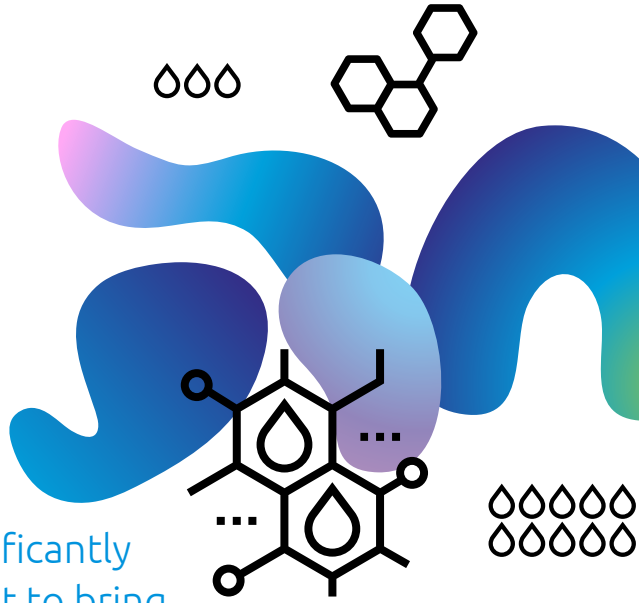
More innovation – from bench to bedside



Idorsia aims to deliver new products with the potential to significantly change the treatment options in their target diseases. We want to bring new perspectives to the discovery, development, and commercialization of innovative treatments, challenging accepted paradigms to answer the questions that matter most.

We have a diversified and balanced innovation portfolio covering multiple therapeutic areas, including CNS, cardiovascular, and immunological disorders, as well as orphan diseases.

The company also has a vaccine platform discovering and developing glycoconjugate vaccines containing synthetic antigenic glycan molecules with and without a carrier protein to prevent infection.

Our Innovation

Innovation Portfolio

QUVIVIQ™ (daridorexant)

TRYVIO™ (aprocitentan)

Lucerastat

Early-stage pipeline

Partner-led portfolio

Innovation Portfolio

Idorsia-led Portfolio

Compound	Target indication	Mechanism of action	P1	P2	P3	R	C	Status
QUVIVIQ™ (daridorexant)	Insomnia	Dual orexin receptor antagonist	■	■	■	■	■	Commercially available as QUVIVIQ in the US, Germany, Italy, Switzerland, Spain, UK, Canada, Austria, and France; approved throughout the EU
TRYVIO™ (aprocitentan)	Systemic hypertension in combination with other antihypertensives	Dual endothelin receptor antagonist	■	■	■	■	□	Approved in the US, launch planned for H2 2024
Aprocitentan	Systemic hypertension in combination with other antihypertensives	Dual endothelin receptor antagonist	■	■	■	■	□	Marketing authorisation application (MAA) under review in the EU
Lucerastat	Fabry disease	Glucosylceramide synthase inhibitor	■	■	■	□	□	Phase 3 primary endpoint not met; open label extension study ongoing
Daridorexant	Pediatric insomnia	Dual orexin receptor antagonist	■	■	□	□	□	Phase 2 in pediatric insomnia ongoing
ACT-1004-1239	Demyelinating diseases inc. MS	ACKR3 / CXCR7 antagonist	■	■	□	□	□	Phase 2 in preparation
Sinbaglustat	Rare lysosomal storage disorders	GBA2/GCS inhibitor	■	□	□	□	□	Phase 1 complete
ACT-777991	Recent-onset Type 1 diabetes	CXCR3 antagonist	■	□	□	□	□	Phase 1 complete
ACT-1014-6470	Immune-mediated disorders	C5aR1 antagonist	■	□	□	□	□	Phase 1
IDOR-1117-2520	Immune-mediated disorders	Undisclosed	■	□	□	□	□	Phase 1 ongoing
IDOR-1134-2831	*Clostridium difficile* infection	Synthetic glycan vaccine	■	□	□	□	□	Phase 1 in preparation

P1: Phase 1, P2: Phase 2, P3: Phase 3, R: Registration, C: Commercially available

