Financial Reporting

idonesia

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.

“This half year has been about running our studies and getting ready for the wave of results and news flow approaching soon.”

Jean-Paul Clozel
Chief Executive Officer

More in the pipeline – Promising compounds

Diversified and balanced pipeline:
CNS, cardiovascular and immunological disorders & orphan diseases

Insomnia

Daridorexant (ACT-541468)
Dual orexin receptor antagonist
Status: Phase 3

Fabry disease

Lucerastat
Glucosylceramide synthase inhibitor
Status: Phase 3

Vasospasm associated with aneurysmal subarachnoid hemorrhage

Clazosentan
Endothelin receptor antagonist
Status: Phase 3

Resistant hypertension management

Aprocitentan
Dual endothelin receptor antagonist
Status: Phase 3

In collaboration with Janssen Biotech, Inc.

Systemic lupus erythematosus

Cenerimod
$S1P_1$ receptor modulator
Status: Phase 2

Acute Coronary Syndrome

Selatogrel
P2Y12 receptor antagonist
Status: Phase 2

Nasal polyposis

ACT-774312
CRTH2 receptor antagonist
Status: Phase 2

Epilepsy

ACT-709478
T-type calcium channel blocker
Status: Phase 1

Psychiatric disorders

ACT-539313
Selective orexin 1 receptor antagonist
Status: Phase 1

Immunology / Cancer Immunotherapy

ACT-1004-1239
Status: Phase 1

Rare CNS diseases

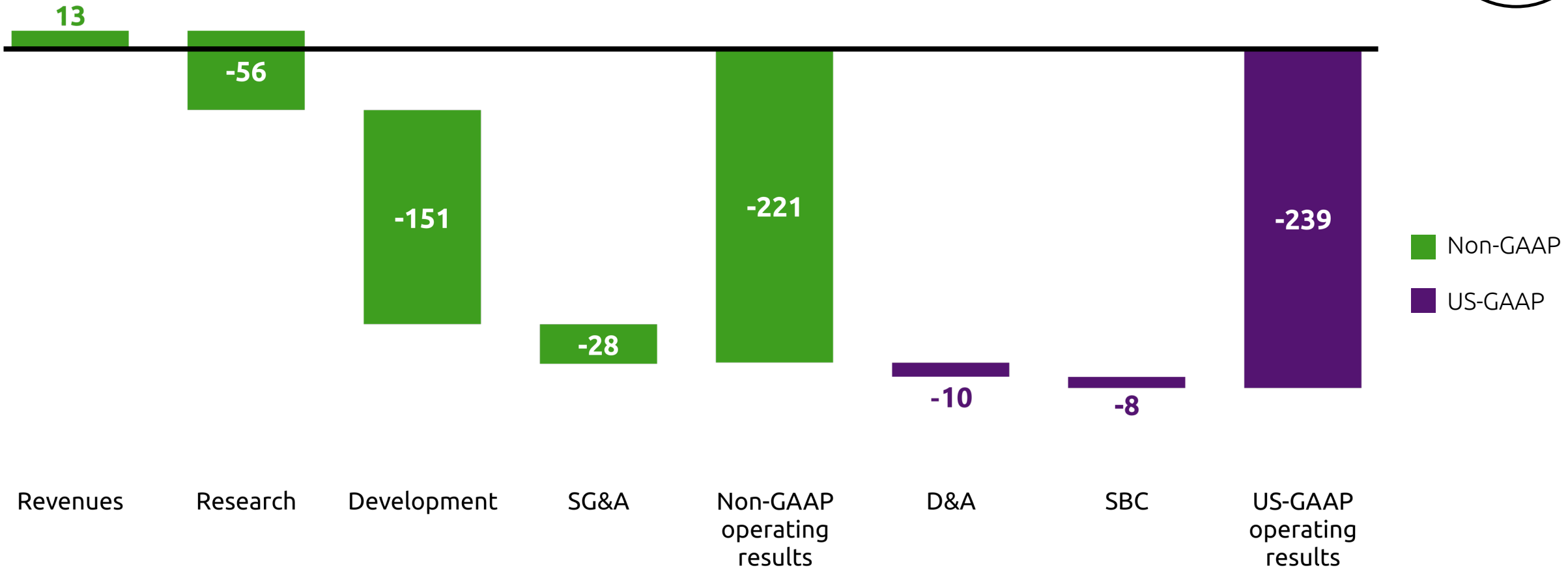
ACT-519276
GBA2/GCS inhibitor
Status: Phase 1

“We fully focus on recruiting patients for our late-stage clinical trials and shaping our commercial strategy.”

