Clinical Development

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 development of innovative compounds, challenging accepted paradigms to answer the questions that matter most. Our key assets have the potential to transform treatment in the target indications.

Drug Discovery and Clinical Development

Development Pipeline

ACT-541468

Aprocitentan

Clazosentan

Lucerastat

Cenerimod

Other Compounds

Idorsia's clinical development comprises a broad spectrum of expertise clustered within multiple departments: therapy area units, strategic development, clinical pharmacology, biostatistics and data management, drug safety, drug regulatory affairs, clinical operations and life cycle management. Life cycle cross-functional teams – under the leadership of a life cycle leader – bring expertise from preclinical development, clinical development and technical operations to the efficient development of new medicines. They steer the compounds from entry-into-human studies through to submission of the dossier to health authorities, approval and maintenance of the license during the commercialization phase until loss of exclusivity of the medicine in the major markets and beyond. Idorsia's clinical development manages clinical programs to the appropriate scientific, medical and operational standards to generate the information required by health authorities worldwide.

Development Pipeline

Compound	Mechanism of Action	Target Indication	Status
ACT-541468	Dual orexin receptor antagonist	Insomnia	Phase 3
Aprocitentan*	Dual Endothelin receptor antagonist	Resistant hypertension management	Phase 3
Clazosentan**	Endothelin receptor antagonist	Vasospasm associated with aneurysmal subarachnoid hemorrhage (aSAH)	Phase 3
Lucerastat	Glucosylceramide synthase (GCS) inhibitor	Fabry disease	Phase 3
Cenerimod	$S1P_1$ receptor modulator	Systemic lupus erythematosus	Phase 2
Selatogrel	P2Y12 receptor antagonist	Acute coronary syndrome (ACS)	Phase 2
ACT-774312	CRTH2 receptor antagonist	Nasal polyposis	Phase 2
ACT-519276	GBA2/GCS inhibitor	Orphan CNS disease	Phase 1
ACT-539313	Selective orexin 1 receptor antagonist	Anxiety	Phase 1
ACT-709478	T-type calcium channel blocker	Epilepsy	Phase 1

* In collaboration with Janssen Biotech to jointly develop and solely commercialize aprocitentan worldwide.
** Market registration trials are being conducted in Japan.

Drug Discovery and Clinical Development

> **Development Pipeline**

ACT-541468

Aprocitentan

Clazosentan

Lucerastat

Cenerimod

Other Compounds

ACT-541468

ACT-541468 is a dual orexin receptor antagonist (DORA) for the treatment of insomnia. It has potential to deliver fast onset of sleep and a duration of action not exceeding a normal night, while preserving natural sleep architecture.

Drug Discovery and Clinical Development

Development Pipeline

> **ACT-541468**

Aprocitentan

Clazosentan

Lucerastat

Cenerimod

Other Compounds

Insomnia – the most commonly reported sleep disorder worldwide – is defined as a combination of dissatisfaction with sleep and a significant negative impact on daytime functioning. Dissatisfaction with sleep refers to difficulty in initiating and/or maintaining sleep on at least three nights per week for at least three months, despite adequate opportunity to sleep.

Insomnia is now recognized as a condition that requires clinical attention, regardless of any other medical problems the patient might have. Insomnia is often underdiagnosed and undertreated. It is estimated that around 70% of people with persistent insomnia never seek medical help.

Current status

In June 2018, Idorsia initiated a Phase 3 registration program with ACT-541468 for the treatment of adult and elderly patients with insomnia. The registration program comprises two confirmatory studies together with a long-term extension study, which will recruit a total of 1,800 patients with insomnia at over 160 sites across 18 countries. As insomnia often presents later in life, around 40% of the recruited population will be aged 65 years or older. The confirmatory polysomnography studies will investigate three doses (10 mg, 25 mg, and 50 mg), on objective and subjective sleep and daytime functioning parameters. Patients will be treated for three months in the two trials, with the opportunity to continue treatment in a 40-week extension study.

The Phase 3 program aims to confirm the positive results observed in the comprehensive Phase 2 clinical program and was developed in consultation with health authorities and is expected to run for around 2 years. In addition, a comprehensive clinical pharmacology program is to be conducted in parallel.