Innovation Portfolio

Partner-led Portfolio

Compound	Target indication	Mechanism of action	Partner Terms	Status P1	P2	P3	R	C	
Daridorexant	Insomnia	Dual orexin receptor antagonist	**Sosei Heptares** License to develop and commercialize for Asia Pacific (ex-China)	■	■	■	■	□	NDA submitted in Japan
Daridorexant	Insomnia	Dual orexin receptor antagonist	**Simcere** License to develop and commercialize for Greater China region	■	■	■	□	□	Phase 3 ongoing
Selatogrel	Acute myocardial infarction	$P2Y_{12}$ inhibitor	**Viatris** Worldwide development and commercialization rights.	■	■	■	□	□	Phase 3 "SOS-AMI" program ongoing
Cenerimod	Systemic lupus erythematosus	$S1P_1$ receptor modulator	**Viatris** Worldwide development and commercialization rights (excluding Japan, South Korea and certain countries in the Asia-Pacific region).	■	■	■	□	□	Phase 3 "OPUS" program ongoing
Daridorexant	Posttraumatic stress disorder (PTSD)	Dual orexin receptor antagonist	**US Department of Defense (DOD)** Idorsia supports a clinical study sponsored by the US DOD to develop new therapies to treat PTSD.	■	■	□	□	□	Phase 2
ACT-709478/ NBI-827104	Epileptic Encephalopathy with Continuous Spike-and-Wave During Sleep (CSCW)	T-type calcium channel blocker	**Neurocrine Biosciences** Global license to develop and commercialize	■	■	□	□	□	Phase 2

P1: Phase 1, P2: Phase 2, P3: Phase 3, R: Registration, C: Commercially available

QUVIVIQ (daridorexant)

Daridorexant is a dual orexin receptor antagonist (DORA) which blocks the binding of the wake-promoting neuropeptides orexins. Rather than inducing sleep through broad inhibition of brain activity, daridorexant blocks only the activation of orexin receptors. Consequently, daridorexant decreases the wake drive, allowing sleep to occur, without altering the proportion of sleep stages.

Chronic insomnia disorder is a condition of overactive wake signaling, which can have a profound effect on patients' lives. It can be defined as a combination of dissatisfaction with sleep quantity or quality and a significant negative impact on daytime functioning. It involves difficulty initiating and/or maintaining sleep at least three times a week for a minimum of three months.

Chronic insomnia disorder as a persistent disorder is quite different from a brief period of poor sleep, and it can take its toll on both physical and mental health. Idorsia's research has shown that poor-quality sleep can affect many aspects of daily life, including the ability to concentrate, mood, and energy levels.

Chronic insomnia disorder is a common problem, with the prevalence being approximately 10%. On this basis, and assuming a US adult population of around 250 million, there are approximately 25 million adults in the US who suffer from chronic insomnia disorder.

The treatment landscape

The goal of treatments for insomnia is to improve sleep quality and quantity, as well as daytime functioning, while avoiding next-morning residual effects. Current recommended treatment of insomnia includes sleep hygiene recommendations, cognitive behavioral therapy, and pharmacotherapy.

With regard to prescription medications, patients are treated with products indicated for insomnia, as well as off-label treatments. The on-label treatment category primarily comprises drugs that induce sleep by enhancing GABA, the primary inhibitory neurotransmitter in the brain, which works by slowing brain activity in a non-targeted manner. There are two main categories of GABA agonists – benzodiazepines and non-benzodiazepines. In addition, other approved insomnia medications include a melatonin receptor agonist and a low-dose tricyclic antidepressant. The first products in a new class of dual orexin receptor antagonists are available in North America and certain Asia-Pacific markets. These have now been joined by daridorexant, which is available in the US and the first countries in Europe. The most widely used off-label treatment for insomnia in the US is a selective serotonin reuptake inhibitor (SSRI) which has an off-target sedation effect.

Global registration program

The Phase 3 registration program comprised two three-month studies, together with a long-term double-blind extension study. The program is now complete, having enrolled around 1,850 patients with insomnia. As insomnia often presents later in life, and elderly patients are more likely to experience fragmented sleep, early awakening, and daytime sleepiness, around 40% of the recruited population was aged 65 years or older.

The placebo-controlled studies investigated the effects of three doses of daridorexant (Study 1: 50 mg and 25 mg; Study 2: 25 mg and 10 mg) on sleep and daytime functioning parameters – objectively

in a sleep lab by polysomnography and subjectively with a daily patient diary at home. The impact of insomnia on patients' daytime functioning was measured daily using the sleepiness domain score from the Insomnia Daytime Symptoms and Impacts Questionnaire (IDSIQ) – a patient-reported outcome (PRO) instrument validated according to the FDA Guidance for Industry, including patient input.

More than 800 patients continued treatment in the 40-week extension study, which measured the effect of all three doses versus placebo, generating data for long-term treatment of insomnia.