André C. Muller
Chief Financial Officer

Operating results

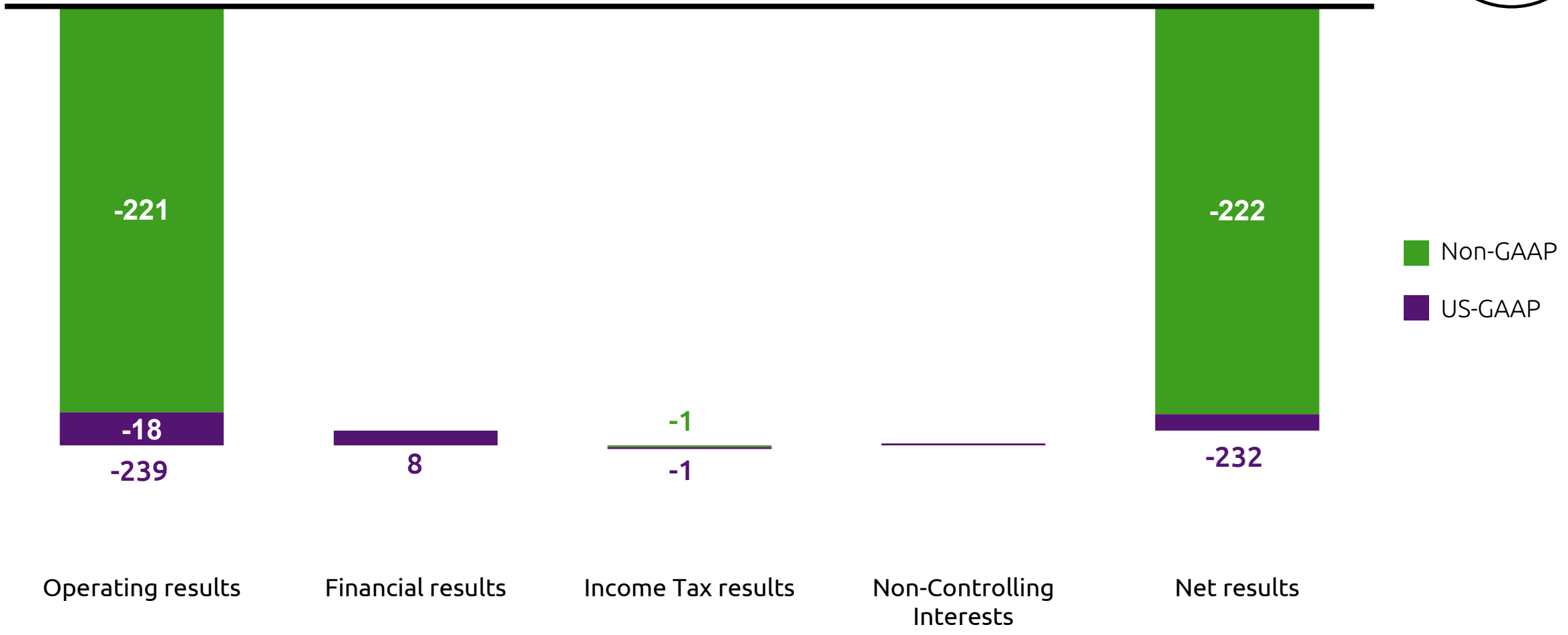
in CHF millions, rounding differences may occur



Financial results as of Jun 30, 2019

Net results

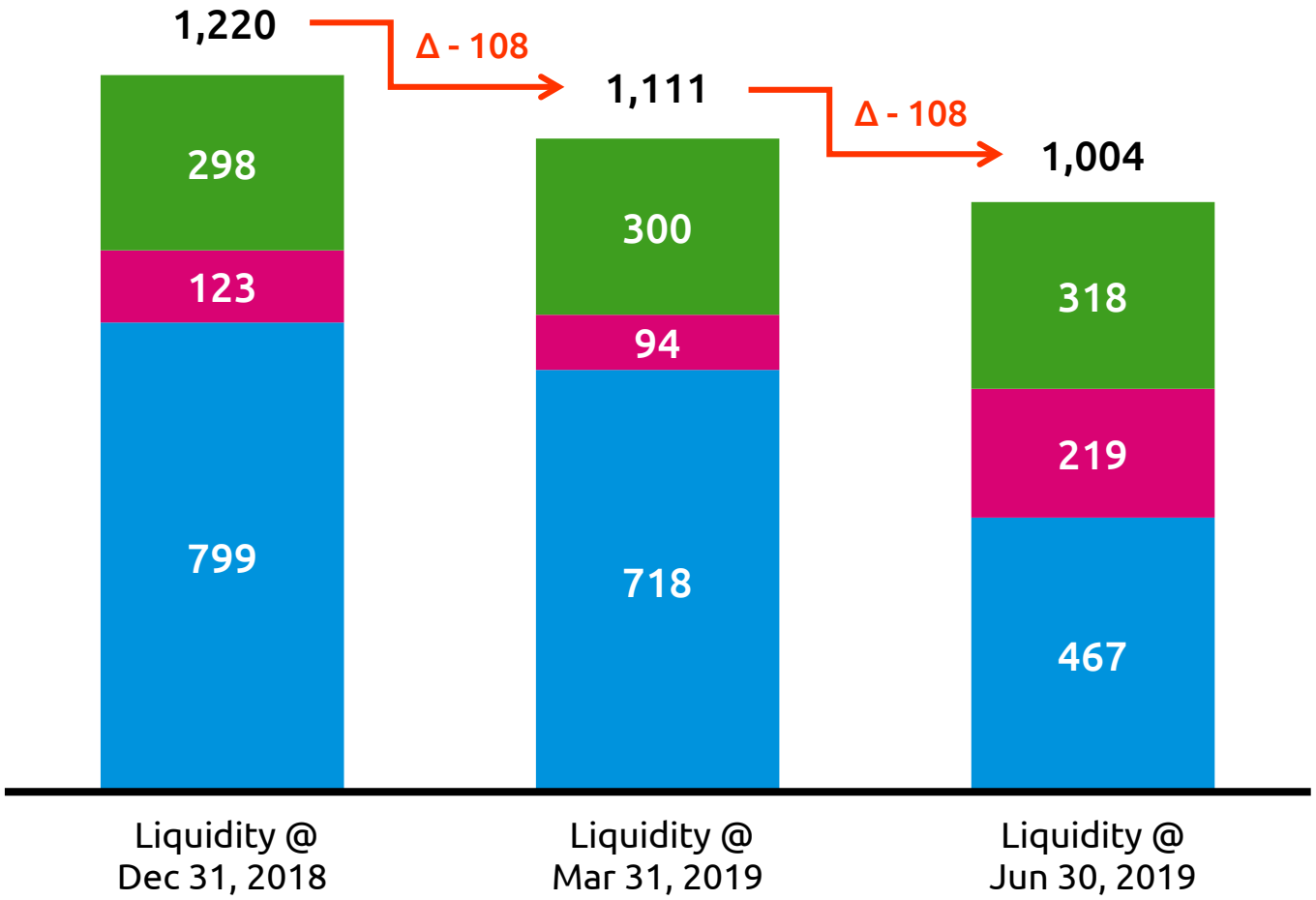
in CHF millions, rounding differences may occur