Available clinical data

The safety and efficacy of ACT-541468 in adult and elderly patients with insomnia was evaluated in a comprehensive Phase 2 program, comprising two studies and included zolpidem as an active reference. Both studies showed the desired effect on sleep maintenance and onset, with a significant dose-response relationship; treatment was generally well tolerated.

The first Phase 2 study in 360 adults (ranging from 18 to 64 years), with a treatment duration of 4 weeks, showed a significant dose dependent decrease in WASO at Day 1 & 2 (average decrease of wake-time after sleep onset from baseline on the first 2 nights of treatment, measured by polysomnography). In addition, ACT-541468 significantly decreased LPS (latency to persistent sleep) in a dose-dependent manner. Treatment with ACT-541468 was generally well tolerated. There were no reports of serious adverse events related to ACT-541468.

The positive readouts of the second Phase 2 study, conducted in 58 elderly patients (ranging from 65 to 85 years), were consistent with the efficacy and safety profile of ACT-541468 for this patient

population. The results of this study also showed a significant decrease in WASO and LPS at Day 1 & 2 in a dose-dependent manner.

Data from an extensive Phase 1 program showed an optimal pharmacokinetic and pharmacodynamic profile for a sleep medication, together with excellent safety and tolerability.

Milestones

2018 Initiation of Phase 3 registration program

2017 Completion of Phase 2 clinical program

2014 Initiation of Phase 1 clinical program

Key scientific literature

– Brisbare-Roch C. et al. Nat Med. 13(2):150-5; 2007.

– Hoever P et al. Clin Pharmacol Ther Clin Pharmacol Ther. 2012; 91(6); 975-985.

– Roth T. 2007;3 Suppl 5:S7-10.

Aprocitentan

Aprocitentan is an orally active dual endothelin (ET) receptor antagonist, which is being investigated for patients whose hypertension is uncontrolled despite the use of three or more antihypertensive drugs.

Drug Discovery and Clinical Development

Development Pipeline

ACT-541468

> **Aprocitentan**

Clazosentan

Lucerastat

Cenerimod

Other Compounds

Hypertension (high blood pressure) is one of the most common medical conditions, and its prevalence continues to rise. According to a recent study, there are about 1.13 billion people living with the condition worldwide, a startling number which has almost doubled in the past 40 years. Left untreated, hypertension can lead to life-threatening conditions such as heart failure, stroke, or kidney disease.

Patients whose blood pressure remains high despite receiving at least three antihypertensive medications from different classes, including a diuretic, at maximal tolerated dose are categorized as having resistant hypertension. Patients with resistant hypertension are typically older and often suffer from obesity, sleep apnea, and/or diabetes mellitus.

Current status

In June 2018, Idorsia initiated PRECISION, a multi-center, double-blinded, placebo-controlled, randomized, parallel-group, Phase 3 study to demonstrate the antihypertensive effect of aprocitentan when added to standard of care in patients with resistant hypertension. Idorsia, in consultation with regulatory agencies, has designed a single study which will efficiently address both the short-term efficacy of aprocitentan and the durability of its effects in long-term treatment.

Patients with history of resistant hypertension will undergo a thorough screening and run-in period. This will confirm the diagnosis of resistant hypertension by excluding pseudo or apparent resistant hypertension. During the screening period, patient's background anti-hypertensive therapies will be transitioned to a standardized fixed combination of a calcium channel blocker (amlodipine), an angiotensin receptor blocker (valsartan), and a diuretic (hydrochlorothiazide).

Patients with true resistant hypertension will then be randomized to receive aprocitentan 12.5 mg, 25 mg, or placebo once-daily. The study consists of 3 sequential treatment periods. The first is a double-bind treatment period designed to demonstrate the effect of aprocitentan on blood pressure at Week 4, compared to placebo. Patients then enter a treatment period where they are treated with 25 mg aprocitentan for 32 weeks. This is followed by a double-blind, randomized withdrawal treatment period where patients will remain either on aprocitentan 25 mg or switch to placebo for 12 weeks. The latter treatment period is designed to demonstrate the durability of the blood pressure lowering effect of aprocitentan. Patients will then enter a 30-day safety follow-up period.

From the initial screened patient population, at least 600 patients will be randomized and at least 300 patients are expected to complete the study. The study will be conducted in approximately 100 sites in around 20 countries.

