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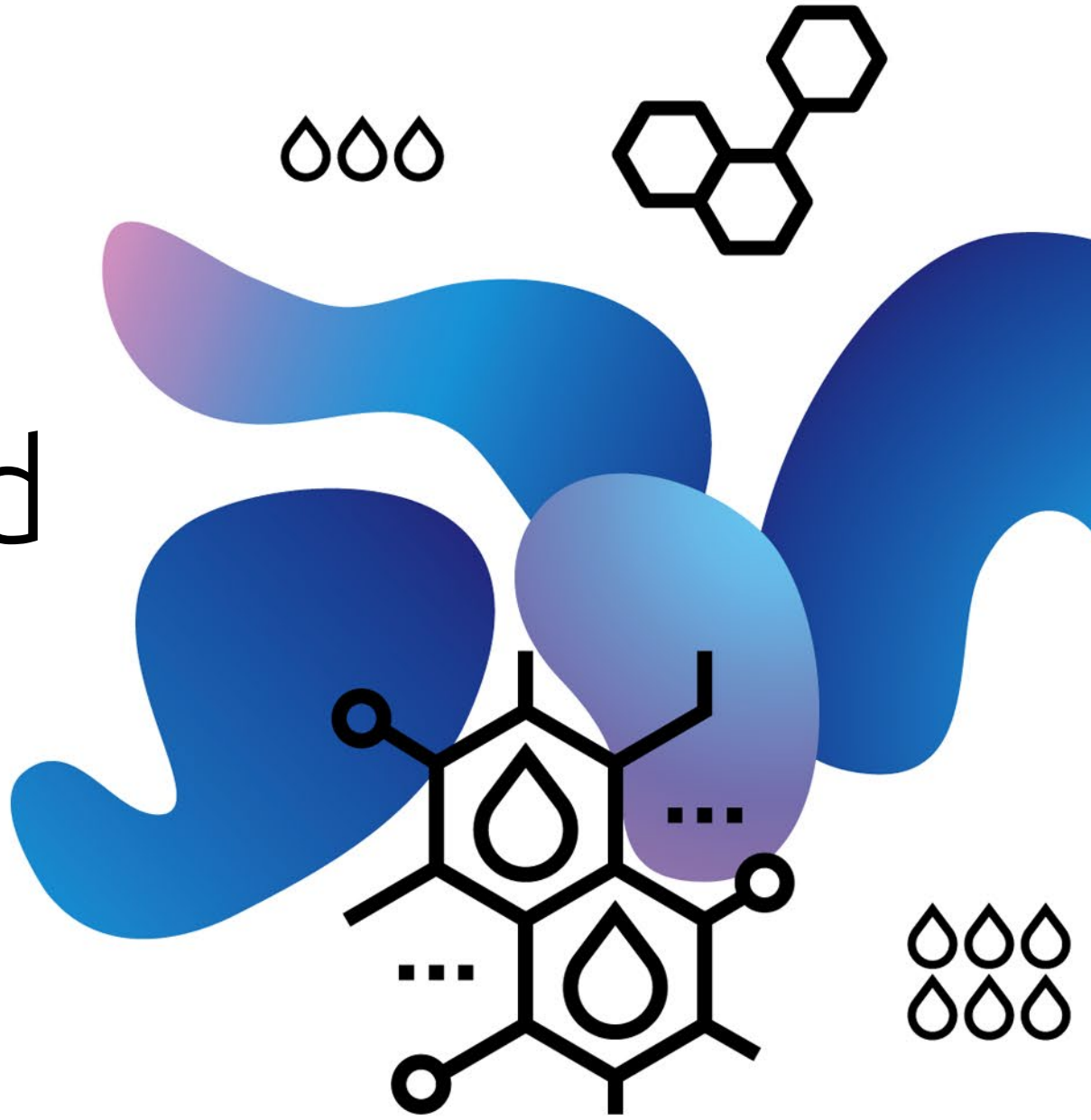
Daridorexant – Successful second pivotal study



Investor Webcast – July 2020

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“I am delighted to see the replicated effect of 25 mg of daridorexant in this large confirmatory study. The consistency of the treatment effect across both studies is remarkable.”