As reported by Mignot E, et al. in the February 2022 issue of *The Lancet Neurology*, the pivotal studies demonstrated that daridorexant significantly improved sleep onset, sleep maintenance and self-reported total sleep time at months 1 and 3 compared to placebo. The largest effect was observed with the highest dose (50 mg), followed by 25 mg, while the 10 mg dose did not have a significant effect. In all treatment groups, the proportions of sleep stages were preserved, in contrast to findings reported with benzodiazepine receptor agonists.

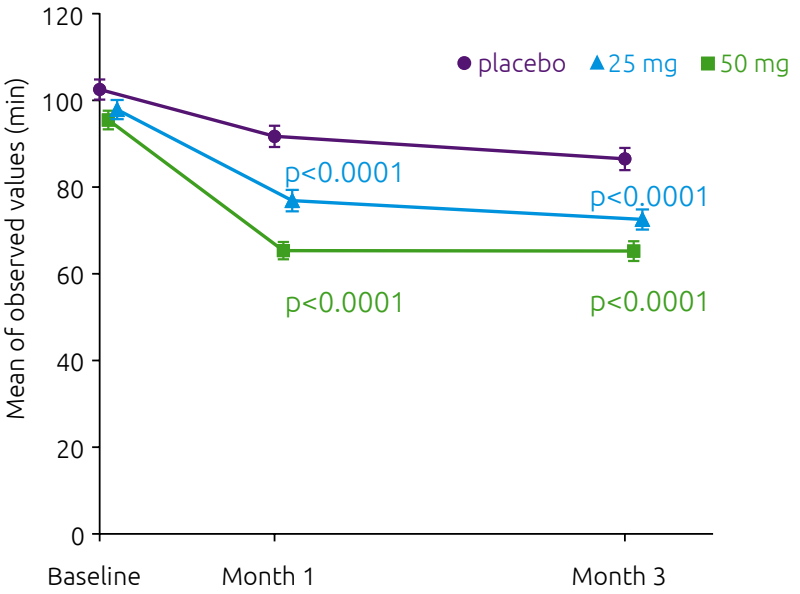
A major focus of the trials was to evaluate the impact of daridorexant on daytime functioning in patients with insomnia, as assessed by the IDSIQ. The sleepiness domain score of the IDSIQ was evaluated as a key secondary endpoint in both pivotal studies, and comparisons to placebo included control for multiplicity. Daridorexant 50 mg demonstrated a highly significant improvement in daytime sleepiness at month 1 and month 3, while the sleepiness domain score was not significantly improved on 25 mg in either study at either timepoint. Daridorexant 50 mg also improved the additional IDSIQ domain scores (alert/cognition, mood) and total score (p values <0.0005 versus placebo not adjusted for multiplicity). Improvements in daytime functioning with daridorexant 50 mg progressively increased over the three months of the study.

The overall incidence of adverse events was comparable between treatment groups. Adverse events occurring in more than 5% of participants were nasopharyngitis and headache. There were no dose-dependent increases in adverse events (including somnolence and falls) across the dosing range. Further, no dependence, rebound insomnia, or withdrawal effects were observed upon abrupt discontinuation of treatment. Across treatment groups, adverse events leading to treatment discontinuation were numerically more frequent with placebo than with daridorexant.

In addition to the results published in *The Lancet Neurology*, the final results of the 40-week extension study with daridorexant became available in April 2021. This study collected information on the safety of long-term treatment, as well as allowing an exploratory analysis of the maintenance of efficacy. There were no new emerging safety findings. Moreover, efficacy for sleep and daytime functioning appeared to be maintained over the longer treatment duration.