Collaboration Agreement with Janssen Biotech

In December 2017, Janssen Biotech, Inc. entered into a collaboration agreement with Idorsia to jointly develop and commercialize aprocitentan and any of its derivative compounds or products. Both

Drug Discovery and Clinical Development

Development Pipeline

ACT-541468

> **Aprocitentan**

Clazosentan

Lucerastat

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Other Compounds

parties have joint development rights over aprocitentan. Idorsia will oversee the Phase 3 development and regulatory submission. The costs will be shared equally between both partners. Janssen will oversee the Phase 3 development and submission for any additional indications.

Available clinical data

In a Phase 2 study that evaluated the efficacy, safety and tolerability of a once-a-day oral regimen of four dose levels of aprocitentan in patients with essential hypertension, 490 patients were randomized to receive either aprocitentan 5, 10, 25, 50 mg, placebo, or lisinopril 20 mg once daily. The results showed a mean reduction from baseline in diastolic blood pressure between 6.3 and 12.0 mmHg in a statistically significant dose-dependent manner for the aprocitentan groups versus a decrease of 4.9 mmHg in the placebo group and a decrease of 8.4 mmHg in the lisinopril group (in the per-protocol population comprised of 410 patients). Systolic blood pressure reductions ranged from 10.3 to 18.5 mmHg in a statistically significant dose-dependent manner in the aprocitentan groups and were 7.7 and 12.8 mmHg in the placebo and lisinopril groups, respectively. These findings were confirmed in all randomized patients (Intent-to-Treat principle) and by 24 hours Ambulatory Blood Pressure Monitoring.

The safety population included 327 patients in the aprocitentan groups, 82 patients in the placebo group and 81 in the lisinopril group. Aprocitentan was well tolerated across all four doses in this patient population. Discontinuation from study treatment due to an adverse event ranged between 1.2% and 3.7% for the aprocitentan groups versus 6.1% in the placebo group and 3.7% in the lisinopril group. The overall frequency of adverse events was similar to those observed in the placebo group. In this study, there were two cases of increased liver enzymes above three times the upper limit of the normal range, one in the placebo and one in the aprocitentan 5 mg group. Four cases of peripheral edema were observed, two in the aprocitentan 25 mg group and two in the aprocitentan 50 mg group. Mean body weight remained unchanged from baseline in the aprocitentan 5, and 10 mg groups, increased by 0.4 kg in the aprocitentan 25 and 50 mg groups, and by 0.3 kg in the placebo group and decreased by 0.3 kg on lisinopril. There was an expected dose-related decrease from baseline in the hemoglobin concentration in the aprocitentan groups (ranging from 1.3 to 6.7 g/L) versus increases of 2.2 and 0.1 g/L in the placebo and lisinopril groups, respectively.

Milestones

2018 Phase 3 study initiated
2017 Collaboration agreement with Janssen Biotech
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

– Iglarz M, et al. Clin Sci 2010; 119:453-63

Clazosentan

Clazosentan is a selective endothelin (ETA) receptor antagonist being developed as an intravenous infusion for the prevention of clinical deterioration due to vasospasm-related delayed cerebral ischemia in patients following an aneurysmal subarachnoid hemorrhage.

Drug Discovery and Clinical Development

Development Pipeline

ACT-541468

Aprocitentan

> **Clazosentan**

Lucerastat

Cenerimod

Other Compounds

Aneurysmal subarachnoid hemorrhage (aSAH) is a sudden life-threatening bleeding occurring in the subarachnoid space. It is caused by the rupture of an aneurysm – a weak, bulging spot on the wall of a cerebral artery. Emergency surgical repair (endovascular coiling or microsurgical clipping) is required to stop the hemorrhage.

The bleeding and the release of a vasoconstrictor (endothelin) by the neighboring vascular endothelium, contributes to many patients experiencing cerebral vasospasm (constriction of arteries in the brain) between 4 and 14 days after aSAH securing. This diminishes blood flow to the brain, and about one third of patients consequently experience worsening of their neurological condition.

Today, patients with vasospasm are typically treated with hemodynamic therapy (the administration of fluids and agents to increase blood pressure) or a more invasive neurovascular intervention, such as balloon angioplasty or intra-arterial administration of vasodilators.

Current status: Global registration study

In February 2019, Idorsia initiated REACT, a prospective multicenter, double-blind, randomized, placebo-controlled, parallel-group, Phase 3 study to investigate the efficacy and safety of clazosentan for the prevention of clinical deterioration due to vasospasm-related delayed cerebral ischemia in adult patients following aSAH.