Guy Braunstein
Head of Global Clinical Development

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

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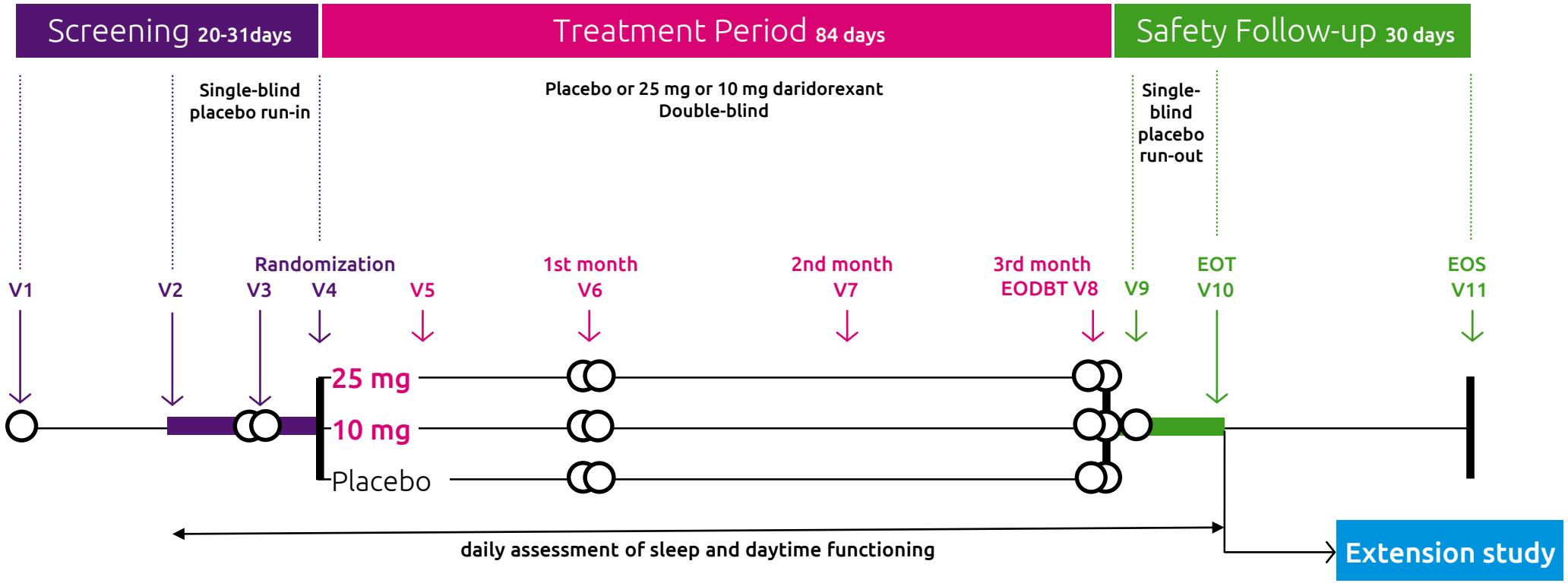
Study design

2nd pivotal study



V = site visit

= 1 polysomnography night

= 2 consecutive polysomnography nights

EODBT = End of double-blind treatment
EOT = End-of-Treatment
EOS = End-of-Study

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Study objectives

2nd pivotal study

Primary objective

- To evaluate the efficacy of 25 mg and 10 mg daridorexant on objective sleep parameters in patients with insomnia.

Secondary objective

- To evaluate the efficacy of 25 mg and 10 mg 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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Primary and secondary endpoints and analysis

2nd pivotal study

Study-wise type 1 error controlled at 0.05 (across 16 comparisons to placebo)

Primary endpoints (night)

- Wakening after sleep onset by PSG
- Latency to persistent sleep by PSG

Two dose levels

- 10 mg vs. placebo
- 25 mg vs. placebo

Secondary endpoints (night and day patients' feeling)