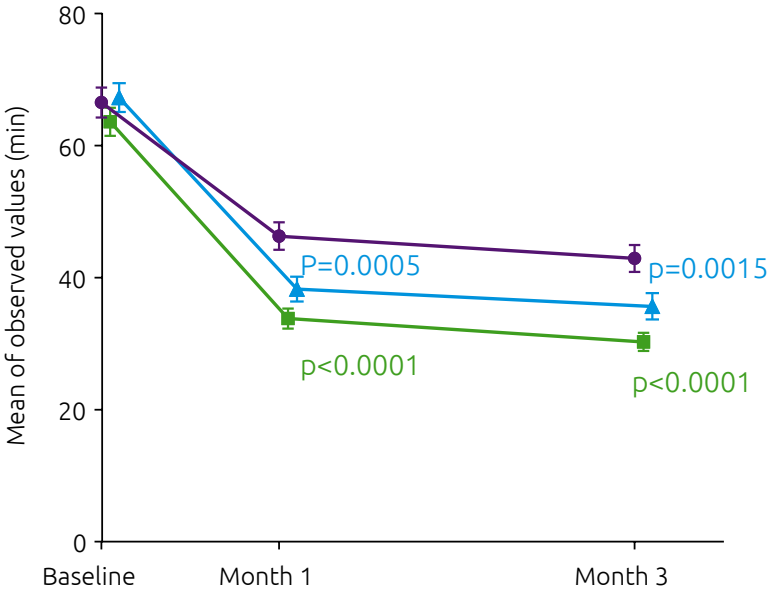
Furthermore, a comprehensive clinical pharmacology program has been conducted, with a total of 18 studies assessing, for example, abuse liability, drug-drug interactions, next-morning driving in healthy participants, the effects of daridorexant on respiratory function in patients with chronic obstructive pulmonary disease or obstructive sleep apnea, and the pharmacokinetics of daridorexant in patients with liver and renal impairment.

Wake time after sleep onset



Mean of observed wake time after sleep onset (WASO) values at study timepoints in study 1.

Latency to persistent sleep

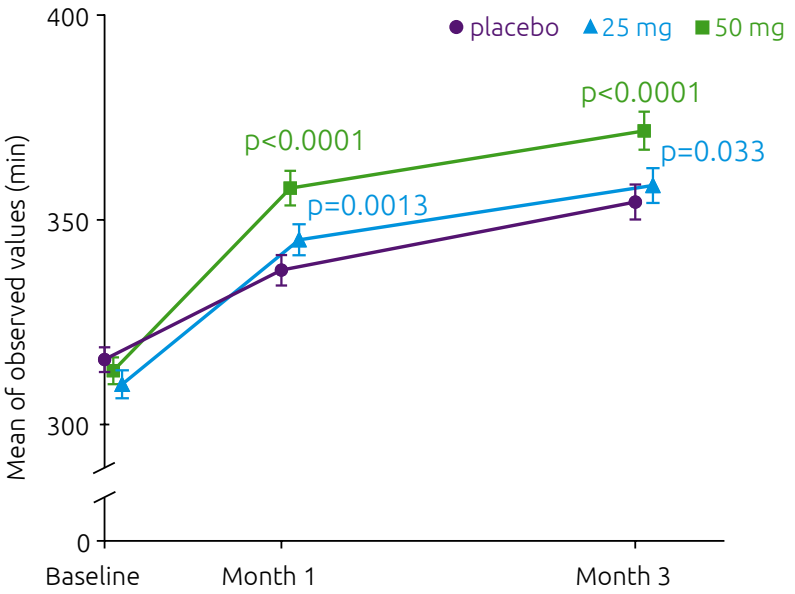


Mean of observed latency to persistent sleep (LPS) values at study timepoints in study 1.

WASO and LPS values are the mean of polysomnography recordings obtained over two consecutive nights during the 3-month double-blind treatment period. Error bars show standard error of the mean. Two-sided p values shown are versus placebo, calculated using the linear mixed effects model for repeated measures.

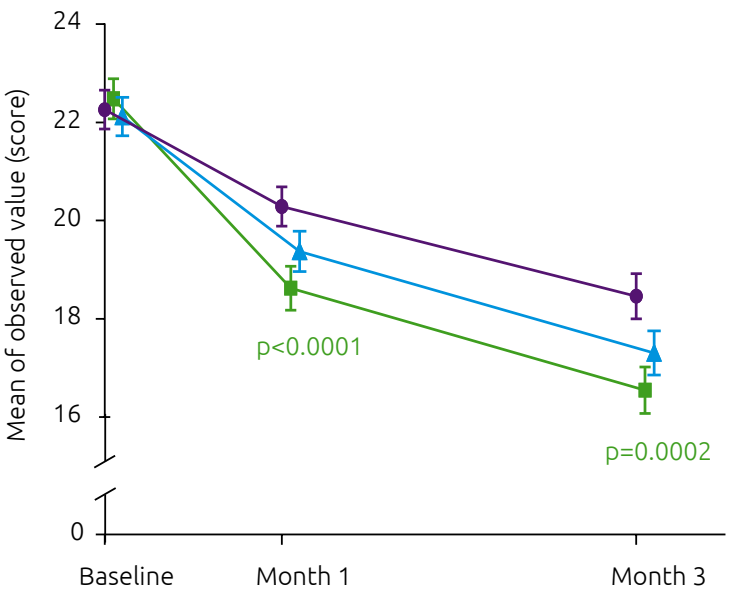
Mignot E, et al. *Lancet Neurol.* 2022; 21: 125–39

Subjective total sleep time



Mean of observed self-reported total sleep time (sTST) values at study timepoints in study 1.