Approximately 400 patients – treated either with microsurgical clipping or endovascular coiling – are expected to be enrolled at 100 sites across 15 countries. Patients will be randomized to receive either clazosentan (15 mg/hr) or placebo for a treatment period of up to 14 days. The study is expected to run for over two years.

REACT will enroll aSAH patients identified as being at high risk of developing delayed ischemic neurological deficit because of high-volume hemorrhage, as assessed by CT scan on hospital admission. Patients experiencing asymptomatic moderate to severe cerebral vasospasm within 14 days of aSAH may also be included.

Available clinical data

Previously, clazosentan was investigated for the prevention of angiographic vasospasm in patients with aSAH in a Phase 2 study, CONSCIOUS-1. This study was followed by two Phase 3 studies, CONSCIOUS-2 and CONSCIOUS-3, to assess the effect of clazosentan on the incidence of cerebral vasospasm-related morbidity and all-cause mortality. The dose of clazosentan (5 mg/h) used in CONSCIOUS-2 did not allow a statistically significant treatment effect to be observed, resulting in the premature termination of CONSCIOUS-3. However, exploratory analysis of the data collected in CONSCIOUS-3 showed that a higher dose of clazosentan, i.e. 15 mg/h, significantly reduced cerebral vasospasm-related morbidity and all-cause mortality, with a 44% relative risk reduction (p=0.0074). This dose also significantly reduced the incidence of delayed ischemic neurological deficit with a 54% relative risk reduction (p=0.0038). In addition, clazosentan reduced the need for rescue therapy for vasospasm. Clazosentan did not improve long-term clinical outcome.

More recently, a pilot study evaluating the early effect of clazosentan on reversing

established cerebral vasospasm in large proximal cerebral artery segments at 3 hours post-initiation, showed that clazosentan acts on some large brain arteries but the real benefit is in the effect on smaller arteries not accessible to endo-arterial therapy. A post-hoc analysis of the effect of clazosentan on reversing established cerebral vasospasm in the entire cerebral vasculature, including smaller distal vessel segments and the cerebellar arteries, showed a clearly visible improvement in vessel diameter at 3 hours, in a significant proportion of patients. Detailed results will be provided in scientific communication.

Those studies have also established an extensive safety profile with over 1,800 patients treated.

Current status: Japanese registration program

A Phase 2 study in Japanese and Korean patients showed that 10 mg/hr clazosentan significantly reduced vasospasm and vasospasm-related morbidity and mortality events. On that basis, a registration program was initiated with clazosentan in Japan in May 2016. aSAH is a significant problem in Japan with a prevalence around twice as high as in the rest of the world.

The program consists of two prospective, multicenter, double-blind, randomized, placebo-controlled studies to assess the efficacy and safety of clazosentan in reducing vasospasm and vasospasm-related morbidity and mortality events in adult patients with aSAH. Patients are randomized to either 10 mg/hr clazosentan or placebo for up to a cumulative maximum of 15 days following the onset of aSAH. The two studies follow the same study design, with one enrolling patients whose aSAH was treated by surgical clipping and the other enrolling patients treated for aSAH by endovascular coiling. The recruitment is ongoing, and results are expected in the first half of 2020, with a rapid turnaround for filing of the dossier with the Japanese health authority.

Milestones

2019 Global Phase 3 study initiated
2016 Japanese Phase 3 program initiated
2006 Orphan status granted in US
2003 Orphan status granted in Europe

Key scientific literature

- Fujimura, et al. Cerebrovasc Dis 2017;44:59–67.
- Macdonald R L, et al. Stroke. 2012; 43(6):1463-9.
- Macdonald R L, et al. The Lancet. Neurology, 2011; 10(7):618-625.
- Macdonald R L, et al. Stroke 2008; 39:3015–3021.
- Vajkoczy P, et al. Journal of Neurosurgery 2005; 103:9-17.
- Roux S. et al. J Pharmacol Exp Ther 1997; 283:1110-1118.

Lucerastat

Lucerastat is an oral monotherapy offering a new treatment approach for patients living with Fabry disease.

Drug Discovery and Clinical Development

Development Pipeline

ACT-541468

Aprocitentan

Clazosentan

> **Lucerastat**

Cenerimod

Other Compounds

Fabry disease is a rare, life-threatening, genetic disorder involving 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 may result in a buildup of Gb3 deposits throughout the body, particularly in the kidneys, heart and nervous system.