- Subjective total sleep time by SDQ
- Sleepiness score during the day by IDSIQ

Two assessment time points

- Month 1
- Month 3

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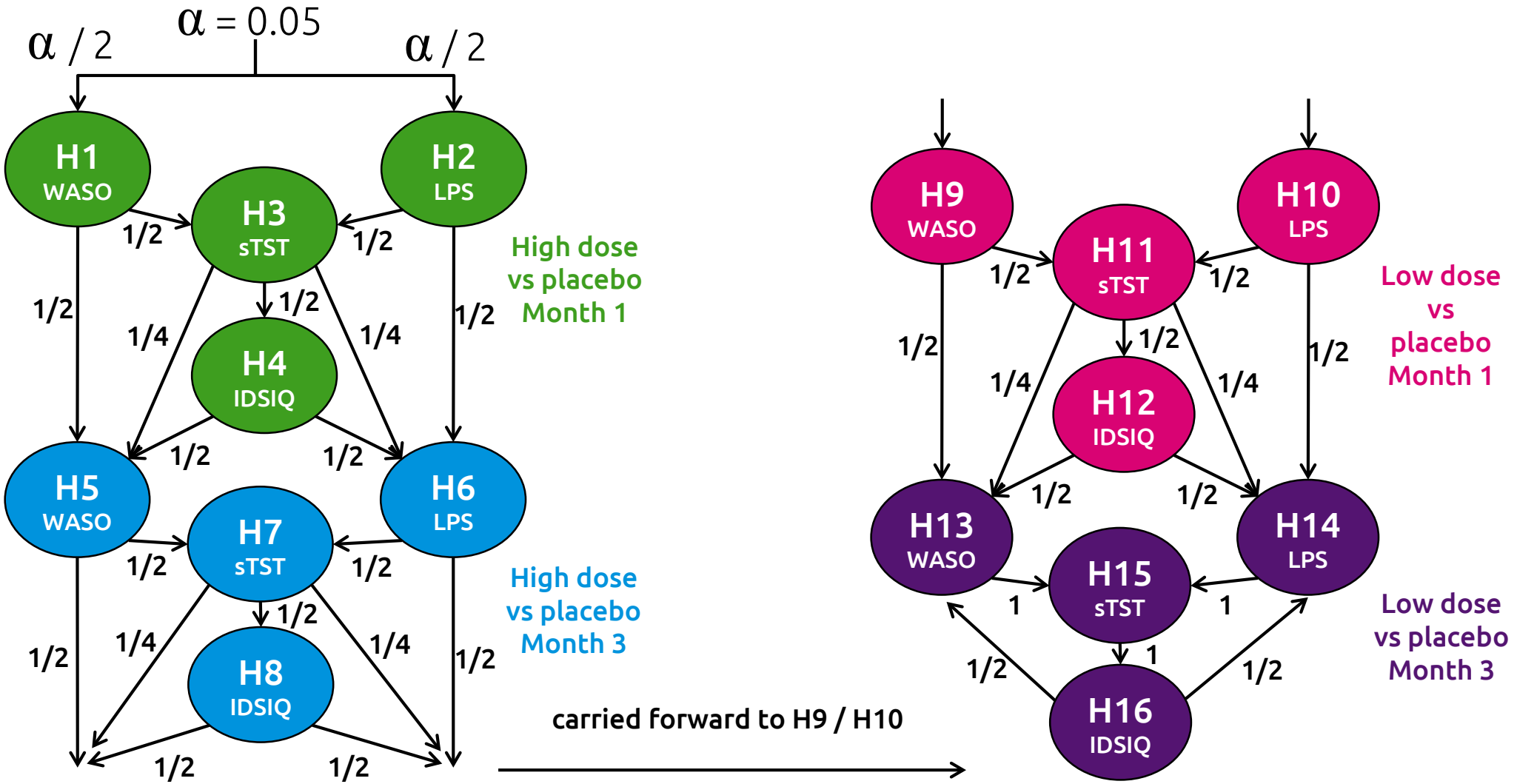
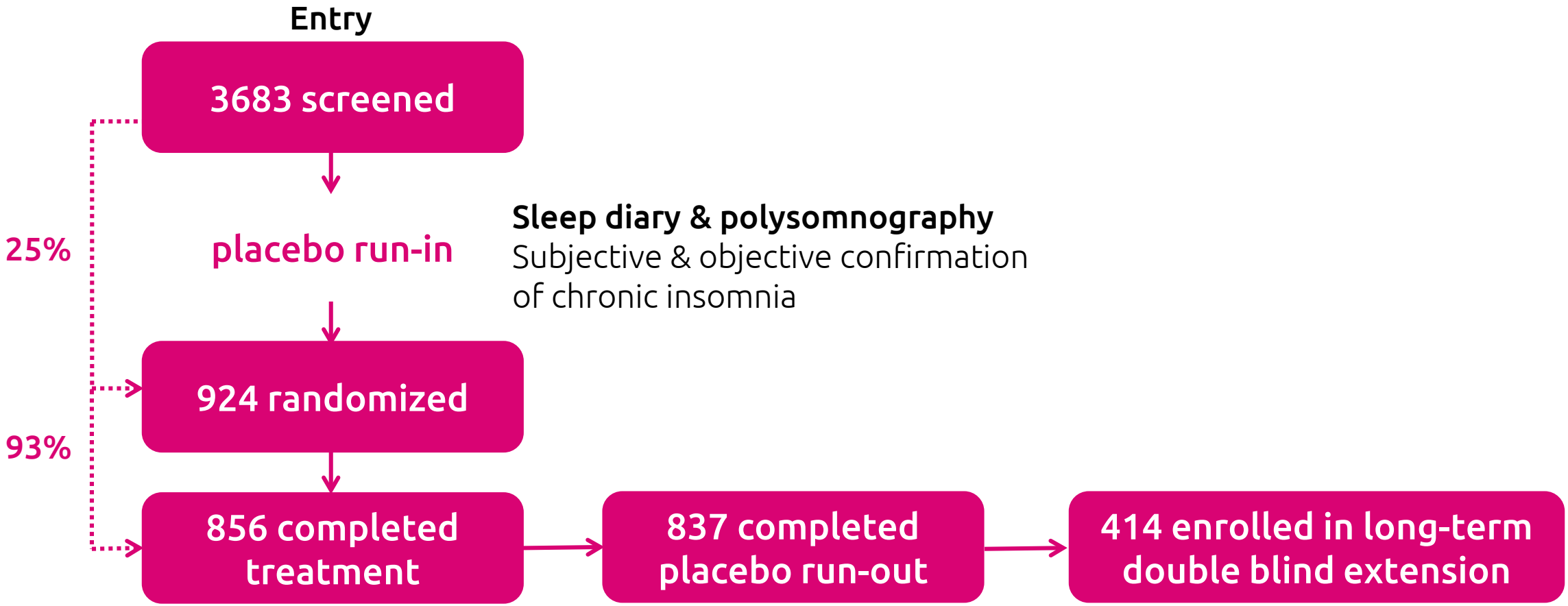
Statistical design and hypothesis testing



