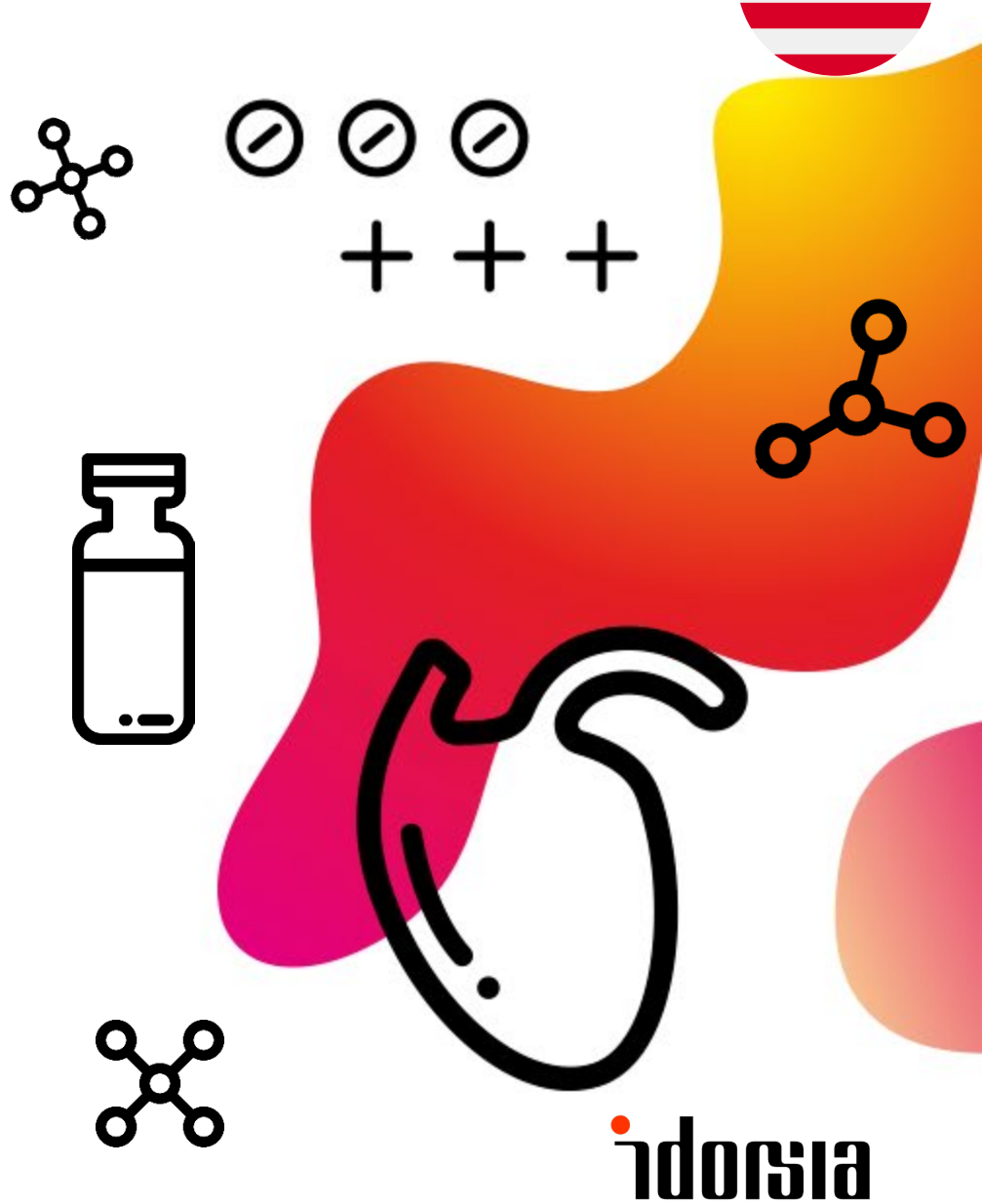
TRYVIO™
(aprocitentan) 12.5mg tablets

Easy to prescribe

- **One dose** for all patients
- No clinically relevant drug-drug interactions
- Manageable side-effect profile
- One-time REMS certification for HCP and Pharmacy only

Easy to use

- **Oral** once-daily tablet, with or without food
- **Long half-life** (approx. 41 hours)



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“The approval of TRYVIO heralds a new era of endothelin research beyond hypertension, where we intend to investigate the utility of aprocitentan for first-in-class applications in new indications.”

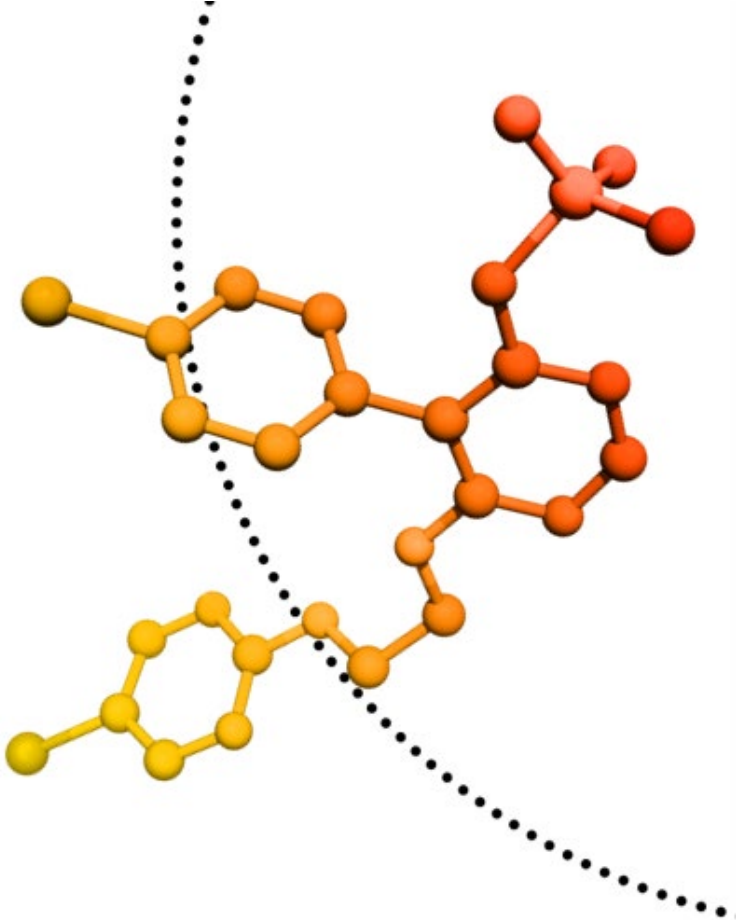
Martine Clozel
Chief Scientific Officer

Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

JERAYGO™ (aprocitentan) for resistant hypertension in the EU

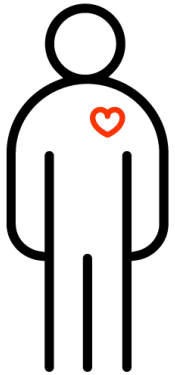
New mode of action in systemic hypertension

JERAYGO™
aprocitentan



Current status

- In April 2024, Idorsia received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) for JERAYGO™ (aprocitentan) as a treatment of resistant hypertension.
- The CHMP has adopted a positive opinion for the use of 12.5 mg JERAYGO orally once daily. The dose can be increased to 25 mg once daily for patients tolerating the 12.5 mg dose and in need of tighter blood pressure control.
- A CHMP positive opinion is one of the final steps before marketing authorization can be granted by the European Commission – a final decision is expected in approximately two months



Aprocitentan is only approved in the US under the tradename TRYVIO™ where it will be made available later in 2024. Market authorization is under review in other countries.

Lucerastat in Fabry disease

Lucerastat is investigational, in development and not approved or marketed in any country.

Fabry disease

Fabry disease is a **rare inherited lysosomal storage disorder** in which a particular **lipid** (a fat-like substance) can't be broken down by the body, leading to its build-up in the cells of the body organs which results in cell and organ damage

Fabry disease is often undetected or misdiagnosed

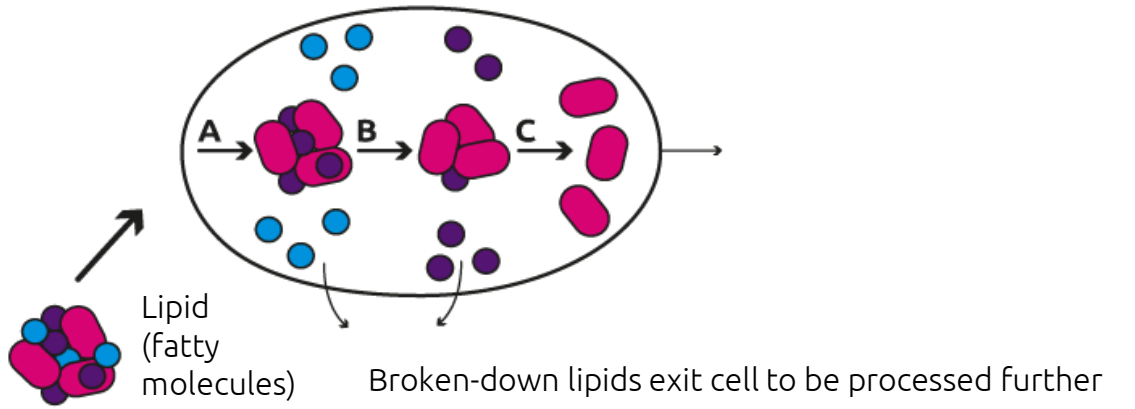
As the disease is progressive, **early diagnosis is essential** to manage the symptoms as soon as possible and reduce the risk of developing serious complications

What is the role of lipids in the body?

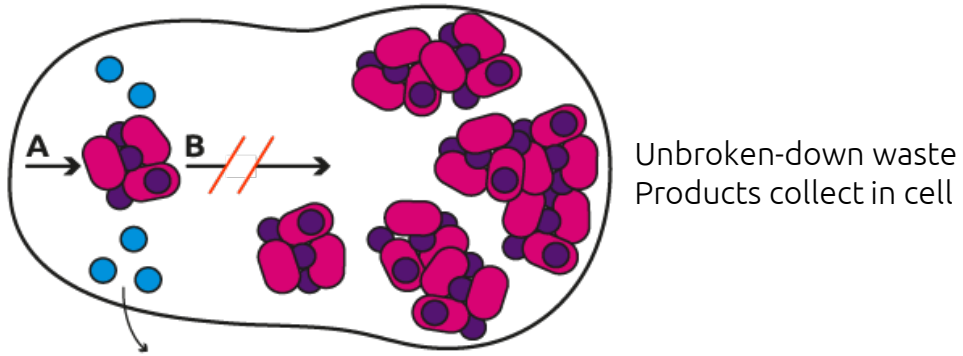
- Lipids are fat-like substances such as fatty acids, oils, waxes and steroids. A well-known example is cholesterol
- Lipids are stored naturally in the body's cells and organs and are vital to their healthy functioning
- Normally, the body is able to process lipids effectively, which keeps them within healthy levels

What happens in patients with lysosomal storage disorders?

Normal breakdown of lipids



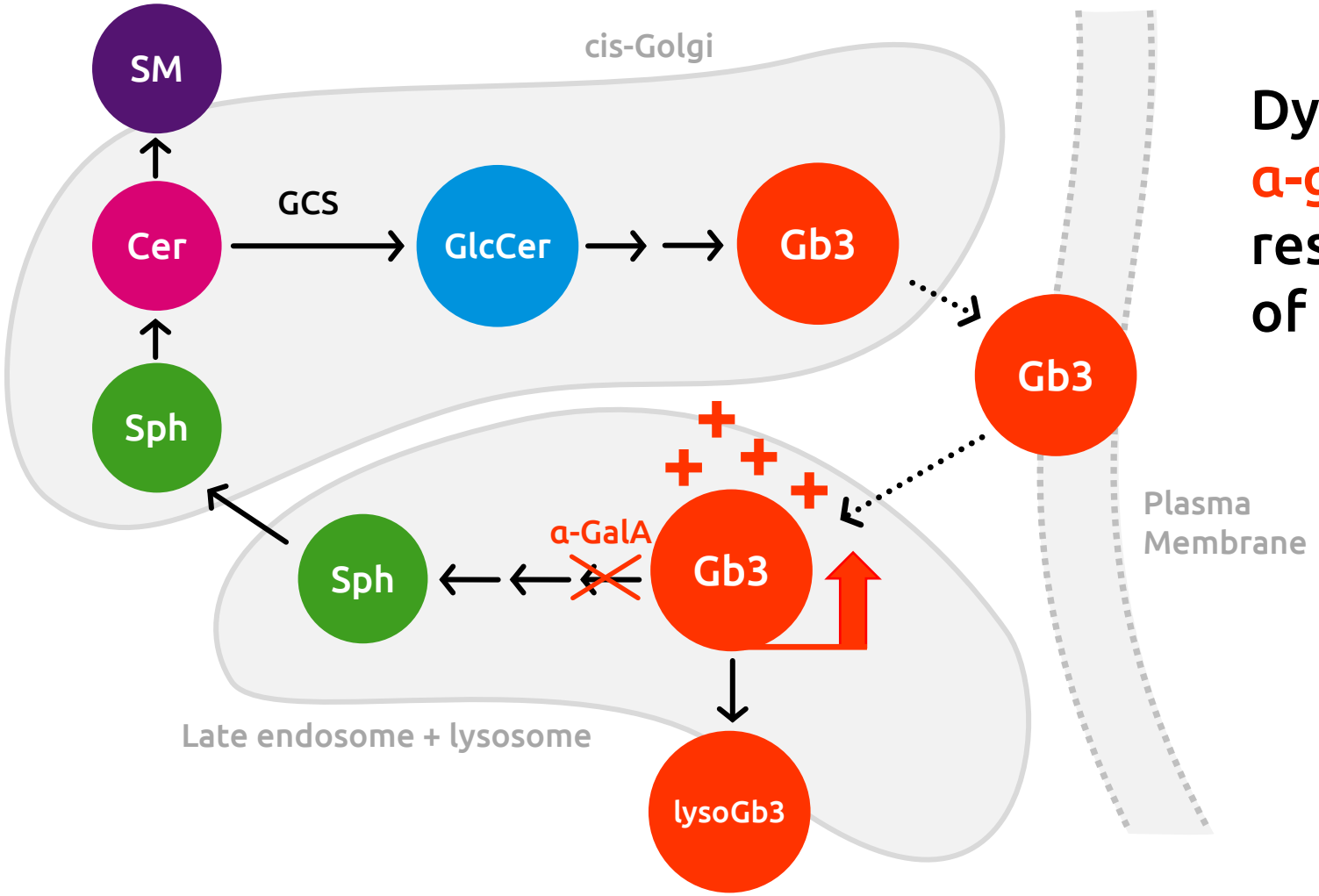
When enzyme to break down lipid is deficient