The symptoms range from neuropathic pain (primarily in the hands and feet) and stomach, skin and eye problems, to hypertension, progressive kidney damage, cardiomyopathy and stroke. Since the 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.

New therapeutic options are needed to treat the underlying mechanism of the disease and provide symptomatic relief.

Current status

In May 2018, Idorsia initiated MODIFY, a multicenter, double-blind, randomized, placebo-controlled, parallelgroup study to determine the efficacy and safety of lucerastat oral monotherapy in adult patients with Fabry disease. The study aims to determine the effects of treatment on neuropathic pain over a 6-month period, as measured by Idorsia's Fabry disease neuropathic pain instrument (validated by health authorities). At the end of the double-blind period, patients will have the option of entering in an open-label extension study. Approximately 108 patients are expected to be enrolled and randomized to lucerastat or placebo in a 2:1 ratio. The study is expected to run for around 20 months.

Lucerastat for Fabry disease has received Orphan Drug designation in the US and in the EU and at the beginning of 2018, the European Medicines Agency (EMA) agreed with Idorsia's paediatric investigation plan for lucerastat for the treatment of pediatric patients with Fabry disease. Idorsia has already initiated activities according to the agreed plan.

Available clinical data

Idorsia preclinical research with a mouse model of Fabry disease has shown that glucosylceramide synthase inhibition with lucerastat reduces the accumulation of Gb3 in kidney and certain nerve endings. Furthermore, Idorsia has shown that lucerastat lowers Gb3 in cultured cells from patients with Fabry disease of both sexes harboring different GLA genetic mutation types.

In an exploratory study in patients with Fabry disease, treatment with lucerastat in addition to ERT demonstrated a marked decrease in plasma levels of metabolic substrates associated with the development of the disease. In this single-

center, open-label, randomized study, 10 patients received lucerastat 1000 mg b.i.d. for 12 weeks on top of enzyme replacement therapy and four patients with Fabry disease received ERT only. A rapid decrease in plasma Gb3, a marker of Fabry disease, and its precursors was observed, demonstrating that lucerastat 1000 mg b.i.d. inhibits GCS and provides alpha-GalA substrate reduction with a fast onset in adult patients with Fabry disease on ERT. The study also demonstrated that lucerastat is well tolerated in patients with Fabry disease.

Milestones

2018 Phase 3 study initiated

2016 Phase 1b study completed

Key scientific literature

- Guérard N, et al. Clin Pharmacol Ther. 2017;103:703-11.
- Guérard N, et al. J Clin Pharmacol. 2017;57:1425-31.
- Guérard N, et al. Orphanet J Rare Dis. 2017; 12(1):9
- Welford R, et al. Molecular Genetics and Metabolism. 2017;120 (Abstract 360): S139.

Drug Discovery and Clinical Development

Development Pipeline

ACT-541468

Aprocitentan

Clazosentan

> **Lucerastat**

Cenerimod

Other Compounds

Cenerimod

Cenerimod is a selective sphingosine-1-phosphate receptor 1 ($S1P_1$) modulator, which potentially offers a novel approach for systemic lupus erythematosus (SLE) – a disease with limited treatment options.

SLE, the most common form of lupus, is an autoimmune disease. In SLE, the body's immune system malfunctions and attacks the body's own tissues, which can affect the skin, joints, gut, blood cells, lungs, and other organs. While the cause of SLE is not fully known, T and B lymphocytes are considered the key immune system cells that contribute to the symptoms of the disease.

Cenerimod blocks the egress of lymphocytes from lymphoid organs, thereby reducing the availability of circulating effector T and B cells that can invade target organs. This pharmacodynamic effect is sustained with continued daily oral dosing and is reversible upon drug discontinuation.

Current status

In December 2018, Idorsia initiated a multiple-dose, efficacy and safety study with cenerimod for the treatment of adult patients with moderately to severely active, autoantibody-positive SLE. The multicenter, randomized, double-blind, placebo-controlled, parallel-group study will enroll around 500 patients, who will be randomized into four cenerimod treatment arms: 0.5, 1, 2, and 4 mg once-daily orally or placebo for up to 12 months. Patients will receive study treatment in addition to background SLE therapy, which will be kept as stable as possible to avoid confounding the treatment effect. The study aims to validate the appropriate dose, patient population and endpoints for further development in SLE.