Financial results as of Jun 30, 2019

Liquidity

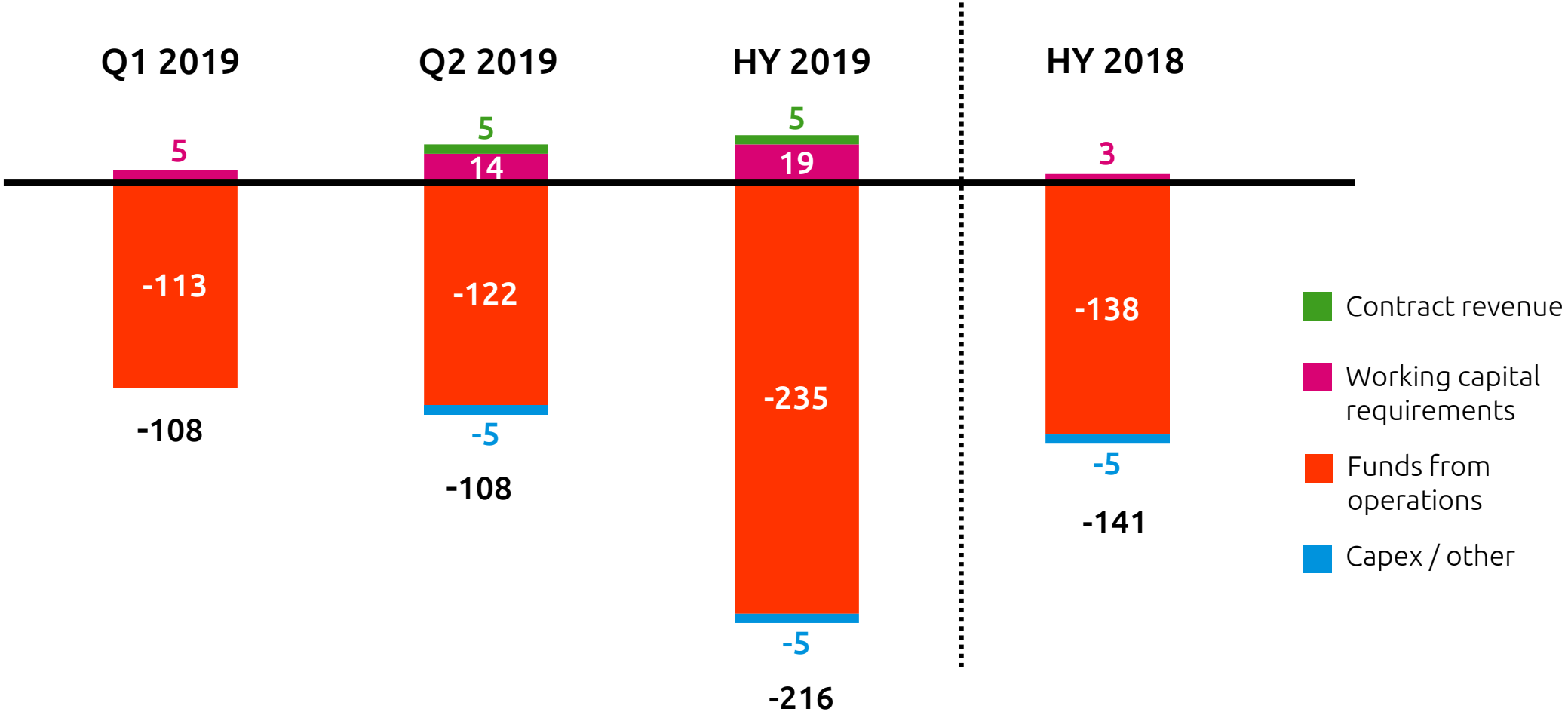
in CHF millions, rounding differences may occur



Financial results as of Jun 30, 2019

Cash flow

in CHF millions, rounding differences may occur



Financial results as of Jun 30, 2019

Financial Guidance for 2019

Unforeseen events excluded, US-GAAP operating expenses of around CHF 570 million and Non-GAAP operating expenses of around CHF 530 million (both measures excluding any potential milestone payments).

“I'm very pleased that the global Phase 3 program with daridorexant is on track to report 3-month efficacy results in the first half of 2020.”