Lipids can't be processed and build up in cell

Fabry disease

Biochemical mechanism



Dysfunctional or absent α-galactosidase A results in accumulation of Gb3 in various organs

Cer	ceramide
GCS	glucosylceramide synthase
GlcCer	glucosylceramide
Gb3	globotriaosylceramide
lysoGb3	globotriaosylsphingosine
α-GalA	α-galactosidase A
SM	sphingomyelin
Sph	sphingosine

Inheritance pattern in Fabry disease

X-linked recessive genetic disease

- GLA gene mutation results in **defective lysosomal enzyme α-GalA**
- In turn, this results in **Gb3 accumulation**

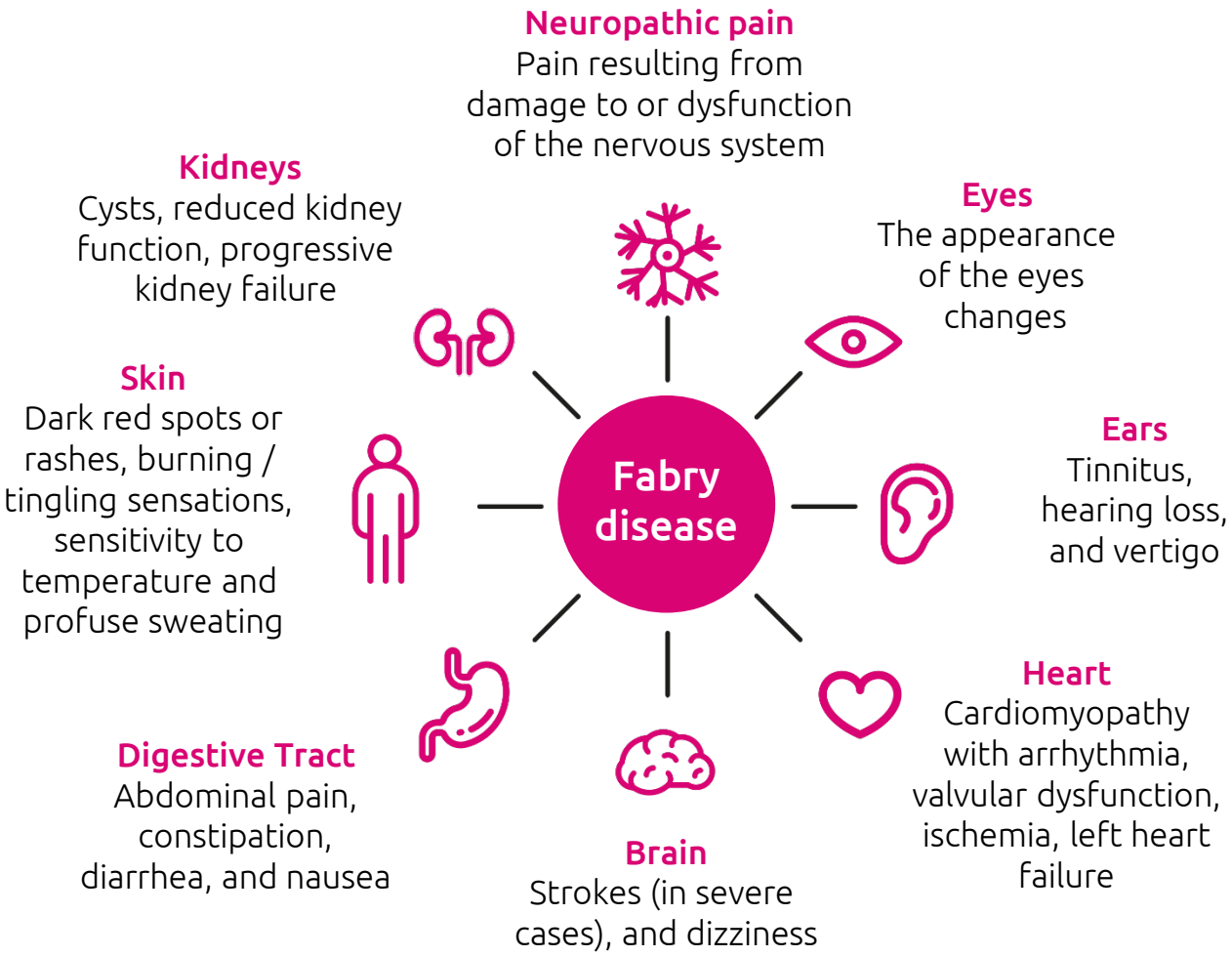
Random X-inactivation in Fabry female 'carriers': both genders affected

Male have generally classical phenotype

Females have higher residual level enzyme and
- are affected later
- progress slower
- have more variable phenotype

Clinical manifestations of Fabry disease

Large spectrum of clinical, heterogeneous manifestations



- **Gradually progressing** in severity from childhood to adulthood
- **Major impact on quality of life**
- **Slow progressive damage** to vital organs over decades
- **Earlier death**

Diagnosis of Fabry disease

Clinical symptoms

Neuropathic pain, GI, hearing loss, hypohydrosis

Clinical events

Stroke, cardiac and renal events

Pedigree analysis

Family members

(between children and parents)

Enzyme assay

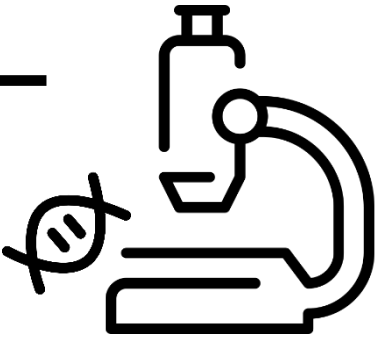
Leukocyte α-GalA

Genotyping

>830 mutations

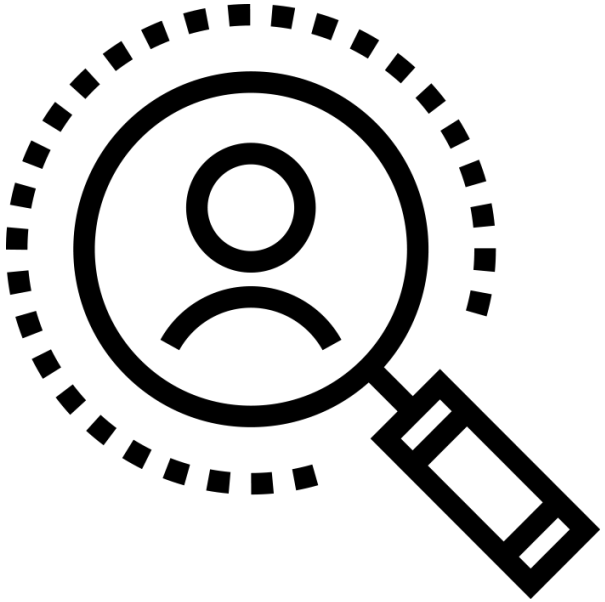
Biomarkers

Gb3 in plasma and urine



Epidemiology of Fabry disease

Patients diagnosed with Fabry disease
in EU-5 and US in 2018



2018	patients, n
EU-5	**3,507**
UK	890
Italy	828
Germany	692
France	562
Spain	535
US	**3,875**
Total	**7,382**

Delveinsight, Fabry Disease – Market Insight, Epidemiology and Market Forecast – 2028

Current therapies in Fabry disease

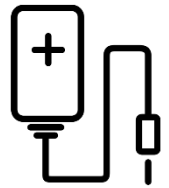
No curative therapy

Symptomatic treatments not satisfactory

Etiological therapies limited

Enzyme replacement therapy

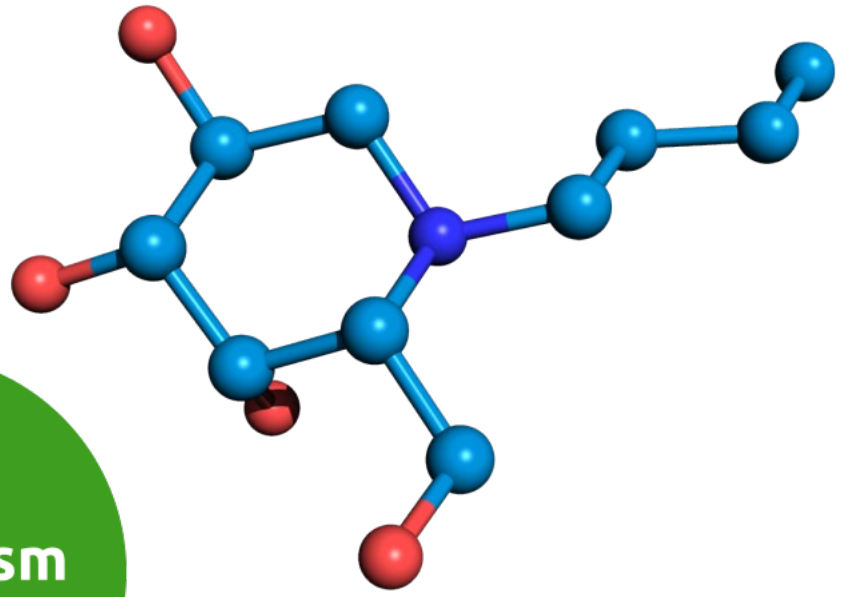
- Fabrazyme (agalsidase beta) (US and EU)
- Replagal (agalsidase alfa) (EU only)
- i.v. infusion, bi-weekly
- Immunogenicity
- Partial efficacy



Chaperone therapy

- Galafold (migalastat) for patients with amenable mutation
- 1 capsule orally, fasted, every other day

Lucerastat in Fabry disease



Novel mechanism of action

Bioavailability
Orally available, highly soluble small molecule with rapid and complete absorption