IDSIQ sleepiness domain



Mean of observed IDSIQ sleepiness domain scores at study timepoints in study 1.

Data for sTST and IDSIQ scores are based on the mean of daily entries in the 7 days before polysomnography nights. Error bars show standard error of the mean. Two-sided p values shown are versus placebo, calculated using the linear mixed effects model for repeated measures.

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

Current status in the US

In January 2022, QUVIVIQ (daridorexant) 25 mg and 50 mg was approved by the US FDA for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance. QUVIVIQ was launched in the US in May 2022. For more information about QUVIVIQ in the US, see the **Full Prescribing Information**.

Current status in the EUCAN region

In April 2022, marketing authorization for QUVIVIQ was granted by the European Commission and subsequently by the Medicines and Healthcare products Regulatory Agency (MHRA) in Great Britain for the treatment of adult patients with insomnia characterized by symptoms present for at least three months and considerable impact on daytime functioning, making it Europe's first approved dual orexin receptor antagonist.

In November 2022, QUVIVIQ was launched in Italy and Germany, followed by Spain in September 2023, UK in October 2023, Austria February 2024 and France in March 2024. For more information about QUVIVIQ in the EU, see the Summary of Product Characteristics. Marketing authorization for QUVIVIQ was also granted by Swissmedic in December 2022, and the company made QUVIVIQ available to patients in Switzerland in June 2023. For more information about QUVIVIQ in Switzerland, see the Patient Information and Information for Healthcare Professionals. Market authorization for QUVIVIQ was also granted by Health Canada in April 2023, and the company made it available to patients in Canada in November 2023. For more information about QUVIVIQ in Canada, see the Product Monograph.

Current status in global clinical development

A post approval study to investigate the efficacy of daridorexant in patients with insomnia and comorbid nocturia is ongoing (NCT05597020).

Idorsia has initiated a Phase 2, double-blind, randomized, placebo-controlled, dose-finding study to assess the efficacy, safety, and pharmacokinetics of multiple-dose oral administration of daridorexant in pediatric patients aged between 10 and <18 years with insomnia disorder (NCT05423717). The primary objective of the study is to characterize the dose-response relationship of daridorexant on objective total sleep time (TST) using polysomnography. The study is expected to enroll around 150 patients, who will be randomized in a 1:1:1:1 ratio to 10 mg, 25 mg, or 50 mg daridorexant, or placebo. The development program has been designed based on advice and agreement with the US FDA and a Paediatric Investigational Plan with the EU PDCO.

Milestones

2024 QUVIVIQ launched in Austria and France
2023 QUVIVIQ launched in Switzerland, Spain, UK, and Canada
2022 QUVIVIQ launched in Italy and Germany
2022 Japanese Phase 3 reports positive results
2022 European Commission approves QUVIVIQ
2022 QUVIVIQ launched in the US
2022 Phase 3 data reported in The Lancet Neurology
2020 Both pivotal studies report positive results
2018 Initiation of Phase 3 registration program
2017 Completion of Phase 2 clinical program
2015 Initiation of Phase 1 clinical program

Key scientific literature

- Fietze I., et al. 2022 Oct;39(10):795-810.
- Kunz, D. et al. CNS Drugs (2022).
- Mignot E, et al. Lancet Neurol. 2022; 21: 125–39
- Dauvilliers, Y., et al. (2020). Ann Neurol 87(3): 347-356.
- Zammit, G., et al. (2020). Neurology 94(21): 1-11.
- Muehlan, C., et al. (2020). J Clin Psychopharmacol 40(2): 157-166.
- Muehlan, C., et al. (2020). J Psychopharmacol 34(3): 326-335.
- Boof, M. L., et al. (2019). Eur J Clin Pharmacol 75(2): 195-205.
- Muehlan, C., et al. (2019). Curr Drug Metab 20(4): 254-265.
- Muehlan, C., et al. (2019). Eur Neuropsychopharmacol 29(7): 847-857.
- Muehlan, C., et al. (2018). Clin Pharmacol Ther 104(5): 1022-1029.
- Treiber, A., et al. (2017). J Pharmacol Exp Ther 362(3): 489-503.
- Brisbare-Roch, C., et al. (2007). Nat Med 13(2): 150-5.