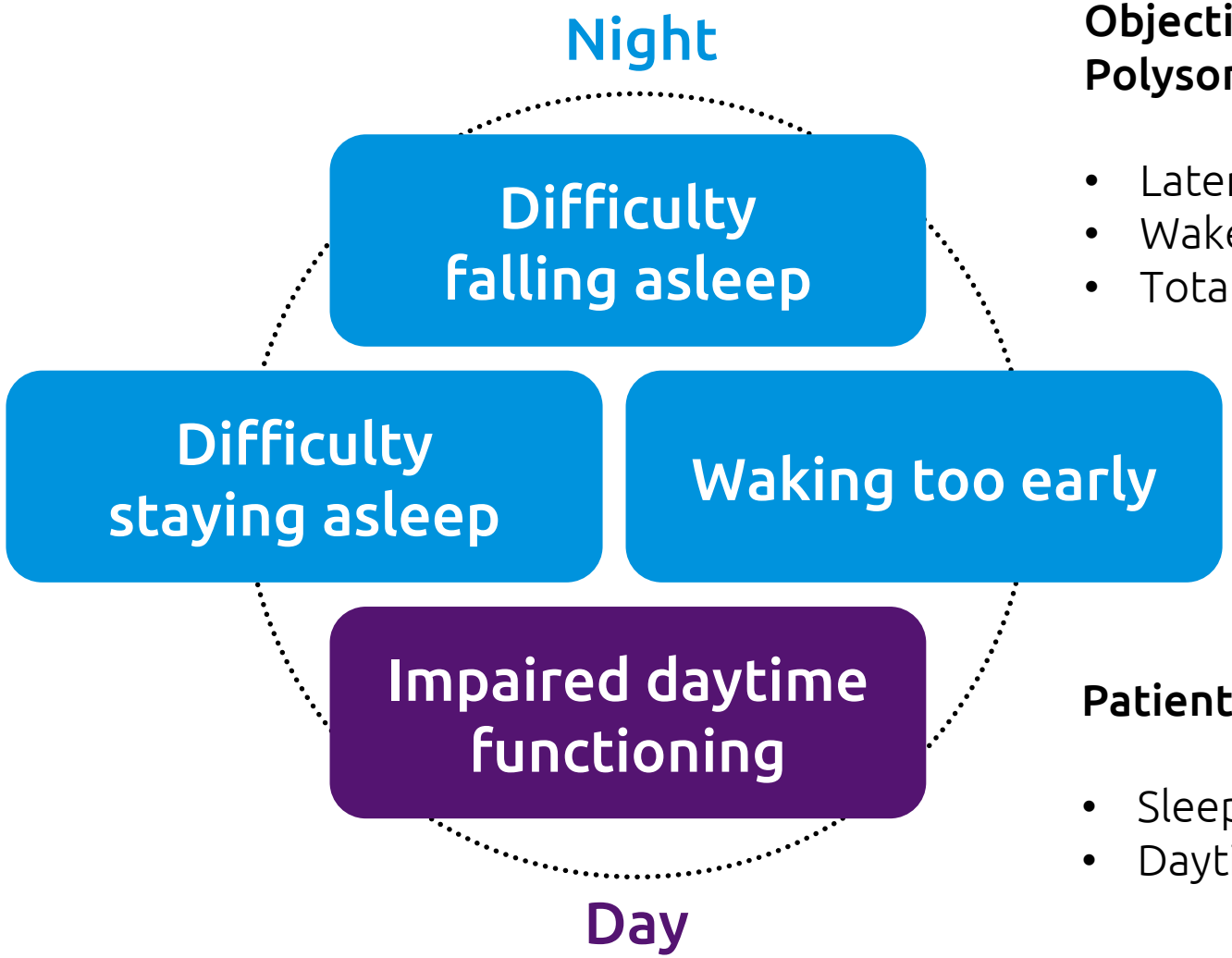
Guy Braunstein
Head of Global Clinical Development

Daridorexant (ACT-541468) – Phase 2 results presented at SLEEP 2019

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

Chronic insomnia disorder

≥ 3 nights/week
≥ 3 months



Objectively measured by Polysomnography (PSG)

- Latency to persistent sleep (LPS)
- Wake after sleep onset (WASO)
- Total sleep time (TST)