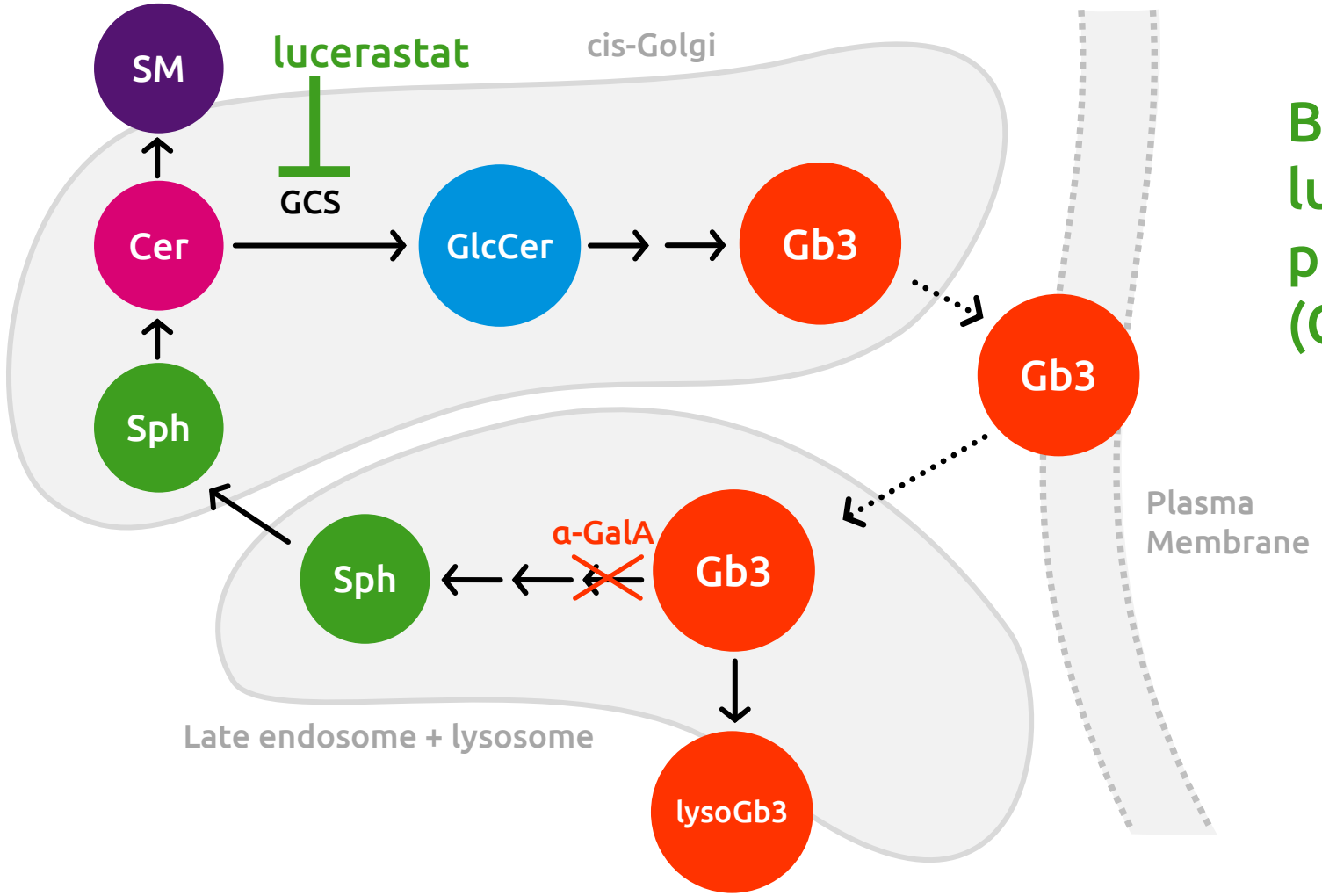
Tissue penetration
Access to most tissues, including peripheral and central nervous system

For all mutations
Potential to treat all Fabry patients irrespective of the underlying enzyme mutation

Lucerastat is investigational, in development and not approved or marketed in any country.

Lucerastat in Fabry disease

Mode of action



By inhibiting GCS, lucerastat reduces the precursor of Gb3 (GlcCer) and Gb3 itself

Cer	ceramide
GCS	glucosylceramide synthase
GlcCer	glucosylceramide
Gb3	globotriaosylceramide
lysoGb3	globotriaosylsphingosine
α-GalA	α-galactosidase A
SM	sphingomyelin
Sph	sphingosine

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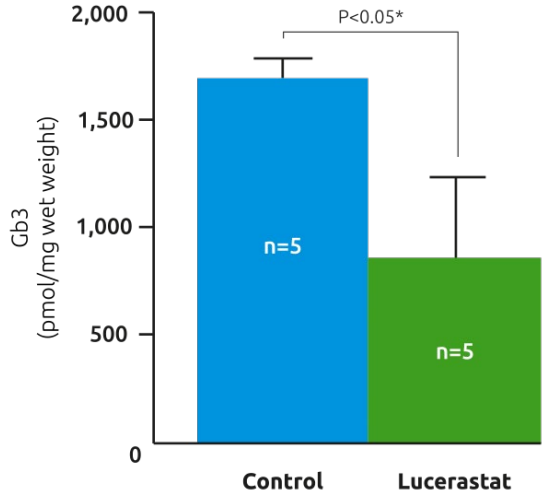
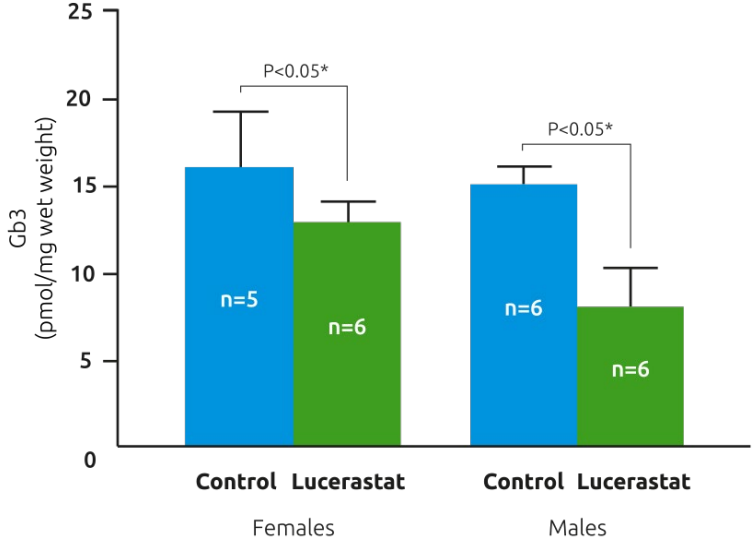
Lucerastat has the potential to reduce Gb3 levels in target organs

Dorsal root ganglia

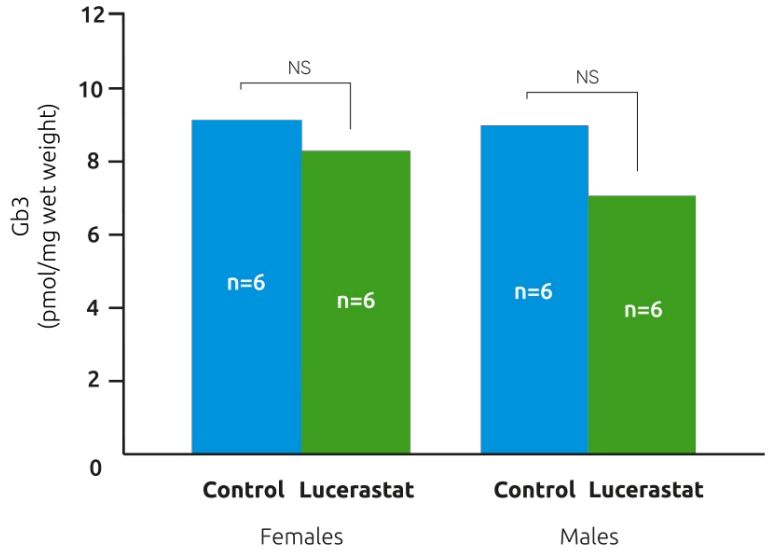


Kidneys



*ANOVA with Bonferroni's multiple testing correction.

Heart



Male and female Fabry mice treated for 20 weeks with lucerastat at 1200 mg/kg/day as food admix and compared to non-treated controls

Idorsia data on file. Data collected in animal models does not necessarily predict human clinical effect.

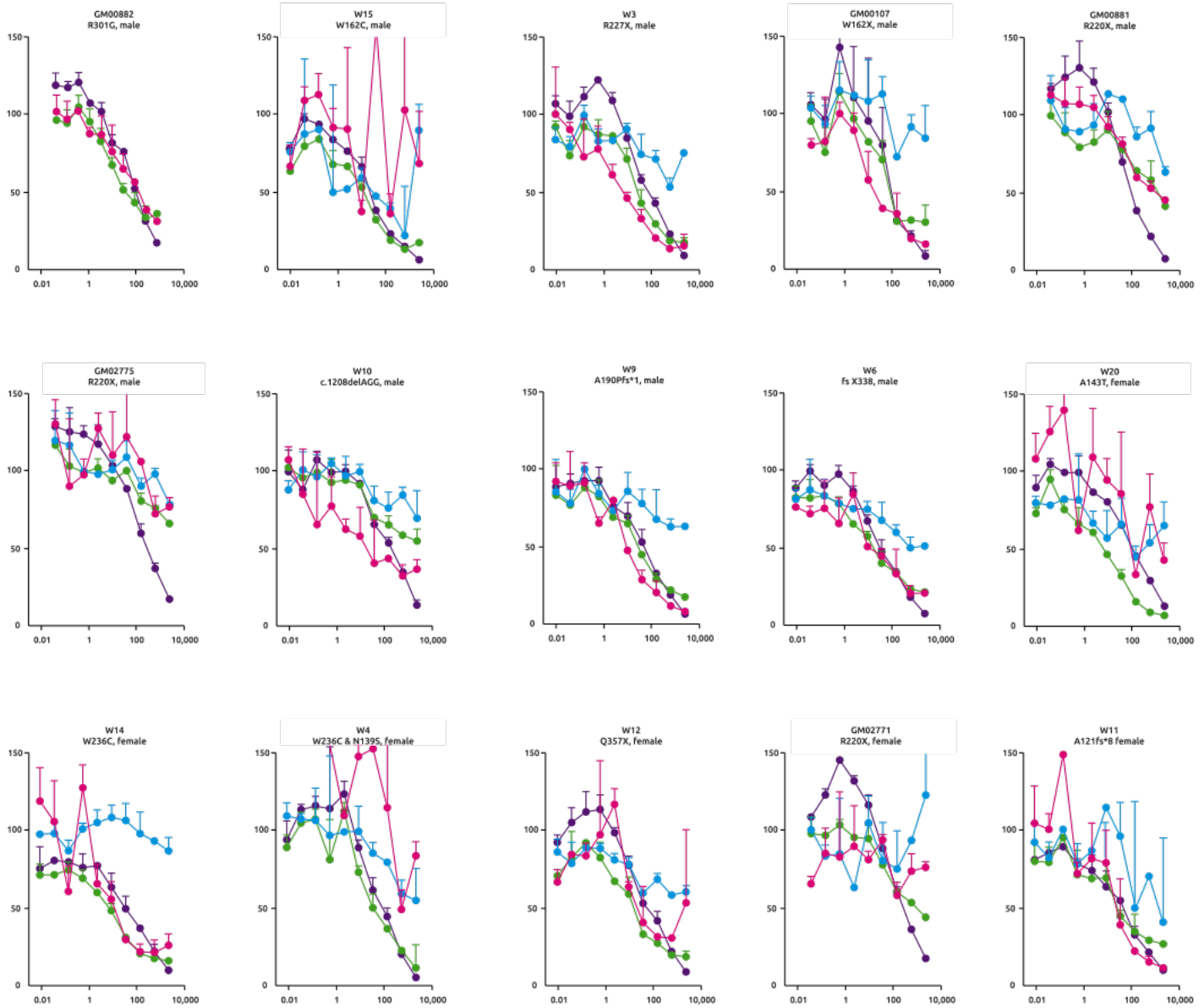
Lucerastat is investigational, in development and not approved or marketed in any country.

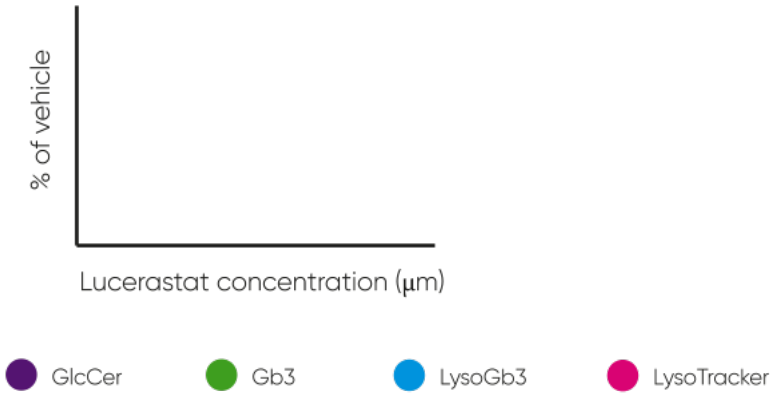
Mutation sensitivity

Proven reduction in Gb3 in all tested mutation types

Effect of different concentrations of lucerastat on GlcCer, Gb3, lysoGb3 lipid levels, and LysoTracker staining in cultured Fabry patients' fibroblasts after 9 days of treatment.