Study patient disposition

2nd pivotal study



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Objective sleep parameters

At 25 mg vs. placebo: highly consistent effect with that of the first pivotal study

The study demonstrated the efficacy of daridorexant in **objective sleep parameters**

1st pivotal study		50 mg vs placebo	25 mg vs placebo
At 1 month	LPS	**significant improvement**	**significant improvement**
	WASO	**significant improvement**	**significant improvement**
At 3 months	LPS	**significant improvement**	**significant improvement**
	WASO	**significant improvement**	**significant improvement**

2nd pivotal study		25 mg vs placebo	10 mg vs placebo
At 1 month	LPS	numerical improvement*	numerical improvement
	WASO	**significant improvement**	numerical improvement
At 3 months	LPS	numerical improvement*	numerical improvement
	WASO	**significant improvement**	numerical improvement

* almost reaching significant improvement

The effect observed at 1 month was **sustained** at 3 months

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Subjective sleep parameters

SDQ

The study demonstrated the efficacy of daridorexant in increasing **patient's assessed total sleep time**

1st pivotal study		50 mg vs placebo	25 mg vs placebo
At 1 month	sTST	**significant improvement**	**significant improvement**
At 3 months	sTST	**significant improvement**	**significant improvement**

2nd pivotal study		25 mg vs placebo	10 mg vs placebo
At 1 month	sTST	**significant improvement**	numerical improvement
At 3 months	sTST	**significant improvement**	numerical improvement

The effect observed at 1 month was **sustained** at 3 months

Daytime functioning

IDSIQ sleepiness domain

The study showed numerical improvement of **patient's daytime functioning**

1st pivotal study		50 mg vs placebo	25 mg vs placebo
At 1 month	IDSIQ	**significant improvement**	numerical improvement
At 3 months	IDSIQ	**significant improvement**	numerical improvement

2nd pivotal study		25 mg vs placebo	10 mg vs placebo
At 1 month	IDSIQ	numerical improvement	numerical improvement
At 3 months	IDSIQ	numerical improvement	numerical improvement

The effect observed at 1 month was **sustained** at 3 months

Overview of treatment emergent adverse events

	1st pivotal study			2nd pivotal study		
	Daridorexant		Placebo	Daridorexant		Placebo
Subjects with at least one event	50 mg n = 308 n (%)	25 mg n = 310 n (%)	n = 309 n (%)	25 mg n = 308 n (%)	10 mg n = 306 n (%)	n = 306 n (%)
AE during the double-blind study period	116 (37.7)	117 (37.7)	105 (34.0)	121 (39.3)	117 (38.2)	100 (32.7)
AEs leading to premature discontinuation of double-blind study treatment	3 (1.0)	7 (2.3)	10 (3.2)	4 (1.3)	6 (2.0)	7 (2.3)
Serious AE	3 (1.0)	2 (0.6)	7 (2.3)	3 (1.0)	3 (1.0)	4 (1.3)
AE of special interest (after blinded, independent adjudication)	2 (0.6)	4 (1.3)	1 (0.3)	7 (2.3)	2 (0.7)	1 (0.3)
AE with fatal outcome*	0	1 (0.3)	0	0	0	0