In December 2017, the US FDA designated the investigation of cenerimod for the treatment of SLE as a Fast Track development program. The Fast Track designation is intended to promote communication and collaboration between the FDA and the company for drugs that treat serious conditions and fill an unmet medical need.

Available clinical data

In the Phase 1 program, cenerimod showed marked and sustained circulating lymphocyte lowering effects. A Phase 2 safety study with cenerimod, which investigated the pharmacodynamics, safety and tolerability of cenerimod in adult patients with SLE, has been conducted. The study enrolled 67 patients to receive either 0.5, 1, 2 or 4 mg/day of cenerimod over a treatment period of 12 weeks. The results of the study showed that cenerimod induces a dose-dependent, sustained reduction in circulating lymphocyte counts that was reversible after treatment discontinuation. Cenerimod was well tolerated at all dose levels. The occurrence of adverse events was similar in all five treatment groups.

Milestones

2018 Initiation of a multiple-dose efficacy and safety study

2015 Initiation of a Phase 2 safety study

Key scientific literature

– Piali L, et al. Pharmacol Res Perspect. 2017 Dec;5(6).
– Borchers AT, et al. Autoimmun Rev. 2010; 9(5):A277-87.
– Pons-Estel GJ, et al. Semin Arthritis Rheum. 2010; 39(4):257-68.
– Govoni M, et al. Lupus. 2006; 15:110-113.
– Rahman A, Isenberg DA. N Engl J Med. 2008; 358:929-39.
– Abu-Shakra M, et al. J Rheumatol 1995; 22(7):1259-64.

Other Compounds

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.

Drug Discovery and Clinical Development

Development Pipeline

ACT-541468

Aprocitentan

Clazosentan

Lucerastat

Cenerimod

> **Other Compounds**

Selatogrel, a P2Y12 receptor antagonist for acute coronary syndrome

Two Phase 2 studies with selatogrel, Idorsia's P2Y12 receptor antagonist, in patients with stable coronary artery disease and acute myocardial infarction have met their pharmacodynamic objectives of significantly inhibiting platelet aggregation. Subcutaneous administration of selatogrel has demonstrated a rapid onset of action, within 15 minutes, with the height of its effect extending over 4-8 hours, depending on the dose. The predefined extent of platelet aggregation inhibition was seen in at least 89% of the patients in both chronic and acute situations across doses. Selatogrel was safe and well tolerated in both studies and there were no treatment-emergent serious bleeds. Idorsia is now preparing for the end of Phase 2 meetings with health authorities where it will discuss a Phase 3 study.

ACT-774312, a CRTH2 antagonist for the treatment of nasal polyposis

ACT-774312 is an oral CRTH2 antagonist being developed for the treatment of nasal polyposis. Idorsia believes that there is a need for new oral therapies to treat allergic and type 2 inflammatory responses. Current evidence suggests that disease pathogenesis in nasal polyposis involves type-2 inflammatory processes and that a CRTH2 antagonist can be effective in reducing ongoing inflammation and nasal polyp burden. A proof-of-concept Phase 2 study has been initiated.

ACT-539313, a selective orexin 1 receptor antagonist (SORA) for anxiety disorders

SORA is a selective orexin 1 receptor antagonist being investigated for the potential treatment of anxiety disorders. It is a potent antagonist, brain-penetrating, and has shown anxiolytic (anxiety-inhibiting) effects after oral administration in four different preclinical models representing different sub-types of anxiety disorders. In these models, it did not induce sleep at anxiolytic doses. A Phase 1 program is ongoing.

ACT-709478, a T-type calcium channel blocker for epilepsy

ACT-709478 is a potent, brain-penetrating, selective triple calcium T-channel blocker for potential use in certain forms of generalized epilepsy. The compound has shown efficacy after oral administration in two animal models of generalized epilepsy.

ACT-519276, a GBA2/GCS inhibitor for Orphan CNS diseases

While Idorsia advances its late-stage pipeline, it also replenishes the early-stage pipeline with new compounds. At the beginning of 2018, Idorsia began Phase 1 clinical development with ACT-519276 for orphan CNS diseases.

Idorsia is an independent biopharmaceutical company based on science and innovation. The company is specialized in the discovery and development of small molecules, to transform 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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Drug Discovery and Clinical Development

Latest update:
February 2019