Each point is the mean of duplicates (±SD)





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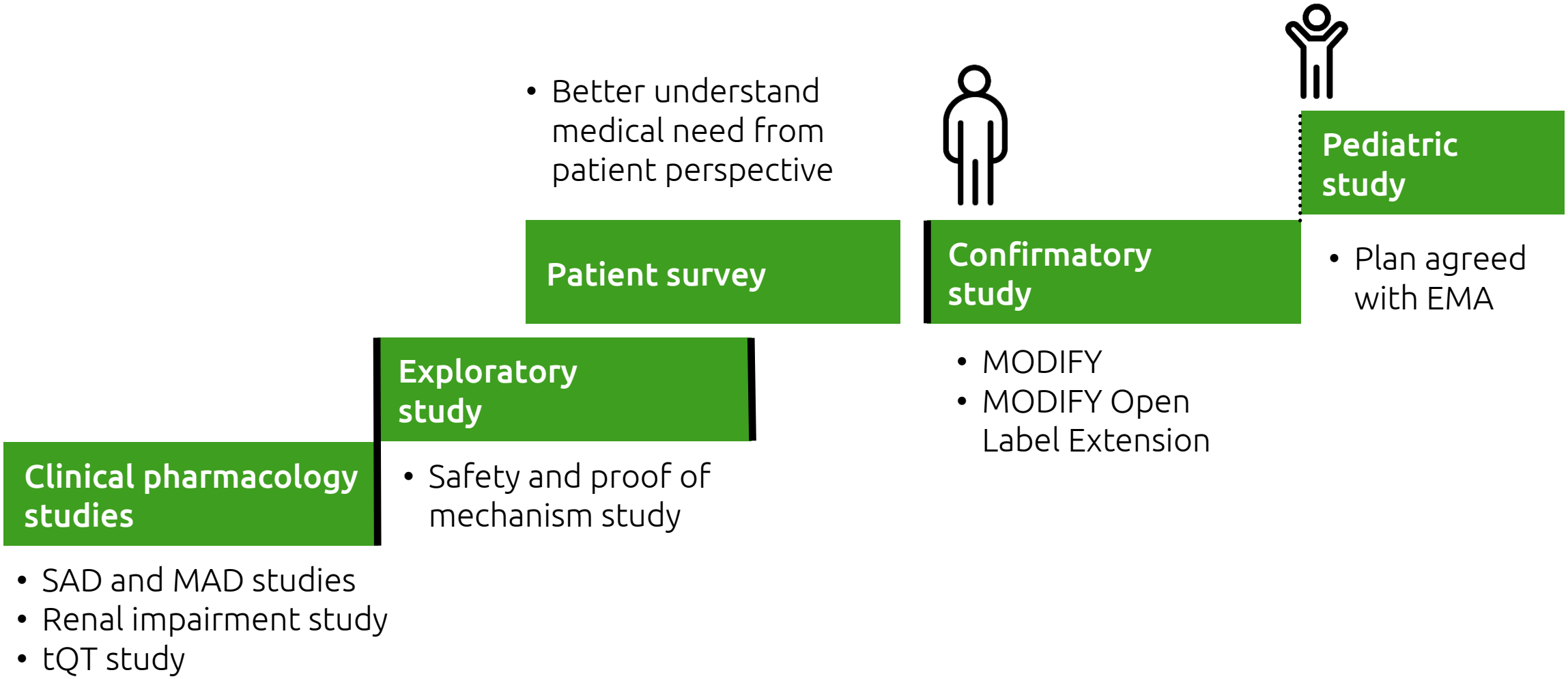
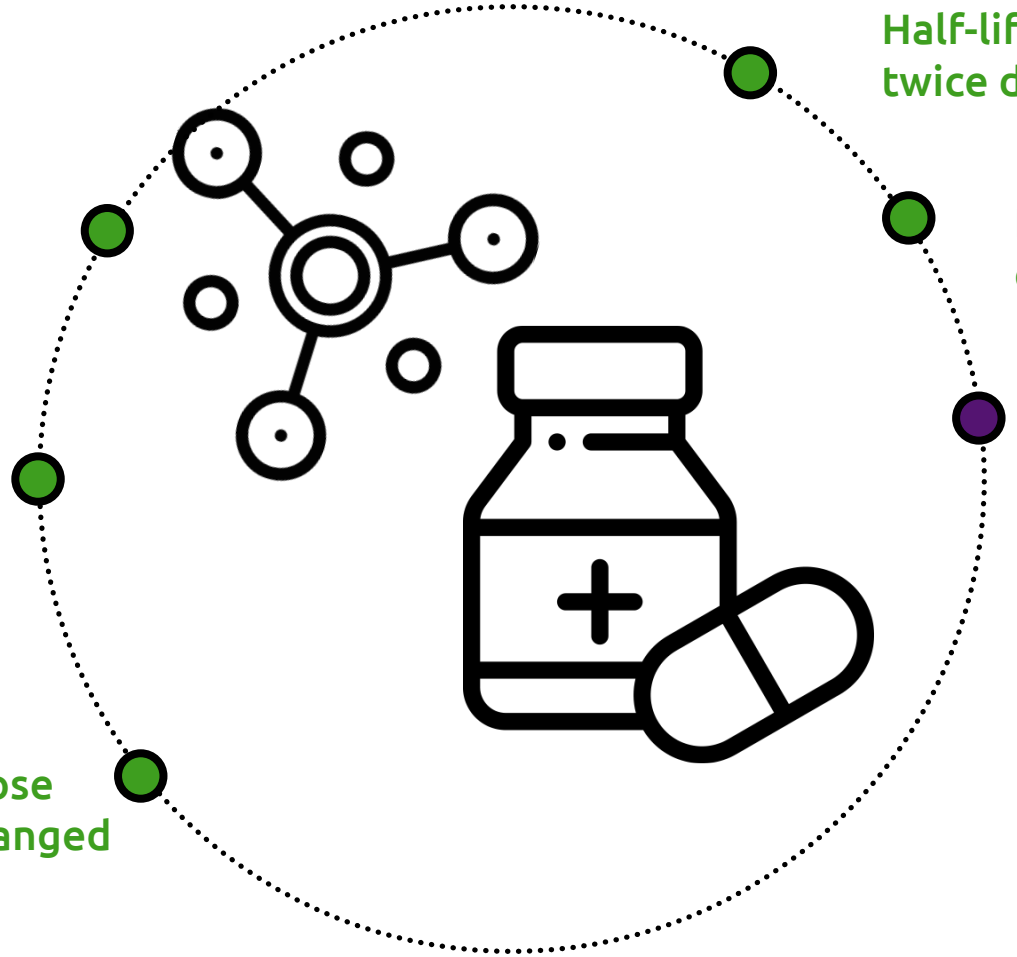
Lucerastat clinical development plan



Lucerastat is investigational, in development and not approved or marketed in any country.

Lucerastat clinical pharmacology



Half-life: approximately 6 hours – twice daily dosing

Dose-proportional exposure

Dose adjustment required in subjects with renal function impairment

Negligible food effect

Low potential for drug-drug interaction

>85% of the dose excreted unchanged in urine

eGFR (mL/min/1.73 m^2)	Dosing regimen (mg b.i.d.)
≥ 60	1000
≥ 45 and < 60	750
≥ 30 and < 45	500
≥ 15 and < 30	250

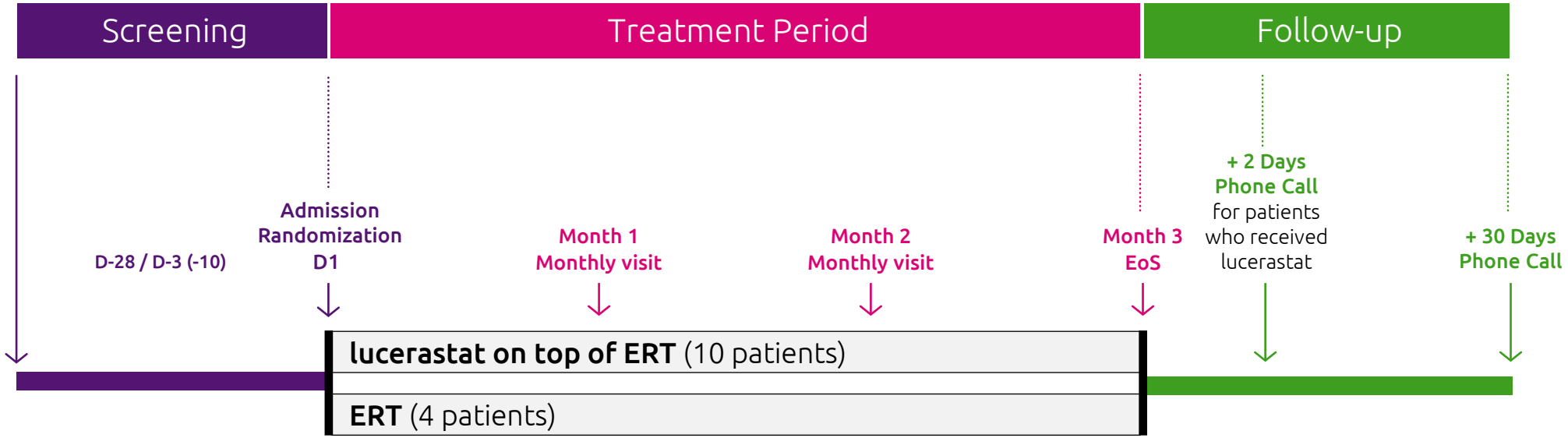
Guérard et al. (2017) Orphanet J Rare Dis
Guérard et al. (2017) J Clin Pharmacol
Guérard et al. (2018) Clin Pharmacol Ther

Lucerastat is investigational, in development and not approved or marketed in any country.

Lucerastat exploratory study design

Phase 1b study

Prospective, single-center, open-label, randomized,
study in 14 male/female adult patients with Fabry disease receiving enzyme replacement therapy (ERT)



Lucerastat is investigational, in development and not approved or marketed in any country.

Lucerastat exploratory study

Primary objective

- **To assess the safety and tolerability**
  of lucerastat 1000 mg b.i.d. for 12 weeks

Secondary objectives

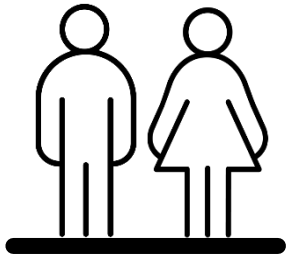
- To investigate the effect of lucerastat on
  plasma biomarker levels following a 12-week treatment
- To assess the effect of lucerastat on renal and cardiac function
- To determine the 12-hour pharmacokinetic profile
  of lucerastat at steady state
- To identify metabolites in plasma

Lucerastat is investigational, in development and not approved or marketed in any country.

Lucerastat exploratory study

Patient demographics

Phase 1b study

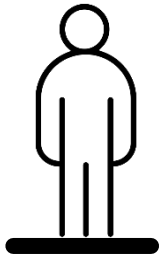


Lucerastat group

- 6 females, 4 males
- Mean age (SD): 47.7 (15.0), range from 18 to 67
- Mean ERT duration in years (SD): 4.5 (2.6)

Medical history:

- All patients had comorbidities, most of them manifestations of Fabry disease
- None of these affected eligibility for the study
- Overall balanced between groups



Control group

- 4 males
- Mean age (SD): 39.8 (19.1), range from 21 to 62
- Mean ERT duration in years (SD): 6.3 (4.2)

Lucerastat is investigational, in development and not approved or marketed in any country.

Lucerastat exploratory study

Safety results

Lucerastat was safe and well tolerated in patients with Fabry disease over 12 weeks on top of ERT

One Serious Adverse Event, unrelated to lucerastat:
Re-occurrence of atrial fibrillation in a patient
with underlying hypertrophic cardiomyopathy

No specific pattern in the nature and distribution
of Treatment-Emergent Adverse Events

No trends for changes from baseline in:
Vital signs, body weight, ECG recordings, clinical laboratory parameters

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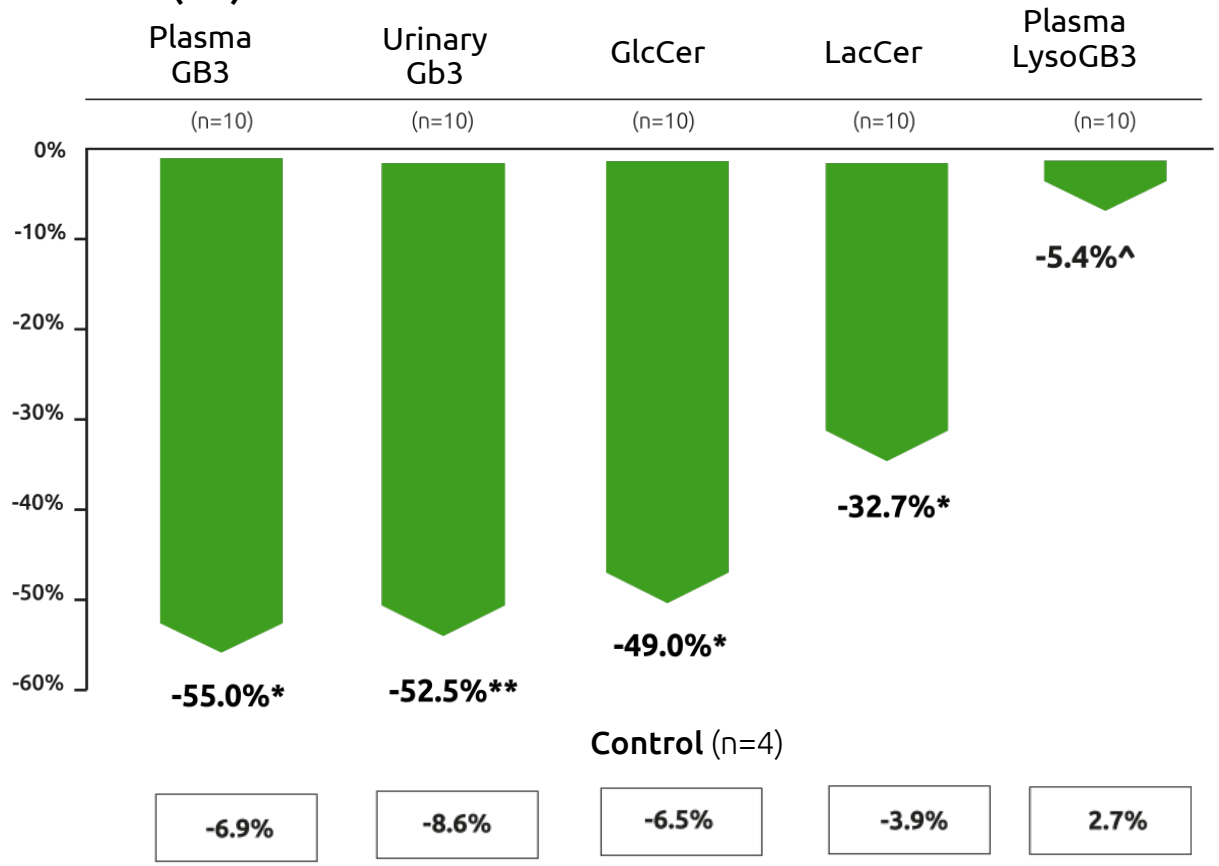
Lucerastat exploratory study