* A 78-year male patient died due to cardiac arrest in the ER after presenting with chest pain. The patient had a history of stroke, hypertension and systolic murmur and the investigator assessed the case as not related to the study drug

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Most frequent adverse events*

	1st pivotal study			2nd pivotal study		
	Daridorexant		Placebo	Daridorexant		Placebo
Preferred Term	50 mg n = 308 n (%)	25 mg n = 310 n (%)	n = 309 n (%)	25 mg n = 308 n (%)	10 mg n = 306 n (%)	n = 306 n (%)
Subjects with at least one event	117 (37.7)	116 (37.7)	105 (34.0)	121 (39.3)	117 (38.2)	100 (32.7)
Nasopharyngitis	21 (6.8)	20 (6.5)	20 (6.5)	13 (4.2)	32 (10.5)	16 (5.2)
Headache	16 (5.2)	19 (6.2)	12 (3.9)	15 (4.9)	12 (3.9)	11 (3.6)
Fatigue	7 (2.3)	7 (2.3)	2 (0.6)	11 (3.6)	7 (2.3)	2 (0.7)
Dizziness	6 (1.9)	7 (2.3)	2 (0.6)	6 (1.9)	4 (1.3)	4 (1.3)
Somnolence	5 (1.6)	11 (3.5)	6 (1.9)	10 (3.2)	6 (2.0)	4 (1.3)
Accidental overdose	4 (1.3)	8 (2.6)	5 (1.6)	4 (1.3)	4 (1.3)	1 (0.3)
Nausea	1 (0.3)	7 (2.3)	3 (1.0)	2 (0.6)	3 (1.0)	3 (1.0)

* Ordered by 50 mg daridorexant

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Clinically relevant adverse events*

	1st pivotal study			2nd pivotal study		
	Daridorexant		Placebo	Daridorexant		Placebo
Adjudicated by Independent Safety Board	50 mg n = 308 n (%)	25 mg n = 310 n (%)	n = 309 n (%)	25 mg n = 308 n (%)	10 mg n = 306 n (%)	n = 306 n (%)
Subjects with at least one event	2 (0.6)	4 (1.3)	1 (0.3)	7 (2.7)	2 (0.7)	1 (0.3)
Narcolepsy-like symptoms related to excessive daytime sleepiness	1 (0.3)	2 (0.6)	1 (0.3)	4 (1.3)	1 (0.3)	1 (0.3)
Narcolepsy-like symptoms related to complex sleep behavior including hallucinations/sleep paralysis**		3			3	
Suicidal ideation	0	0	0	1 (0.3)	1 (0.3)	0
Narcolepsy-like symptoms related to cataplexy	0	0	0	0	0	0
Other Adverse Events						
Somnolence	5 (1.6)	11 (3.5)	6 (1.9)	10 (3.2)	6 (2.0)	4 (1.3)
REM sleep abnormal	3 (1.0)	0	0	1 (0.3)	0	0
Fall	1 (0.3)	1 (0.3)	8 (2.6)	3 (1.0)	4 (1.3)	3 (1.0)
Depressed mood	1 (0.3)	1 (0.3)	0	1 (0.3)	1 (0.3)	0
Overdose	1 (0.3)	1 (0.3)	0	2 (0.6)	2 (0.7)	2 (0.7)
Syncope	1 (0.3)	0	2 (0.6)	0	1 (0.3)	0

* Ordered by 50 mg daridorexant

** treatment arm not disclosed to maintain the blinded nature of the extension study

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Two positive pivotal studies

Remarkable consistency between studies

		1st pivotal study				2nd pivotal study			
		Daridorexant 50 mg		Daridorexant 25 mg		Daridorexant 25 mg		Daridorexant 10 mg	
		1 month	3 months	1 month	3 months	1 month	3 months	1 month	3 months
Primary endpoints	**WASO**	√	√	√	√	√	√	NS*	NS*
	LPS	√	√	√	√	NS*	NS*	NS*	NS*
Secondary endpoints	**sTST**	√	√	√	√	√	√	NS*	NS*
	IDSIQ	√	√	NS*	NS*	NS*	NS*	NS*	NS*

* Numerical trend

Safety and tolerability profile consistent between both pivotal studies

- No dose-dependent treatment emergent adverse events
- Low rate of clinically relevant adverse events
- No next morning hang-over effect
- No sign of rebound insomnia
- No withdrawal symptoms