TRYVIO (aprocitentan)

Aprocitentan is a once-daily, orally active, dual endothelin receptor antagonist, which inhibits the binding of ET-1 to ETA and ETB receptors. Aprocitentan has a low potential for drug-drug interaction and a mechanism of action that is ideally suited to lower blood pressure in adult patients whose hypertension is not adequately controlled on other drugs.

Hypertension is one of the leading causes of cardiovascular disease worldwide, impacting an estimated 1.3 billion people globally. Approximately 10% of these people have uncontrolled blood pressure (BP), despite receiving at least three antihypertensive medications from different classes, at optimal doses. Compared with adults whose hypertension is well controlled, adults with uncontrolled hypertension have greater risk of heart attack, stroke, end-stage renal disease and death.

The effects of ET-1 bear many similarities with the pathophysiology of hypertension, and ET-1 is a major driver of aldosterone production. Until the approval of TRYVIO, no systemic antihypertensive medications targeted the ET pathway, as approved antihypertensive therapies focus on the regulation of salt and water (diuretics), antagonism of the renin–angiotensin–aldosterone (RAAS) system, reduction of influx of extracellular calcium into the cell (calcium channel blockers), sympatholytic activity (beta blockers, central alpha-agonist agents), or non-selective vasodilatory effects.

TRYVIO was evaluated as a monotherapy in a Phase 2 study in patients with hypertension, and as an add-on therapy in a Phase 3 study called PRECISION in patients with confirmed resistant hypertension. In PRECISION, aprocitentan was well tolerated and superior to placebo in lowering blood pressure at week 4, with a sustained effect at week 40.

Global registration study

The efficacy of TRYVIO (aprocitentan) was evaluated in a multipart, Phase 3 multicenter study (PRECISION, NCT03541174) in adults with systolic blood pressure (SBP) ≥140 mmHg who were prescribed at least three antihypertensive medications. The trial included a placebo run-in period, which was followed by three parts as described below. Prior to the placebo run-in period, all patients were switched to standard background antihypertensive therapy consisting of an angiotensin receptor blocker, a calcium channel blocker, and a diuretic, which was continued throughout the study. Patients with concomitant use of beta blockers continued this treatment throughout the study.

Following the 4-week placebo run-in period, 730 patients were randomized equally to aprocitentan at either 12.5 mg, 25 mg, or placebo once daily during the initial 4-week double-blind (DB) treatment period (part 1). At the end of 4 weeks, all patients entered the single-blind treatment period (part 2) where they received 25 mg aprocitentan once daily for 32 weeks. At the end of the 32 weeks, patients were re-randomized to receive either 25 mg aprocitentan or placebo, once daily, during a 12-week DB-withdrawal period (part 3).
The primary efficacy endpoint was the change in sitting SBP (SiSBP) from baseline to Week 4 during part 1, measured at trough by unattended automated office blood pressure (uAOBP). The key secondary

endpoint was the change in SiSBP measured at trough by uAOBP from Week 36 (i.e., prior to randomized withdrawal to 25 mg aprocitentan or placebo in part 3) to Week 40.

Patients had a mean age of 62 years (range 24 to 84 years) and 60% were male. Patients were White (83%), African American (11%) or Asian (5%). Approximately 10% were Hispanic. The mean body mass index (BMI) was 34 kg/m2 (range 18 to 64 kg/m2). At baseline, 19% of patients had an eGFR 30–59 mL/min/1.73 m2 and 3% had an eGFR 15–29 mL/min/1.73 m2. At baseline, 24% of patients had a urine albumin-to-creatinine ratio (UACR) of 30–300 mg/g and 13% had a UACR >300 mg/g. Approximately 54% of patients had a medical history of diabetes mellitus, 31% ischemic heart disease, and 20% congestive heart failure. At baseline, 63% of patients reported taking four or more antihypertensive medications.

TRYVIO 12.5 mg was statistically superior to placebo in reducing SiSBP at Week 4 (part 1). The treatment effect was consistent for sitting diastolic BP (SiDBP). 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. Most of the BP-lowering effect occurred within the first two weeks of treatment with TRYVIO. TRYVIO is not approved for use at a 25 mg dose. The efficacy for the 25 mg aprocitentan dose as measured in the primary end point of change in sitting SBP (SiSBP) from baseline to Week 4 in part 1, was similar to the 12.5 mg dose and thus aprocitentan 12.5 mg is the approved dose in the US.