Results: rapid and additional reduction in Gb3 when added to enzyme replacement therapy

Phase 1b study

- **Lucerastat was safe and well tolerated** in patients with Fabry disease over 12 weeks on top of ERT
- **Pharmacokinetic findings consistent** with previous studies in healthy subjects
- **Proof of mechanism achieved with lucerastat:**
  Lucerastat significantly reduced Fabry disease-elevated Gb3
  and other relevant biomarkers

Mean % (SD) biomarker reduction from baseline at week 12



*P<0.0001,**statistical significance not calculated, ^non-significant

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Fabry patients survey

Goals

Better understand patients' disease and needs from the patient perspective

1

Investigate key aspects of Phase 3 study MODIFY with respect to symptoms: neuropathic pain and gastrointestinal symptoms

2

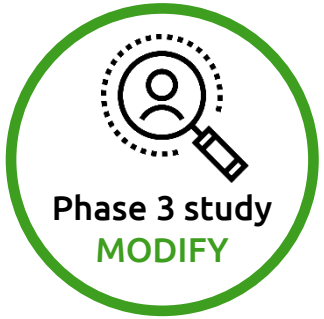
Complement existing information/data from the literature

3

In addition, collect information on:

- Use of enzyme replacement therapy (ERT)
- Impact on daily life
- Participation in clinical trials

Designing the confirmatory study: MODIFY



- **Informed design** based on patients survey
- **Development of endpoint measurement** – neuropathic pain, based on Brief Pain Inventory instrument, modified for Fabry's neuropathic pain according to FDA guidelines for PRO
- **Development and validation of electronic tool** to collect pain and gastro-intestinal daily data
- **Input from patient organization and from specialists**
- **Input from regulatory agencies including FDA**, and in Europe through scientific advice and the VHP procedure

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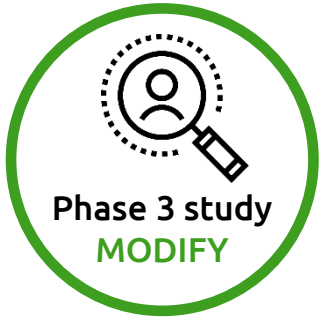
MODIFY: Objectives



Primary objective

- **To determine the effect of lucerastat on neuropathic pain** in patients with Fabry disease

Secondary objectives

- **To determine the effect of lucerastat on gastro-intestinal symptoms** (abdominal pain and diarrhea) in patients with Fabry disease and GI symptom(s) at baseline
- **To confirm the effect of lucerastat on biomarkers** of Fabry disease
- **To determine the safety and tolerability** of lucerastat in patients with Fabry disease

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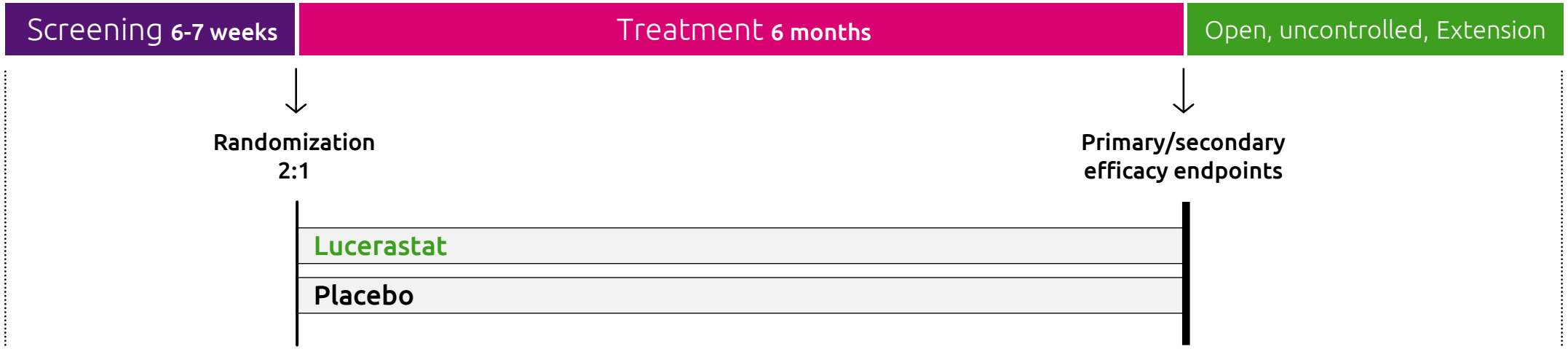
MODIFY: Study design

Phase 3 study
MODIFY



Site visits
Screening, Randomization,
Months 1, 2 (phone), 3, 4 (phone), 5, 6
+ 2 FU visits (phone)

Stratification by
- Sex
- ERT use (on ERT at screening vs never treated/previously treated)

Lucerastat dose
- 1000 mg b.i.d.
- Adjusted in subjects with moderate renal failure

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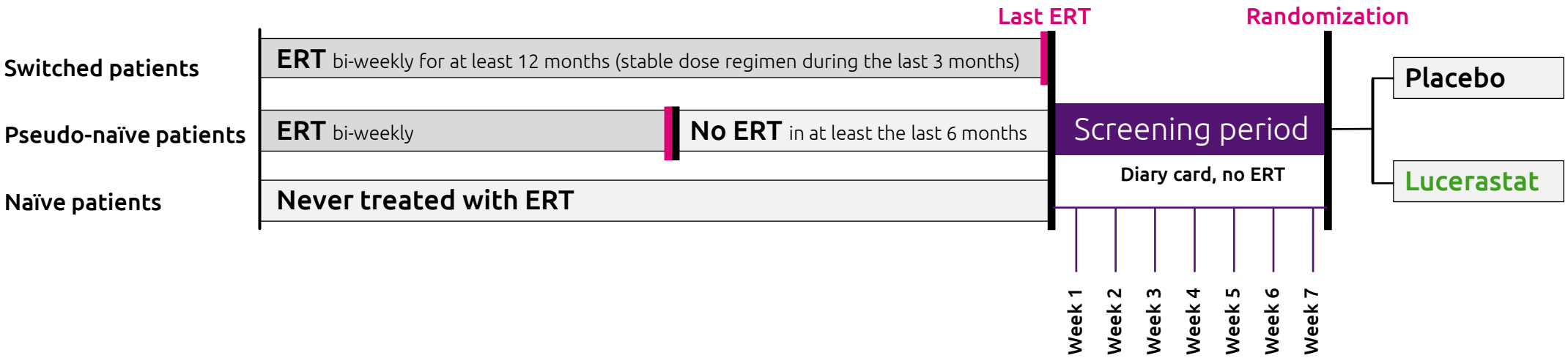
MODIFY: Patient population

Phase 3 study
MODIFY



- Confirmed Fabry disease – presence of at least 1 mutation in GLA (the gene coding for α-galactosidase A) as measured with genetic test
- Neuropathic pain in the last 3 months preceding the screening period
- Three options for ERT status at baseline

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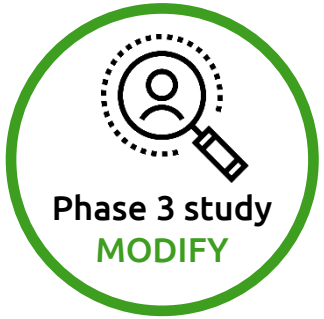
MODIFY: Study endpoints



Primary efficacy endpoint

- The primary efficacy endpoint is a response to study treatment on neuropathic pain, defined as a reduction from baseline to Month 6 of at least 30% in the "modified" BPI-SF3 score of "neuropathic pain at its worst in the last 24 hours".

Secondary efficacy endpoints

- Change from baseline to Month 6 in the average daily 11-point Numerical Rating Scale (NRS-11) score of "abdominal pain at its worst in the last 24 hours" in subjects with GI symptoms at baseline.
- Change from baseline to Month 6 in the number of days with at least one stool of a Bristol Stool Scale (BSS) consistency Type 6 or 7 in subjects with GI symptoms at baseline;
- Change from baseline to Month 6 in plasma globotriaosylceramide (Gb3).

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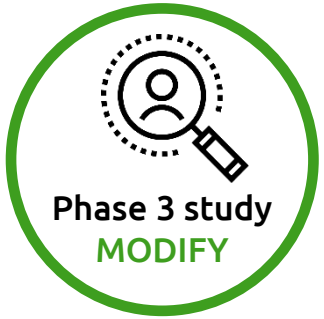
MODIFY: Results



- October 2021 MODIFY did not meet the primary endpoint of reducing neuropathic pain during 6 months of treatment versus placebo
- Substantial and consistent reduction of plasma Gb3 – confirming the pharmacological activity of lucerastat
- Based on historical patient data, mean estimated glomerular filtration rate (eGFR) – a measure of kidney function – was decreasing prior to the study. During the 6 months of the MODIFY study, eGFR increased in both arms of the study (as measured by the eGFR slope), with a slightly higher increase observed in the lucerastat group than in the placebo group.
- Lucerastat was well tolerated
- Lucerastat will therefore be further characterized in the Open label extension (OLE) study

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MODIFY: Open label extension study

- To determine the long-term safety and tolerability of lucerastat oral therapy and to further evaluate its clinical effects on renal and cardiac function in adult patients with Fabry disease over an additional period of up to 72 months
- October 2022: Interim analysis of the OLE study – all patients continuing in the study have now been treated with lucerastat for at least 12 months
- The analysis corroborated the long-term effect on the reduction of plasma Gb3 and showed that the signal seen on kidney function after 6 months of treatment is still observed after the longer treatment duration, supporting a potential positive long-term effect on kidney function
- The analysis also showed a safety and tolerability profile consistent with that observed during the 6-month randomized treatment period

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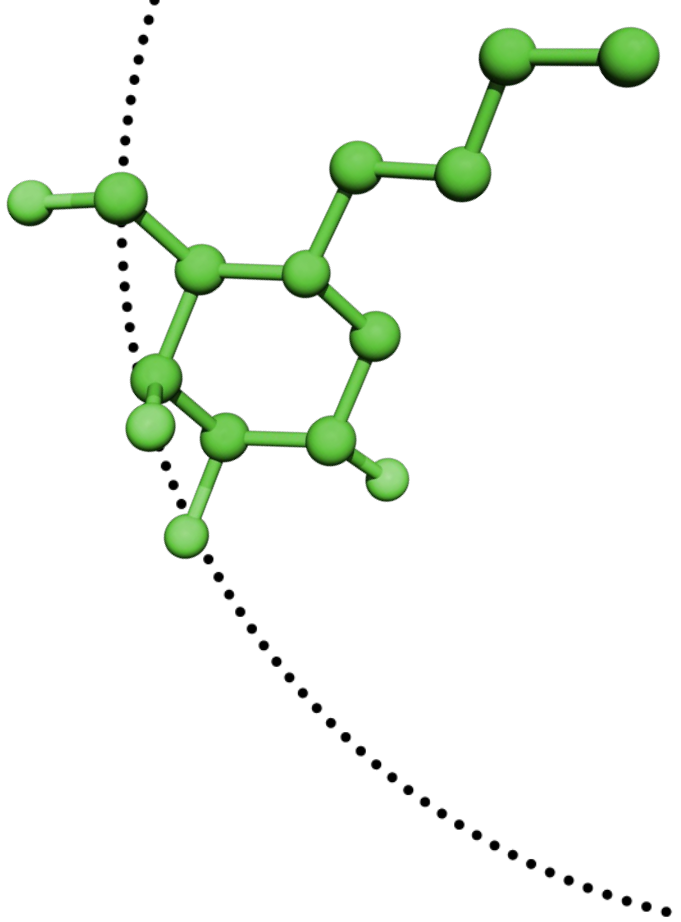
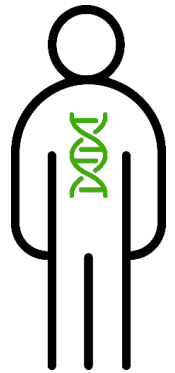
Lucerastat for Fabry disease

Glucosylceramide synthase inhibitor

An oral substrate reduction therapy investigated for the treatment of adult patients with Fabry disease.