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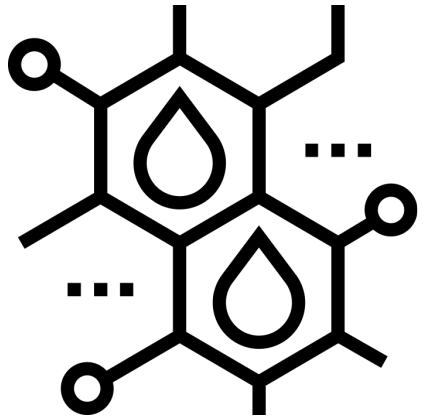
“The whole company is united in the effort to file the NDA with the US FDA around the end of this year and to prepare for a successful launch.”

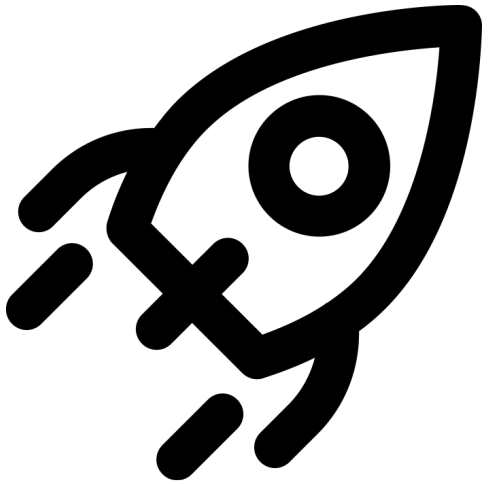
Jean-Paul Clozel
Chief Executive Officer

Roadmap to a successful launch

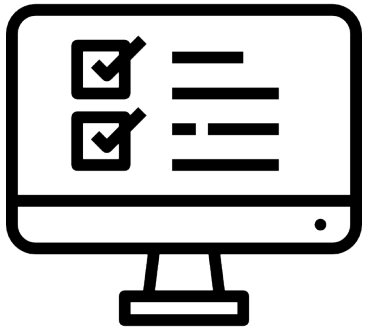
The second pivotal study confirms the findings of the first