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).

The most frequently reported adverse reactions to TRYVIO during the 4-week double-blind placebo-controlled treatment period (part 1) of the PRECISION study were edema/fluid retention and anemia. During the initial 4-week double-blind placebo-controlled treatment period (part 1), 0.8% of patients experienced an adverse reaction of hypersensitivity (i.e., rash, erythema, allergic edema) on TRYVIO compared to no reports in patients treated with placebo. One patient experienced allergic dermatitis requiring hospitalization while receiving aprocitentan 25 mg. TRYVIO is contraindicated in patients who are hypersensitive to aprocitentan or any of its excipients. Use of TRYVIO is contraindicated in pregnancy.

Lowering BP reduces the risk of fatal and non-fatal cardiovascular events, primarily strokes and myocardial infarctions. These benefits have been seen in controlled trials of antihypertensive drugs from a wide variety of pharmacologic classes. There are no controlled trials demonstrating reduction of risk of these events with TRYVIO.

Current status in the US

In March 2024, TRYVIO™ (aprocitentan) 12.5 mg was approved by the US FDA 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. For more information see the Full Prescribing Information including BOXED Warning (PI and Medication Guide). The company is preparing to make TRYVIO available during the second half of 2024.

TRYVIO™ (aprocitentan) 12.5mg tablets

Current status in the EU

A marketing authorisation application (MAA) for aprocitentan was submitted to the EMA at the end of January 2023

Milestones

2024 Approved as TRYVIO (aprocitentan) by the US FDA
2023 MAA submitted to the EMA
2022 Phase 3 data simultaneously presented as late-breaker at AHA and published in The Lancet
2022 Phase 3 study successful
2018 Phase 3 study initiated
2017 Positive results for the dose-response study
2015 Initiation of Phase 2 dose-response study
2014 Initiation of Phase 1 clinical program

Key scientific literature

- Schlaich M, et al. The Lancet 2022; Nov 7 online.
- Iglarz M, et al. Clin Sci 2010; 119:453-63
- Clozel M. Can J Physiol Pharmacol 2022, Mar 4 online.
- Verweij P., et al. Hypertension. 2020; 75:956–965
- Danaietash P et al. J Clin Hypertension 2022; 24(7):804-813

Lucerastat

Lucerastat is an oral inhibitor of glucosylceramide synthase, offering a potential new treatment approach for all patients living with Fabry disease, irrespective of the mutation type of the GLA gene.

Fabry disease is a rare genetic, lysosomal storage disorder. It is caused by mutations in the GLA gene, leading to a deficiency or dysfunction of alpha-galactosidase A (alpha Gal A), an enzyme that normally breaks down a fatty substance known as globotriaosylceramide (Gb3) in the cells of the body. Over time, this results in an accumulation of Gb3 deposits throughout the body, leading to progressive pathophysiology in the cardiovascular system, the nervous system, and organs including the kidneys, heart, skin, ears, and eyes.

Fabry disease affects a patient's life expectancy and quality of life. Since most symptoms are non-specific, 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.

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Lucerastat, an oral inhibitor of glucosylceramide synthase (GCS), acts by reducing the synthesis of the lipid Gb3 as opposed to supporting the breakdown of Gb3, thus reducing damaging build-up. This is known as Substrate Reduction Therapy (SRT).

Global registration study

MODIFY was a Phase 3 study to determine the efficacy and safety of lucerastat oral monotherapy in adult patients with Fabry disease. 118 patients were randomized in a 2:1 ratio to receive either lucerastat (80 patients) or placebo (38 patients). At the end of the 6-month double-blind period, 107 patients entered an ongoing open label extension (OLE) study, which aims 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 48 months.

In October 2021, the company reported that lucerastat 1000 mg b.i.d. did not meet the primary endpoint of reducing neuropathic pain during 6 months of treatment versus placebo. However, observations were made 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. After 6 months of treatment, lucerastat demonstrated a substantial reduction in levels of the Fabry disease biomarker plasma Gb3. A nominally significant ($p<0.0001$) difference was observed between lucerastat and placebo in the change in plasma Gb3 from baseline to month 6, with a decrease of approximately 50% in plasma Gb3 in the lucerastat treatment group, compared to an increase of 12% in the placebo group.

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. No clinically meaningful changes in vital signs or ECGs or marked laboratory abnormalities were observed. Two patients in each group (lucerastat 2.5%; placebo 5.4%) discontinued treatment due to adverse events. Serious adverse events were reported in 5 patients (6.3%) in the lucerastat group and in 1 patient (2.7%) in the placebo group.