- Lucerastat for Fabry disease has received orphan drug designation in the US and the EU
- MODIFY did not meet the primary endpoint
- Observations on renal function and cardiac echocardiography which, if confirmed with longer-term data, would indicate a treatment effect on the main organs affected by the disease
- Interim analysis showed that the signal seen on kidney function after 6 months of treatment is still observed after the longer treatment duration
- The OLE study continues, and the company is consulting with health authorities about the regulatory pathway for lucerastat





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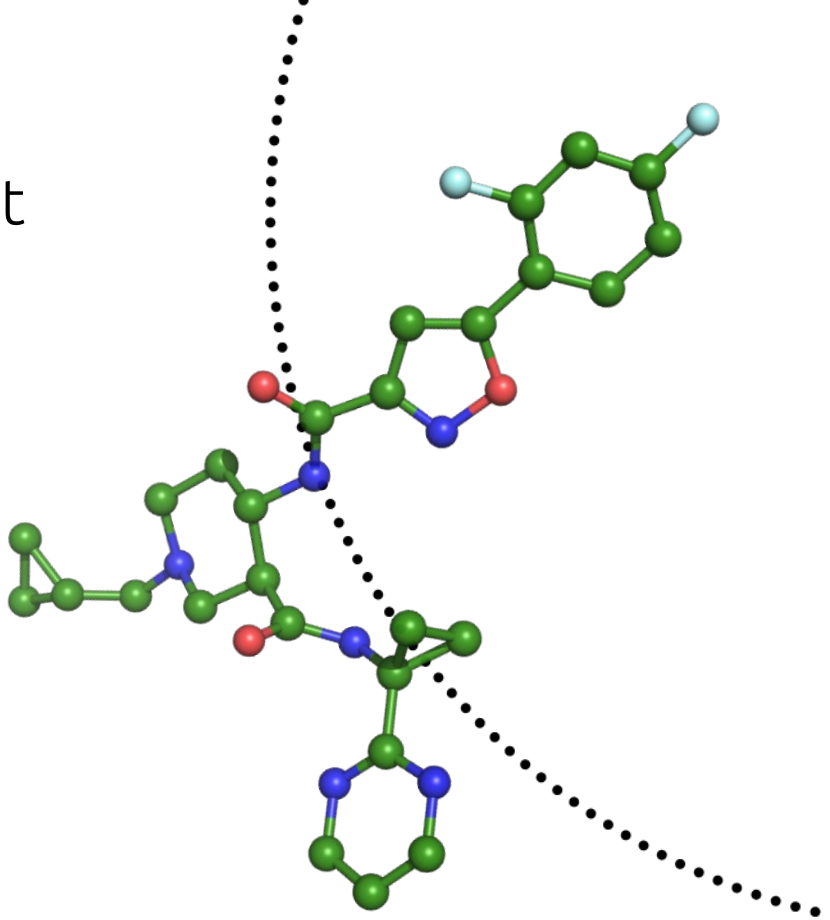
Idorsia's other clinical development assets

ACT-1004-1239

A first-in-class, potent, selective ACKR3/CXCR7 antagonist

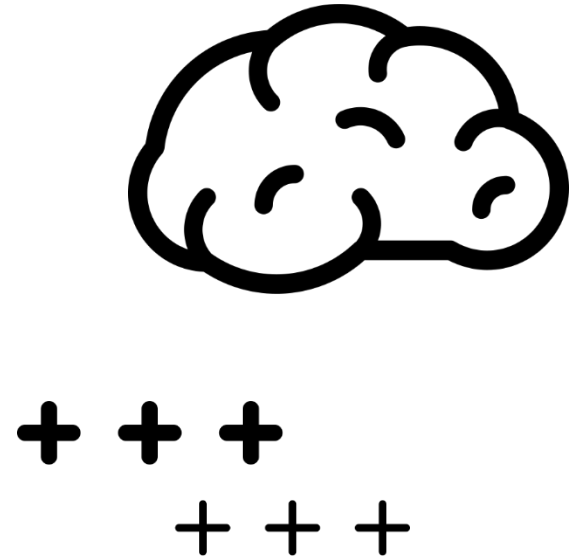
- Preclinical data has shown both anti-inflammatory and promyelinating effects
- The Phase 1 SAD and MAD studies have been completed, and following feedback from the US FDA, we are currently preparing the plan for a Phase 2 study in multiple sclerosis



ACT-1004-1239 is investigational, in development and not approved or marketed in any country.

Sinbaglustat

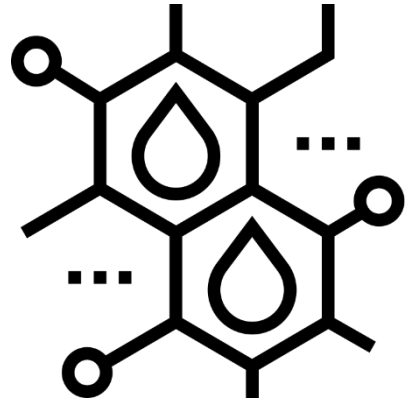
GBA2/GCS inhibitor



- Sinbaglustat, a non-lysosomal glucosylceramidase / glucosylceramide synthase (GBA2/GCS) inhibitor, has potential for the treatment of rare lysosomal storage disorders
- Following a Phase 1 clinical pharmacology program, the company ran a natural history study called “RETRIEVE” which collected disease information from pediatric patients with early onset of rare lysosomal storage disorders (LSDs).
- Based on this information, the company is now considering development options for sinbaglustat.

Sinbaglustat is investigational, in development and not approved or marketed in any country.

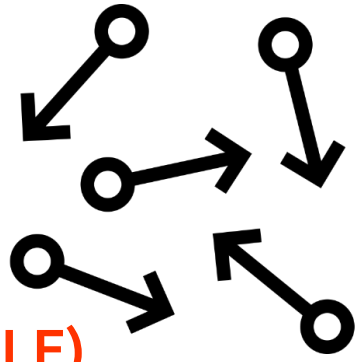
Other early-stage pipeline assets



- **ACT-1014-6470**, a C5aR1 antagonist, is currently investigated in a Phase 1 program with the target indication in immune-mediated disorders
- **ACT-777991**, a CXCR3 antagonist, is currently investigated in a Phase 1 program with the target indication of recent-onset Type 1 diabetes
- **IDOR-1117-2520** is currently investigated in a Phase 1 program with the target indication in immune-mediated disorders
- **IDOR-1134-2831** is a synthetic glycan vaccine targeting *Clostridium difficile* infection. A clinical pharmacology program is currently in preparation to test ID-090 with healthy volunteers and patients. A study in patients will elucidate the potential of ID-090 to prevent recurrence of *C. difficile* infection (therapeutic approach) in a patient population at an early timepoint of clinical development.

These compounds are investigational, in development and not approved or marketed in any country.

ACT-709478 (NBI-827104)



A potent, selective, orally-active, and brain penetrating T-type calcium channel blocker

Investigated by Neurocrine Biosciences in a Phase 2 open label extension (OLE) study for the treatment of a rare form of pediatric epilepsy known as epileptic encephalopathy with continuous spike and wave during sleep (EE-CSWS)

- ~7,000 people have EE-CSWS in the US
- Neurocrine Biosciences has a global license to develop and commercialize Idorsia's ACT-709478
- Rare Pediatric Disease Designation and Orphan Drug Designation from the US FDA for ACT-709478 in EE-CSWS
- While the blinded-study did not meet the primary endpoint, ACT-709478 was generally well tolerated and Neurocrine continues to analyze the totality of data coming from the OLE study to determine next steps.

ACT-709478 is investigational, in development and not approved or marketed in any country.

More knowledge – Powered by science

Focus on small molecules

- Based on organic chemistry
- Suitable for acute and chronic diseases
  - Suitable for oral use
    - Clear patent protection

Vaccine platform

- Discovering and developing glycoconjugate vaccines
- Containing synthetic antigenic glycan molecules
- +/- carrier protein to prevent infection

Target selection

- High medical need – patient focused
- Therapeutic novelty

State-of-the-art technologies

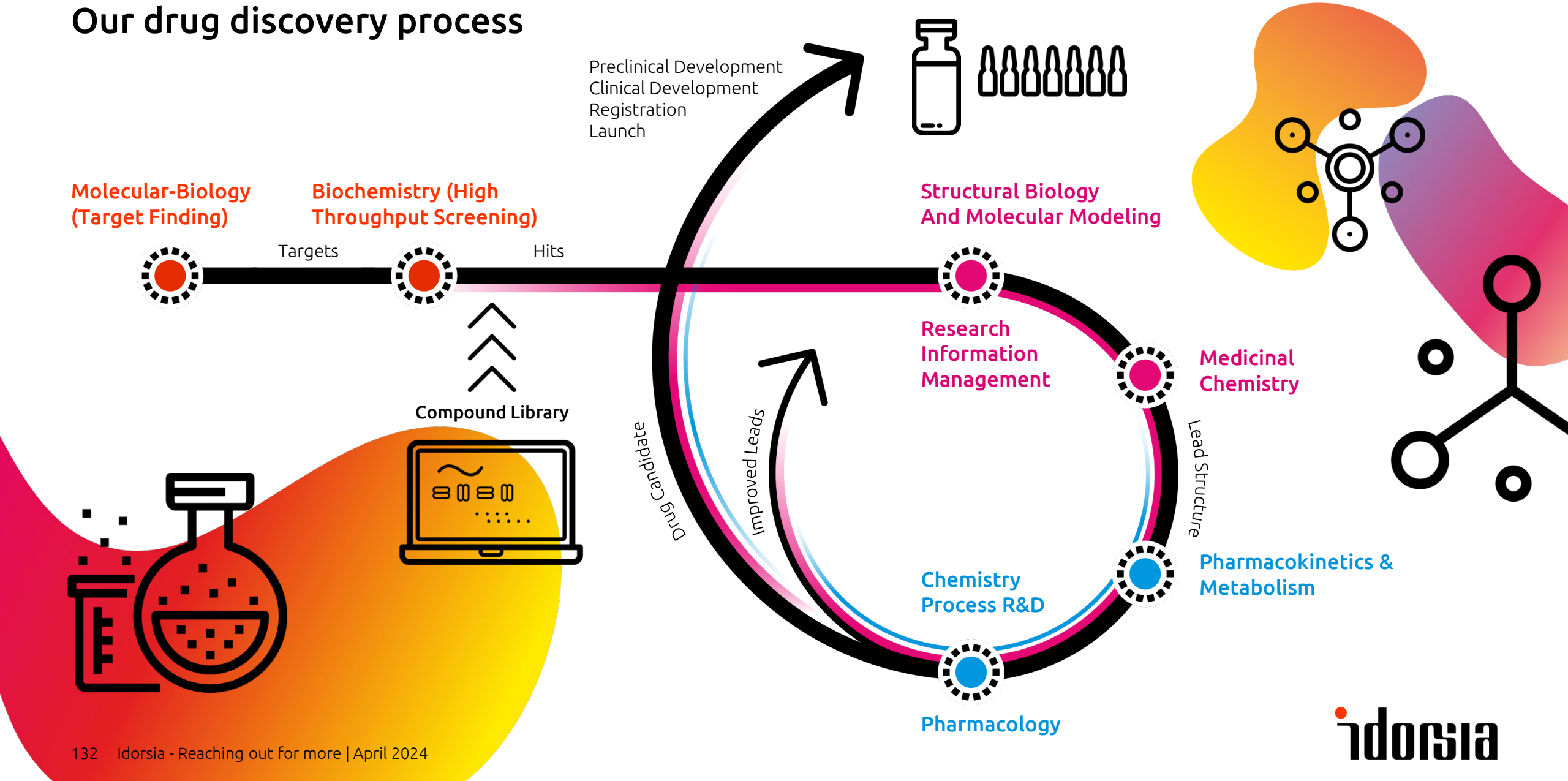
- Artificial intelligence
- Computer modelling
- High throughput screening

Industry leading talent

- Experienced team
- Top-quality organic chemists
- Medical expertise in multiple therapeutic areas