NDA to be filed around the end of the year – meeting with FDA set for Autumn

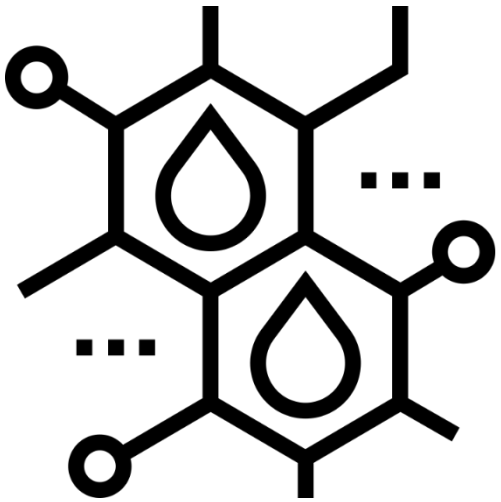


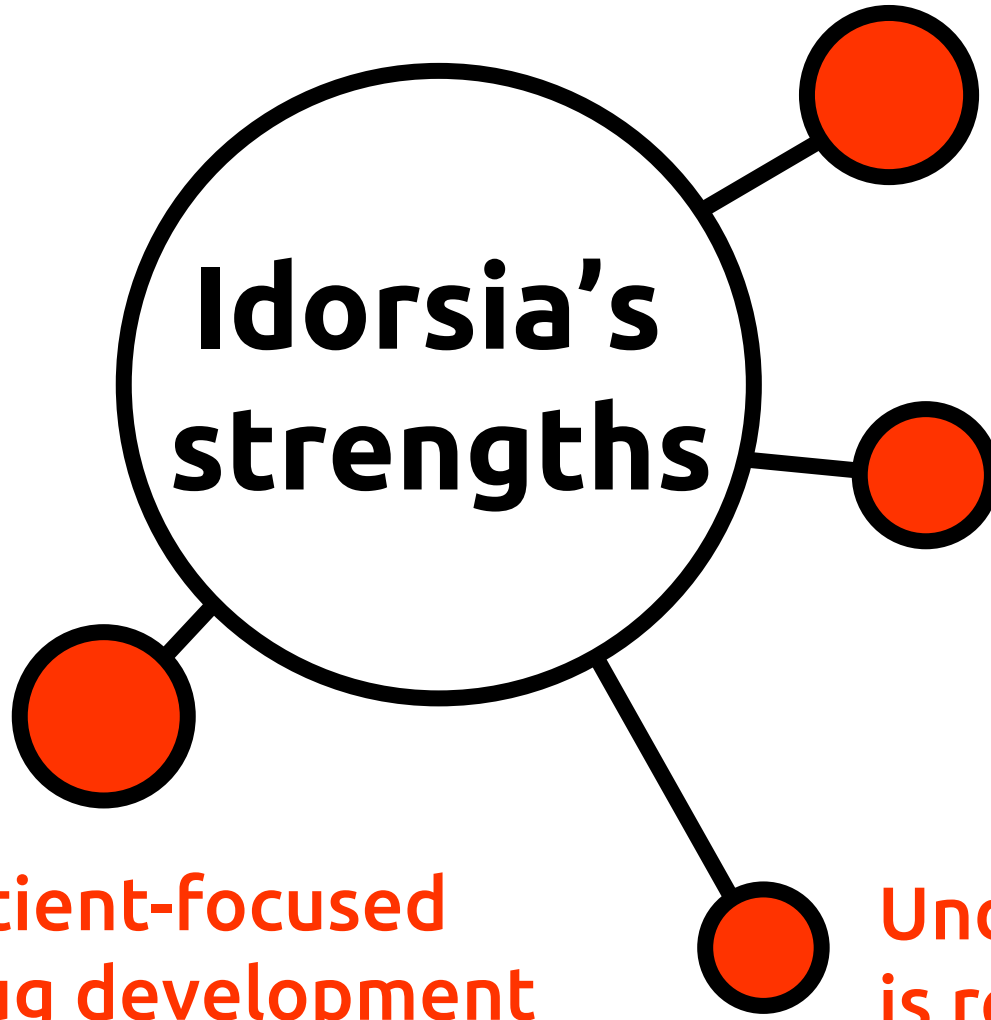
We have a unique drug for patients with insomnia



The whole company is preparing for the commercial launch of daridorexant

Daridorexant illustrates:

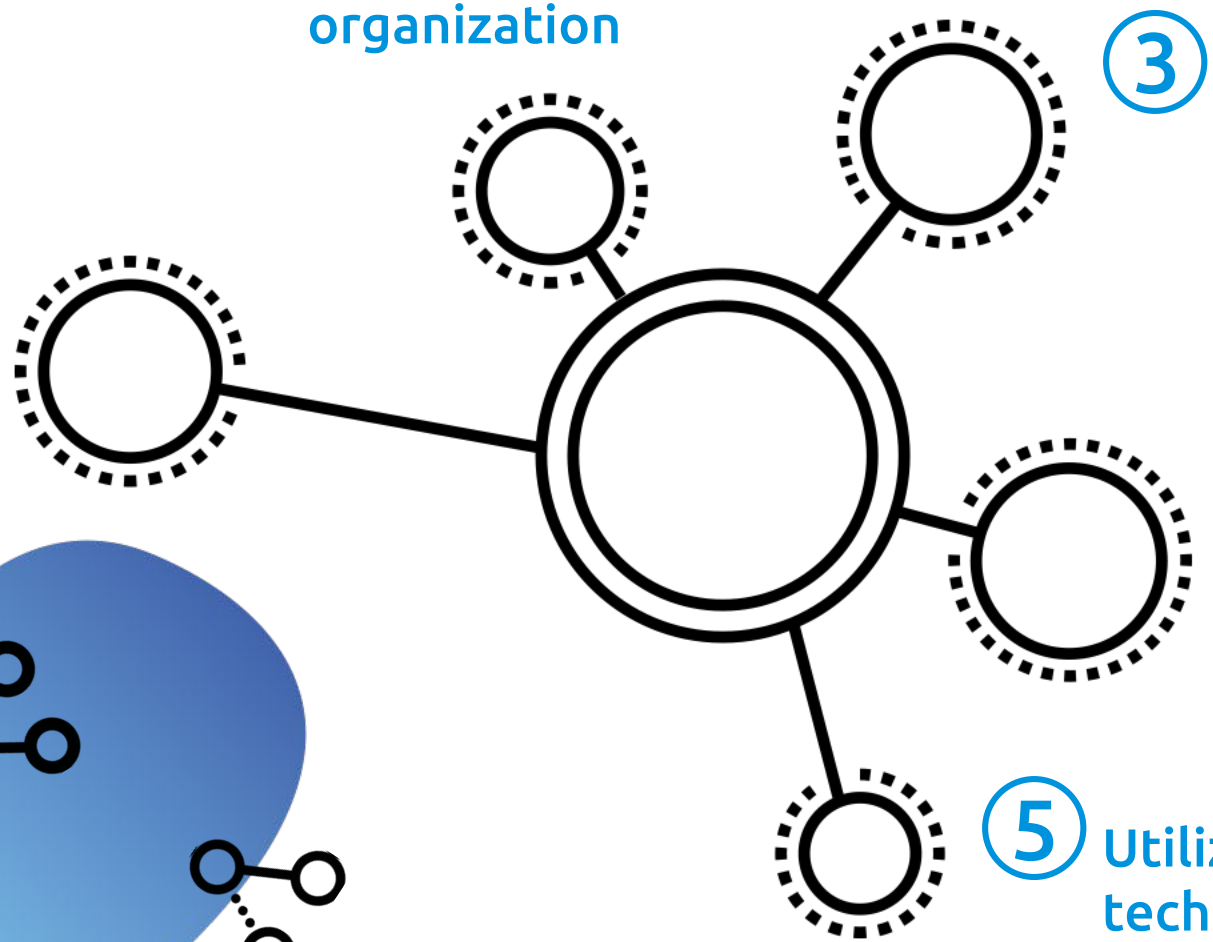




Our Strategic Priorities

Daridorexant is a key component of our strategy for value creation

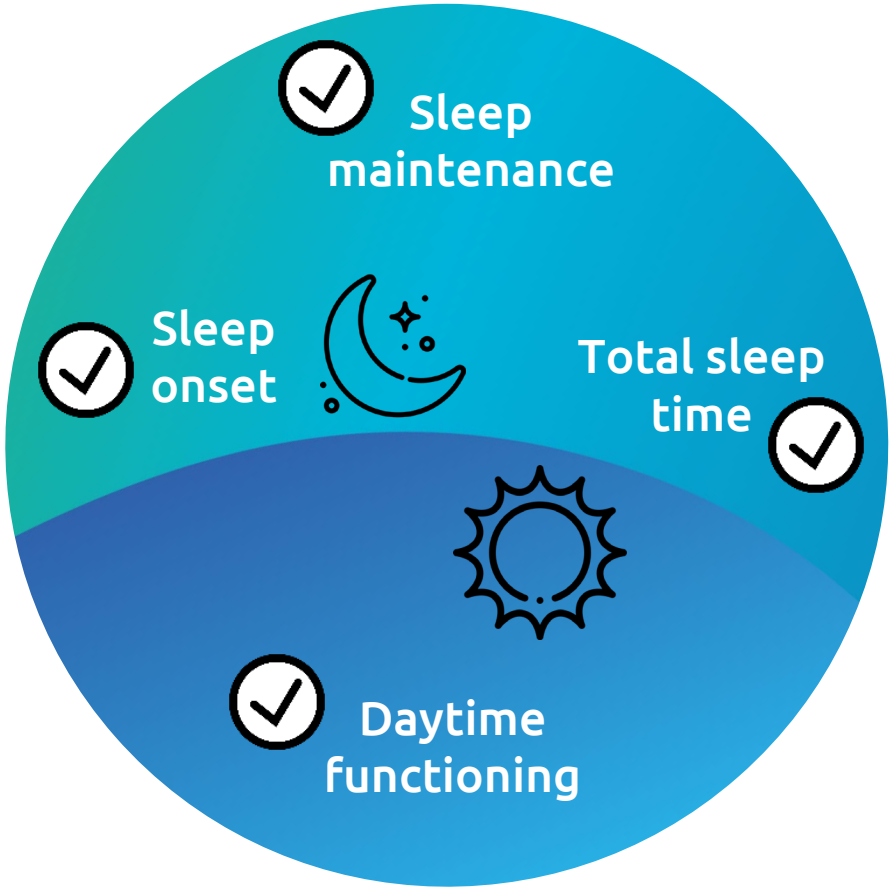
1. Deliver at least **three products to market**
2. **Build a commercial organization**
3. **Bring Idorsia to profitability** in a sustainable manner
4. Create a **pipeline with a sales potential of CHF 5 billion**
5. **Utilize state-of-the-art technologies**



Program conclusion

The program with daridorexant demonstrated statistically significant and clinically meaningful improvements at month 1 and at month 3

Efficacy during the night and the day



Safety and tolerability profile consistent between both pivotal studies

- No dose-dependent treatment emergent adverse events
- Low rate of clinically relevant adverse events
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- No sign of rebound insomnia
- No withdrawal symptoms