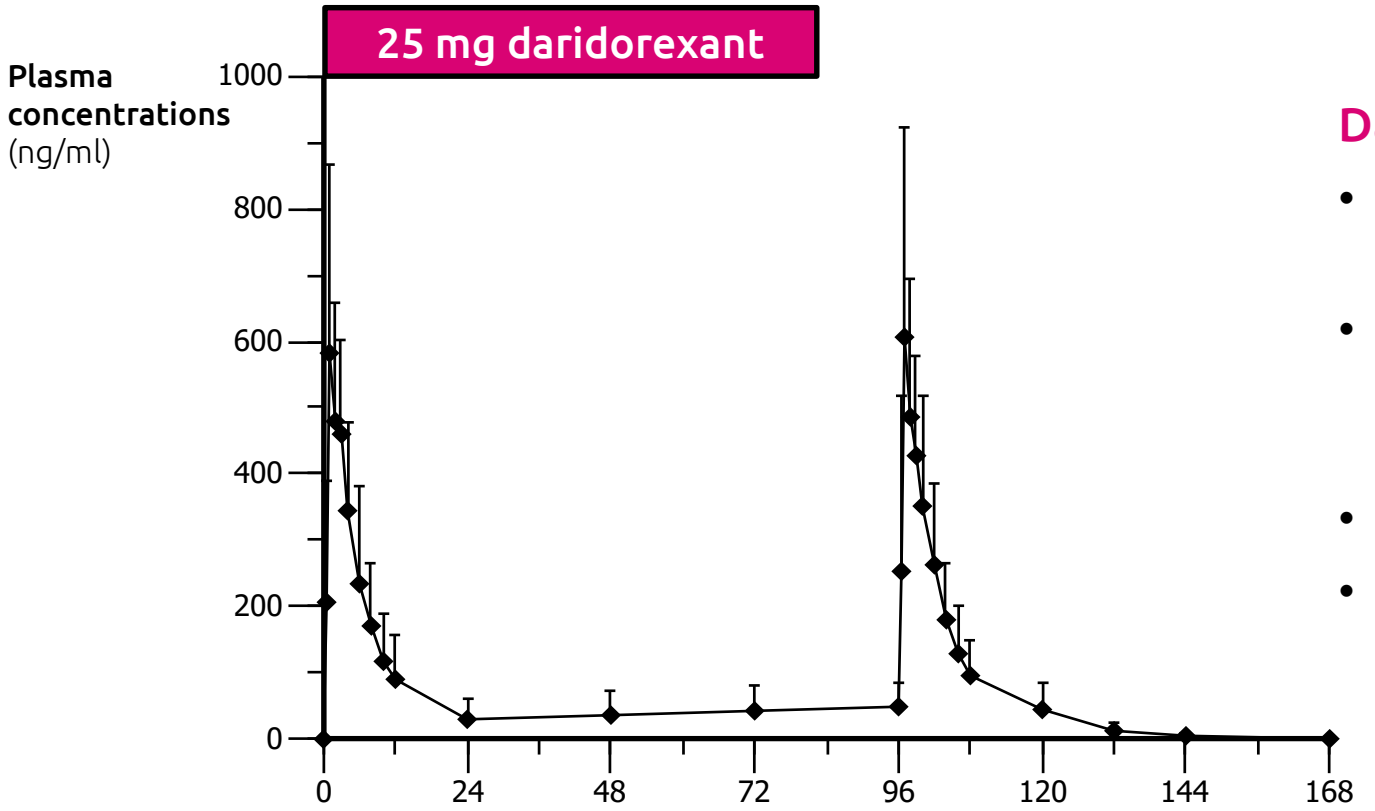
Patient reported outcome

- Sleep parameters
- Daytime functioning

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

Rationale for development of daridorexant

- There remains a need for effective and safe treatments for chronic insomnia disorder.
- 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 next-day functioning
- Fast absorption
- No accumulation over time

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

Two Phase 2 studies completed

Adult study: parallel group design

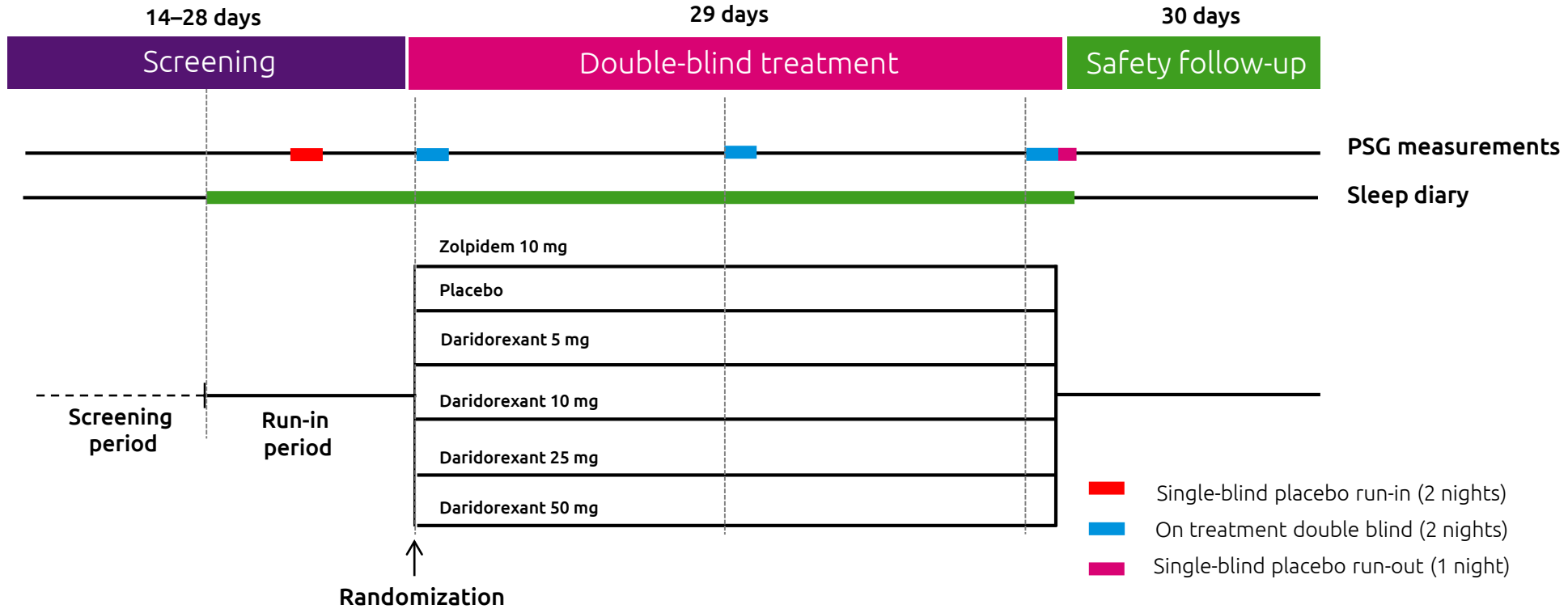
- 4-week treatment to assess effect after single dose and durability of effect over time
- Short off treatment period at the end to assess withdrawal
- 4 dose levels (5 mg, 10 mg, 25 mg and 50 mg)
- Placebo and zolpidem arms
- Objective and subjective sleep parameters