More joy – Transforming the horizon

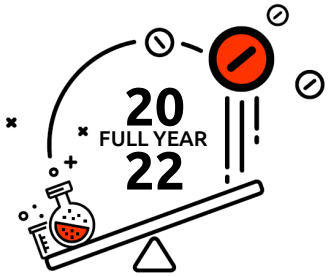
Our drug discovery process

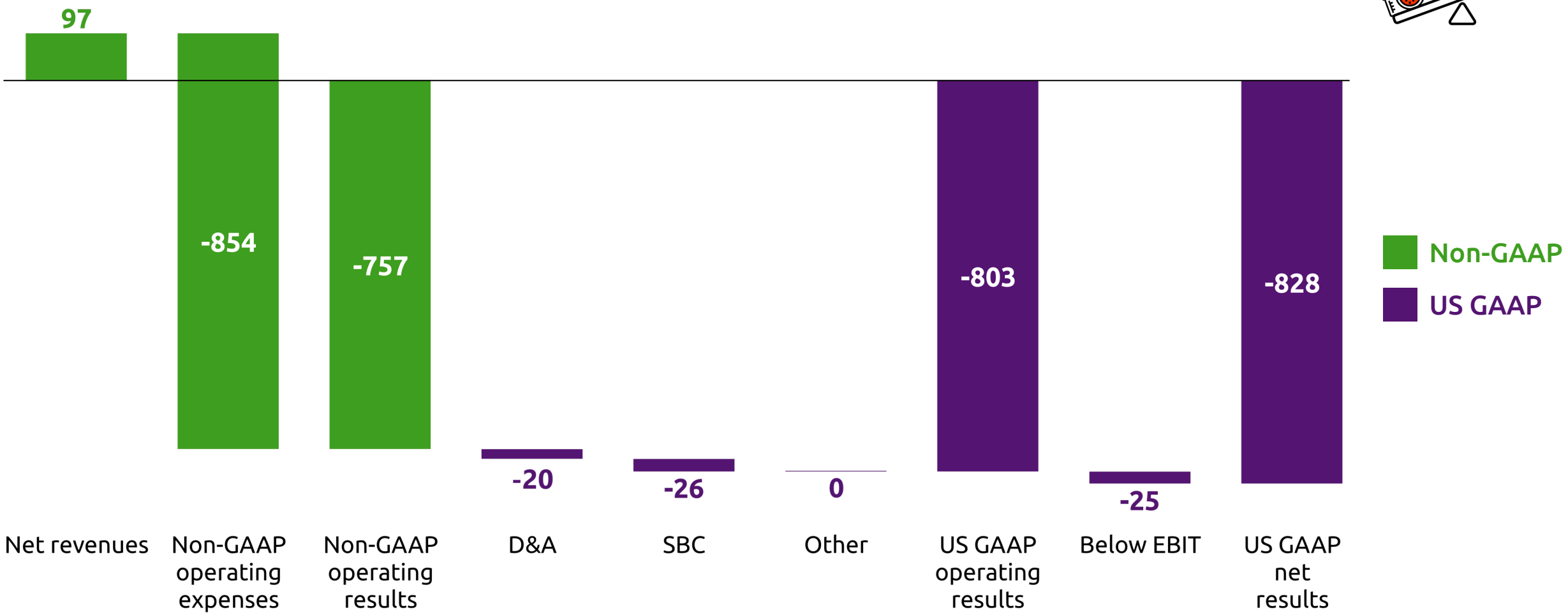


Financial information FY 2022

US GAAP net results

in CHF millions, rounding differences may occur

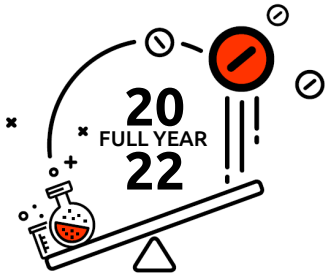


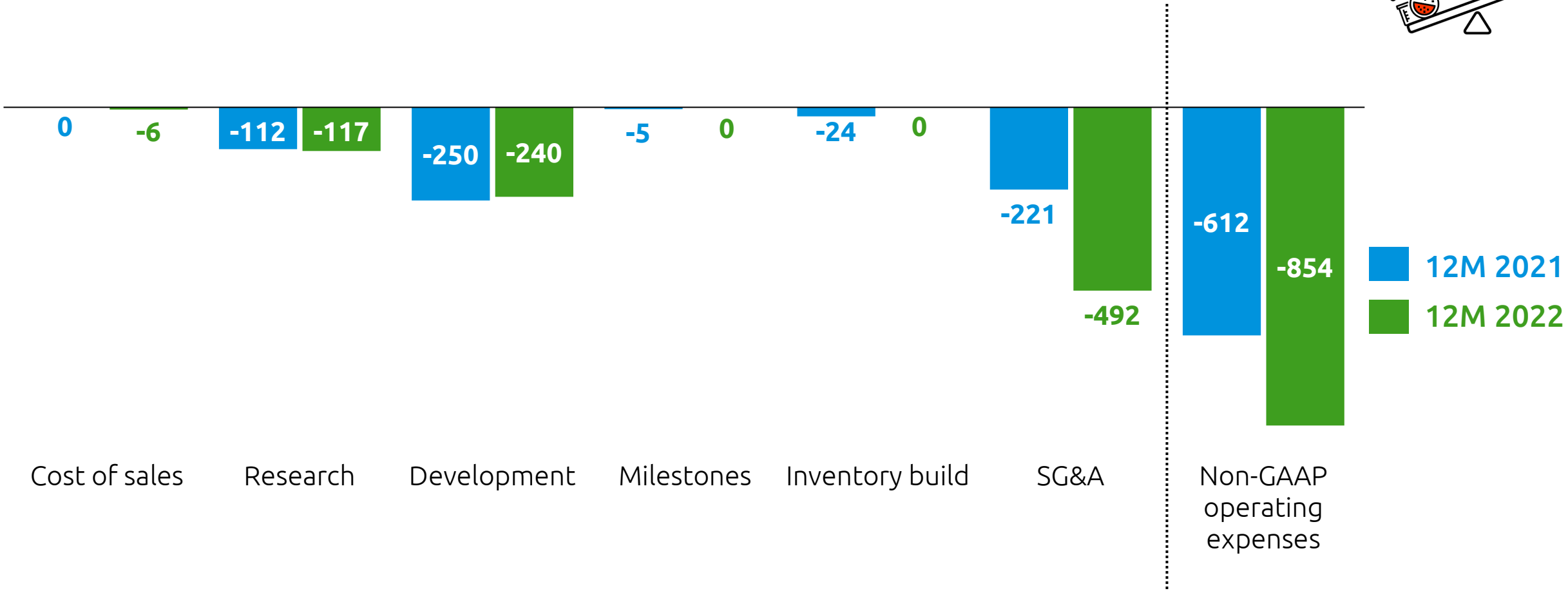


Financial results as of Dec 31, 2022

Non-GAAP operating expenses

in CHF millions, rounding differences may occur





Financial results as of Dec 31, 2022

Financial information 9M 2023

US GAAP/Non-GAAP Net Sales

in CHF millions, rounding differences may occur

		Q1	Q2	Q3	Nine months
QUVIVIQ daridorexant 25mg, 50mg tablets	United States	3.0	5.8	6.2	15.0
	Germany, Italy, Spain and Switzerland	1.3	1.6	2.2	5.1
	QUVIVIQ™	4.3	7.4	8.4	**20.2**
PIVLAZ clazosentan	**PIVLAZ® (Japan)**	13.5	18.9	1.3	**33.7**
	Net Sales	**17.7**	**26.4**	**9.7**	**53.9**

Impact from Nxera deal (previously known as Sosei)

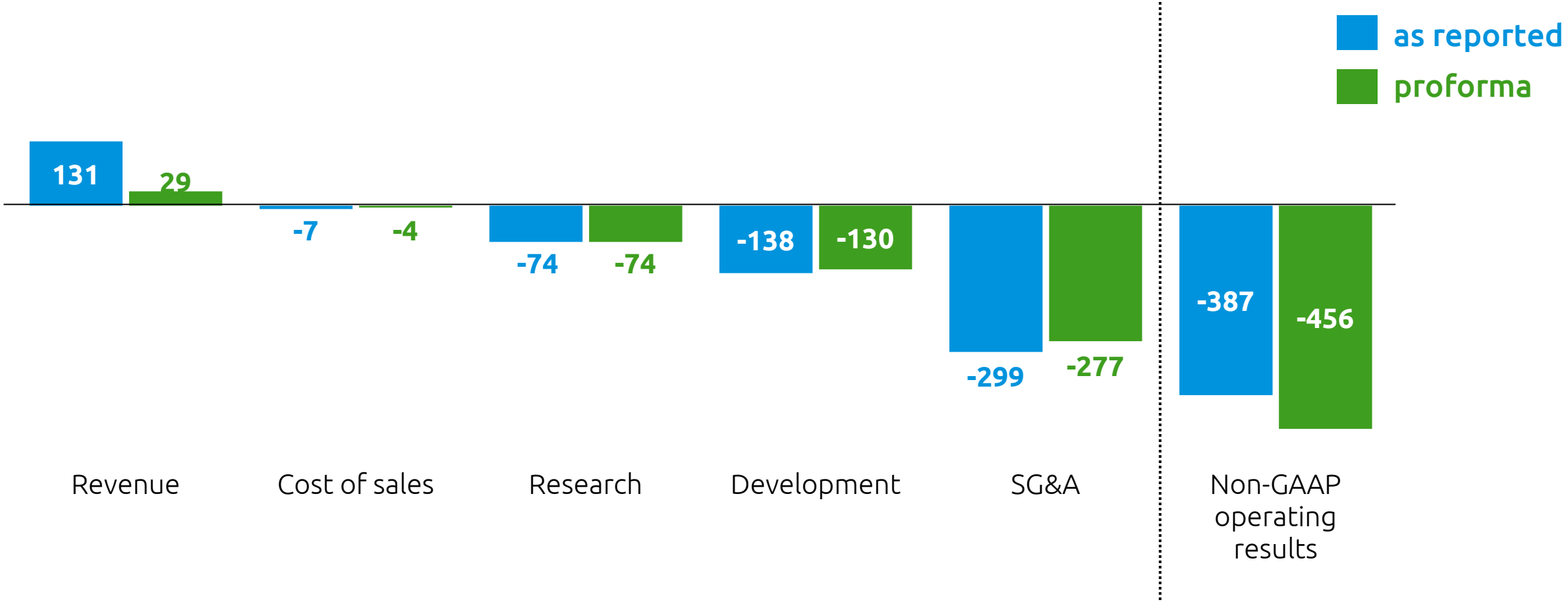
in CHF millions, rounding differences may occur

Initial cash received	396
Approx. cash to be received	4
Total cash from Nxera Deal	**400**

Gains on sale of disposal group	302
Contract revenue from QUVIVIQ license	68
Impairment of intangible assets	(7)
Total profit from Nxera Deal	**363**

Non-GAAP operating results

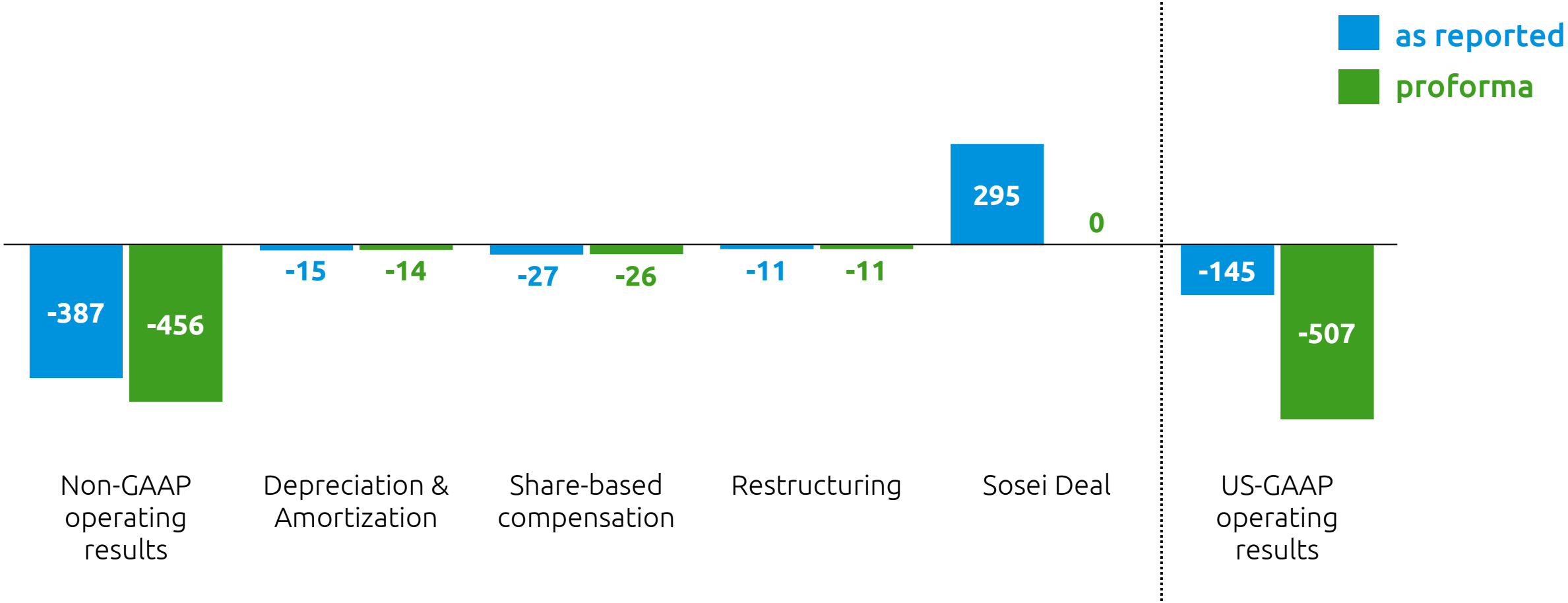
in CHF millions, rounding differences may occur