Lucerastat for Fabry disease has received orphan drug designation in the US and the EU and is under review in Japan.

Current status

In October 2022, Idorsia conducted an interim analysis of the OLE study, where all patients who are continuing in this 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. The OLE study continues, and the company is consulting with health authorities about the regulatory pathway for lucerastat.

Milestones

2021 Phase 3 open label extension study continues
2021 Phase 3 study completed – primary endpoint not met
2018 Phase 3 study initiated
2016 Phase 1b study completed

Key scientific literature

- Guérard N., et al. Clin Pharmacol Ther. 2018; 103(4):703-11.
- Welford RWD., et al. Hum Mol Genet 2018; 27(19): 3392-3403

Early-stage pipeline

Idorsia has developed platforms of expertise in families of molecular targets which allow high productivity in the generation of innovative compounds potentially addressing a wide range of high unmet medical needs.

ACT-1004-1239

ACT-1004-1239 is 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, plans for a Phase 2 study in multiple sclerosis are under preparation.

Sinbaglustat

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.

ACT-1014-6470

ACT-1014-6470, a C5aR1 antagonist, is currently investigated in a Phase 1 program with the target indication in immune-mediated disorders.

ACT-777991

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

IDOR-1117-2520 is currently investigated in a Phase 1 program with the target indication in immune-mediated disorders.

IDOR-1134-2831

IDOR-1134-2831 is a synthetic glycan vaccine targeting *Clostridium difficile* infection. A clinical pharmacology program is currently in preparation to test IDOR-1134-2831 with healthy volunteers and patients. A study in patients will elucidate the potential of IDOR-1134-2831 to prevent recurrence of *C. difficile* infection (therapeutic approach) in a patient population at an early timepoint of clinical development.

Partner-led portfolio

For Idorsia, sophisticated partnerships are a way of gaining strategic access to technologies or products and fully exploiting our discovery engine and clinical pipeline. In general, we seek suitable external project partners to maximize the value of internal innovation.

Daridorexant (Sosei Heptares)

Daridorexant is licensed to Sosei Heptares in the Asia Pacific (ex-China) region and a New Drug Application is under review with the Japanese Ministry of Health, Labor and Welfare (MHLW).

Asia Pacific (ex-China) region: Australia, Brunei, Cambodia, Indonesia, Japan, Laos, Malaysia, Myanmar, New Zealand, Philippines, Singapore, South Korea, Thailand, Taiwan, and Vietnam.

Daridorexant (Simcere)

In the Greater China region (Mainland China, Hong Kong, and Macau), daridorexant is licensed to Simcere, which has initiated a Phase 3 study with daridorexant in Chinese patients.

Selatogrel and cenerimod (Viatris)

A joint development committee will oversee the development of the ongoing Phase 3 programs for selatogrel ("SOS-AMI") and cenerimod ("OPUS") through regulatory approval. Viatris has worldwide commercialization rights for both selatogrel and cenerimod (excluding, for cenerimod only, Japan, South Korea and certain countries in the Asia-Pacific region).

Daridorexant (DOD)

Idorsia supports a clinical study sponsored by the US Department of Defense (DOD) to develop new therapies to treat posttraumatic stress disorder (PTSD). The Phase 2 study will evaluate the safety, tolerability, and efficacy of potential therapeutic interventions, including daridorexant, in active-duty US service members and veterans with PTSD (NCT05422612).

ACT-709478

Neurocrine Biosciences has a global license to develop and commercialize ACT-709478 (NBI-827104), Idorsia's novel T-type calcium channel blocker. ACT-709478 is investigated in a Phase 2 open label extension (OLE) study for the treatment of pediatric subjects with Epileptic Encephalopathy with Continuous Spike-and-Wave During Sleep (CSCW), a rare form of pediatric epilepsy. 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.

Idorsia is an independent biopharmaceutical company based on science and innovation. The company is specialized in the discovery, development, and commercialization of innovative small molecules, with the aim of transforming the horizon of therapeutic options. It is headquartered in Allschwil/Basel, Switzerland and is quoted on the SIX Swiss Exchange (tickersymbol: IDIA). All trademarks are legally protected by their respective owners.

Disclaimer This fact sheet has the sole purpose to provide members of the public with general information about the activities of Idorsia. The forward-looking statements in this fact sheet are based on current expectations and belief of company management, which are subject to numerous risks and uncertainties.

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Our Innovation

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