Elderly study: cross over design

- 2-night treatment
- 4 dose levels identical to adults
- Placebo-controlled
- Objective and subjective parameters

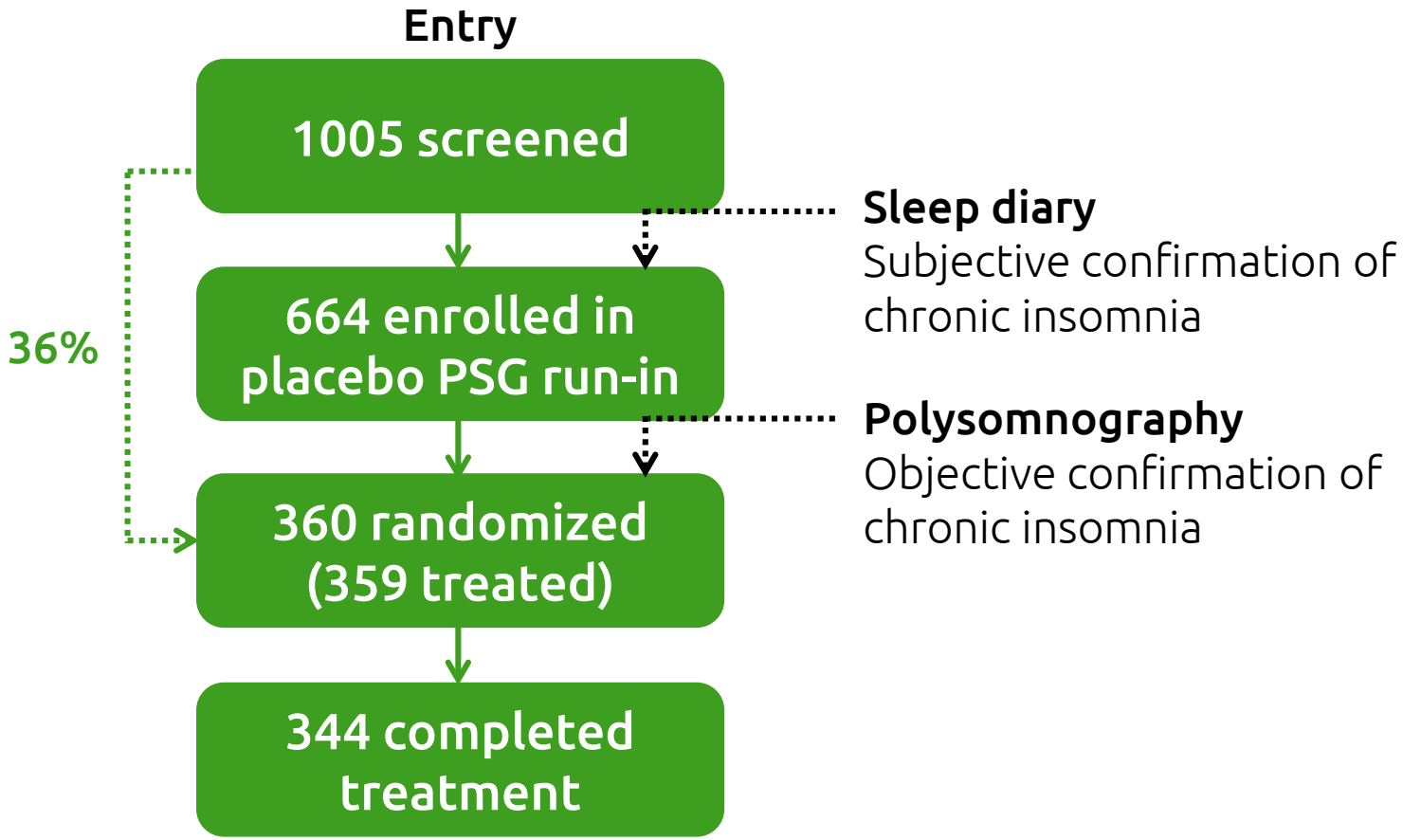
Daridorexant is investigational, in development and not approved or marketed in any country.

Adult study design



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

Adult study patient disposition



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Demographics and baseline characteristics

Adult study (N = 359)

Demographic characteristic	
Female, n (%)	230 (64)
Mean age, years (SD)	45 (11)
Mean BMI, kg/m^2 (SD)	25 (3)
White race, n (%)	321 (89)

This study was conducted at 38 sites in six countries (Germany, Hungary, Israel, Spain, Sweden, and the United States) at hospitals and sleep centers.