Financial results as of September 30, 2023

US GAAP operating results

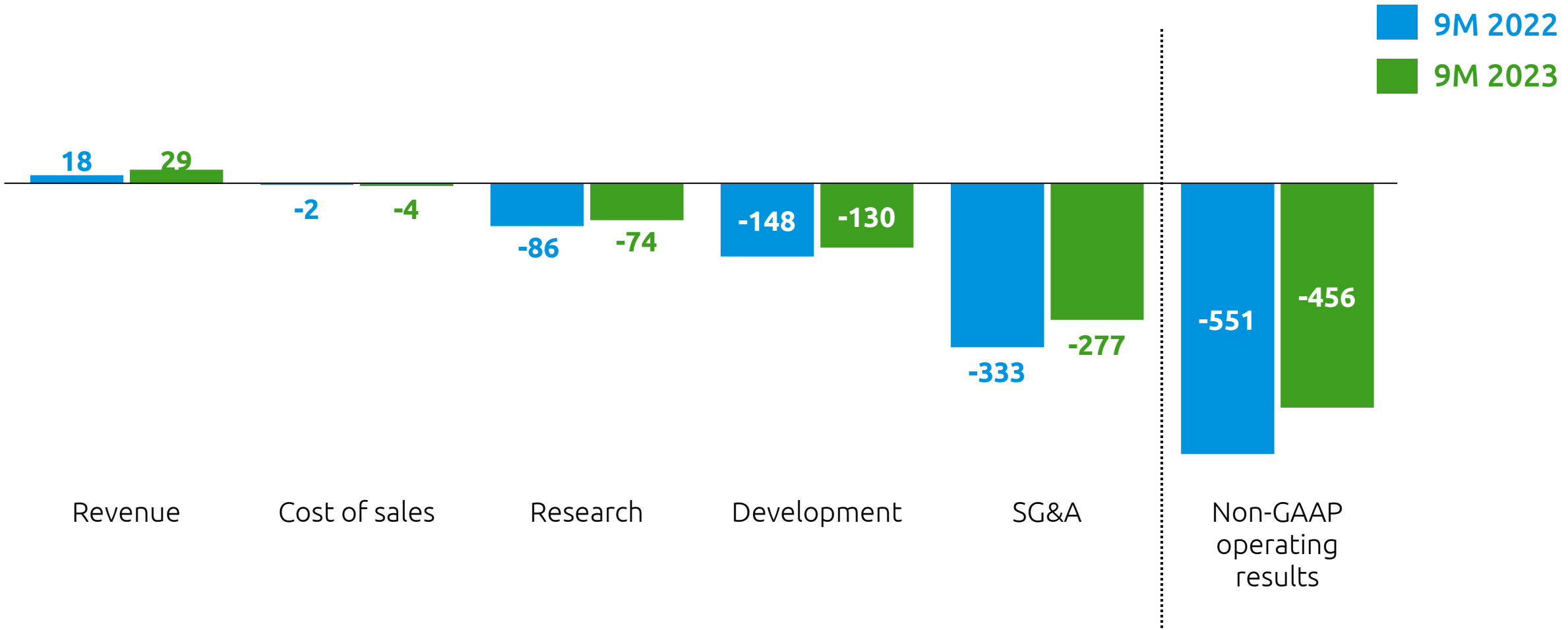
in CHF millions, rounding differences may occur



Financial results as of September 30, 2023

Proforma Non-GAAP operating results

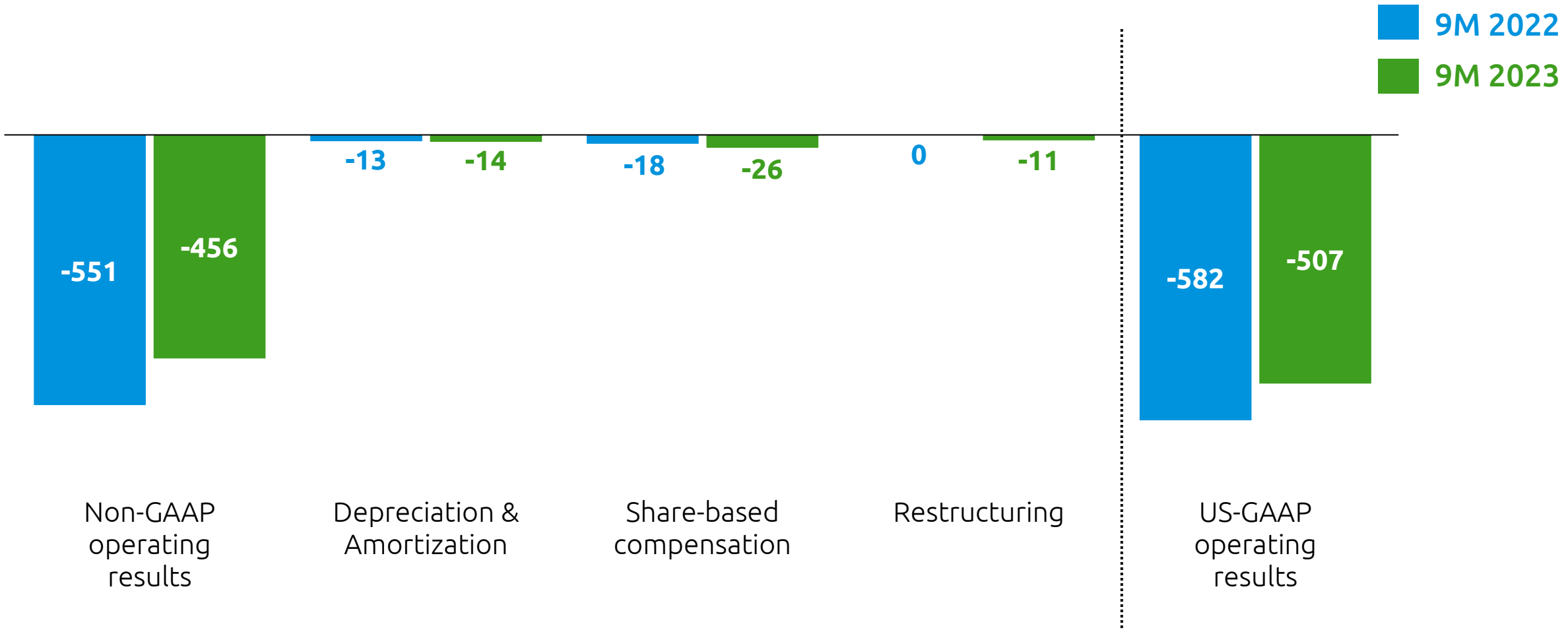
in CHF millions, rounding differences may occur



Financial results as of September 30, 2023

Proforma US GAAP operating results

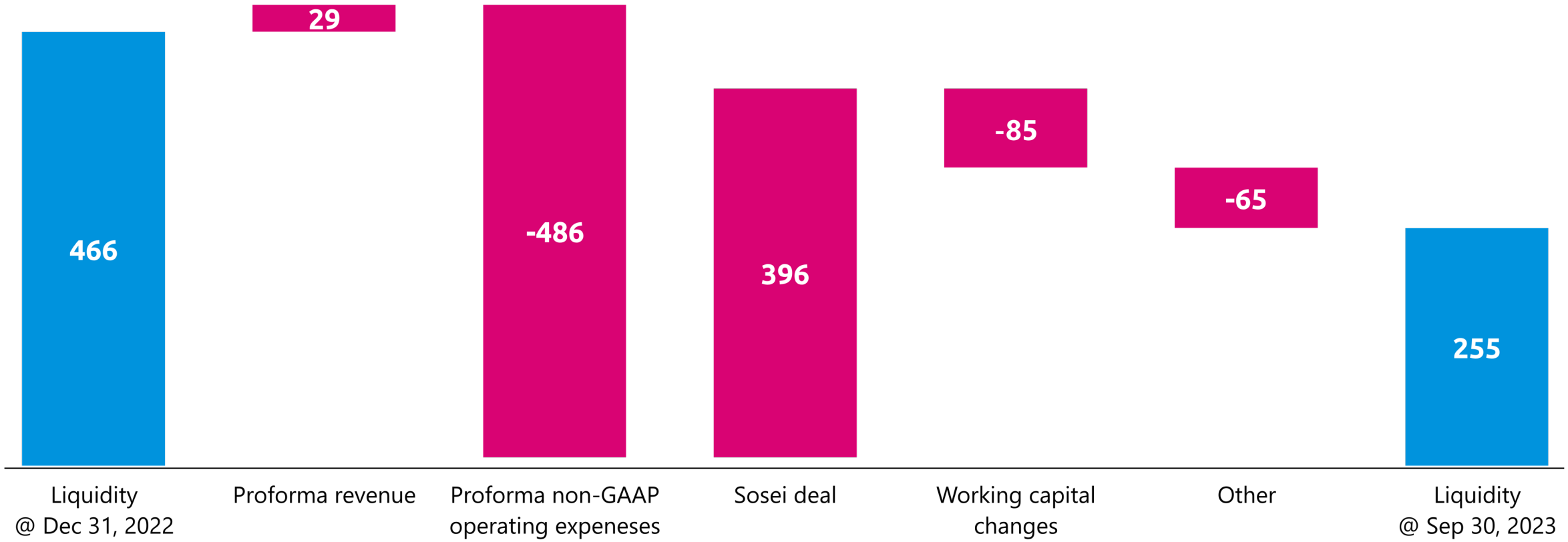
in CHF millions, rounding differences may occur



Financial results as of September 30, 2023

Cash flow

in CHF millions, rounding differences may occur



Financial results as of September 30, 2023

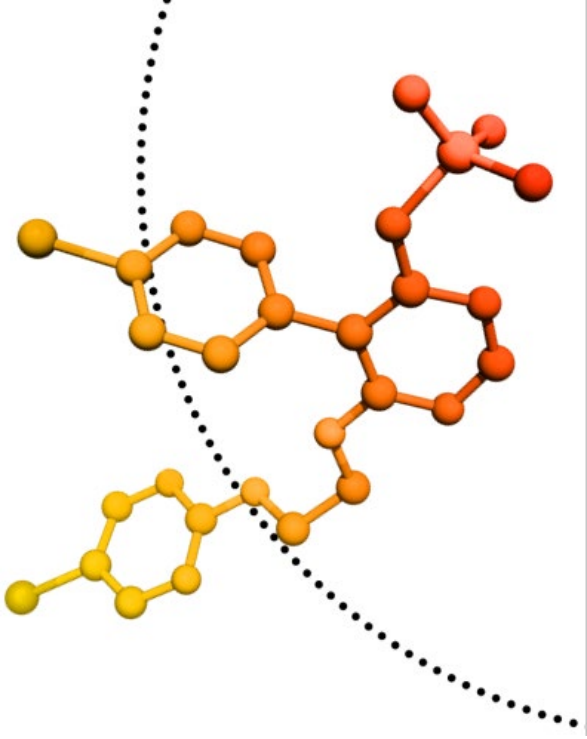
Indebtedness

in CHF millions, rounding differences may occur

*Total Indebtedness does not include conditional payments to J&J of up to CHF 306 m for the reacquisition of worldwide rights to aprocitentan

Financial results as of September 30, 2023

Reacquisition of aprocitentan rights



- Idorsia reacquired all worldwide rights to aprocitentan
- Johnson & Johnson entitled up to CHF 306 million
  - If aprocitentan is approved in the US (90%)
  - If aprocitentan is approved in EU (10%)
- Idorsia to pay J&J
  - 30% on aprocitentan out-license deal
  - 10% on other out-license deals
  - Tiered royalties on annual net sales

Financial Guidance for 2023*

US GAAP operating loss of around **CHF 670 million** and non-GAAP operating loss of around **CHF 600 million**

***Both metrics include the restructuring charge, exclude APAC operations in 2023 until the closing of the Nxera Deal and the one-off impact of such transaction, and exclude any unforeseen events**
Non-GAAP metrics do not include Depreciation and Amortization, and Shared-Based Compensation

Idorsia has a **strong and visionary leadership team** with the power and drive to create more remarkable innovations and more new medicines

Idorsia Executive Committee

Idorsia Leadership Team

Kerstin Niggemann
Head Pharmacological Sciences

Olivier Lambert
Head of Technical Operations

Markus Riederer
Head Translational Sciences

Alex Khatuntsev
Head of Global Human Resources

Julien Gander
Group General Counsel

Eva Caroff
Head Chemical Sciences

Andrew C. Weiss
Head of Investor Relations & Corporate Communications

Be prepared for more