Baseline sleep parameters Mean (SD)	
WASO, min	97.5 (38.6)
LPS, min	71.8 (39.3)
TST, min	318.5 (56.6)
sWASO, min	80.4 (43.0)
sLSO, min	55.9 (27.1)
sTST, min	316.8 (52.6)
KSS	6 (1.7)
ISI©	21.2 (2.8)

BMI, body mass index ; ISI©, insomnia severity index©; KSS, Karolinska sleepiness scale; LPS, latency to persistent sleep; SD, standard deviation; sLSO, subjective latency to sleep onset; sTST, self-reported TST; sWASO, subjective WASO; WASO, wake after sleep onset

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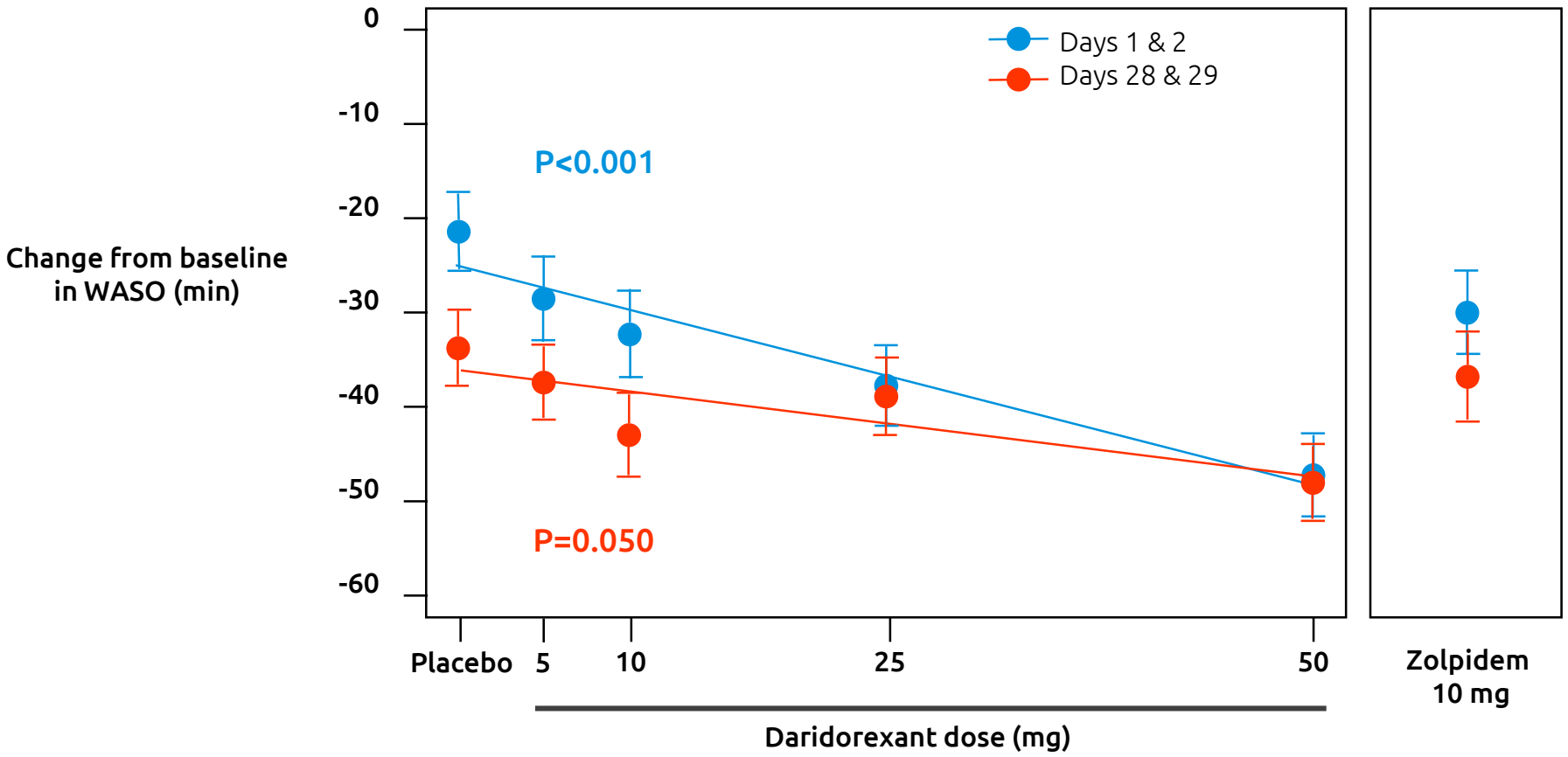
Wake after sleep onset (WASO)

Adult study



Data shown as mean (SE)

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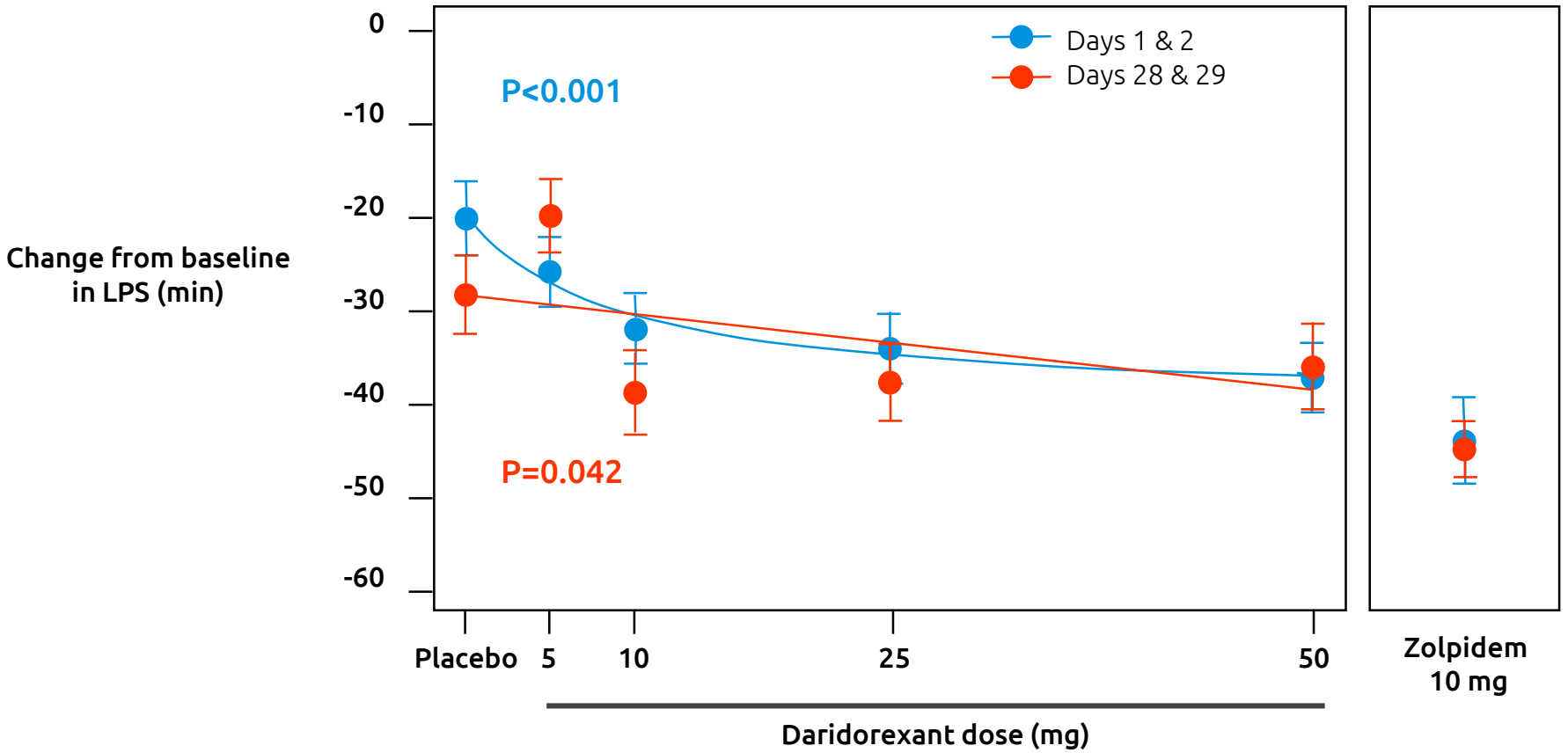
Latency to persistent sleep (LPS)

Adult study



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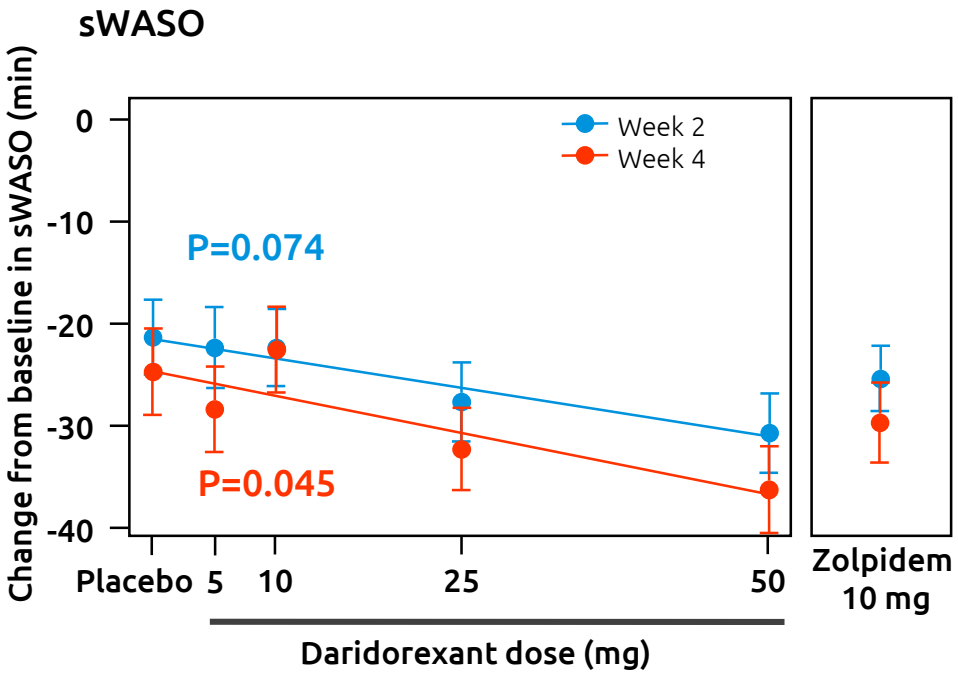
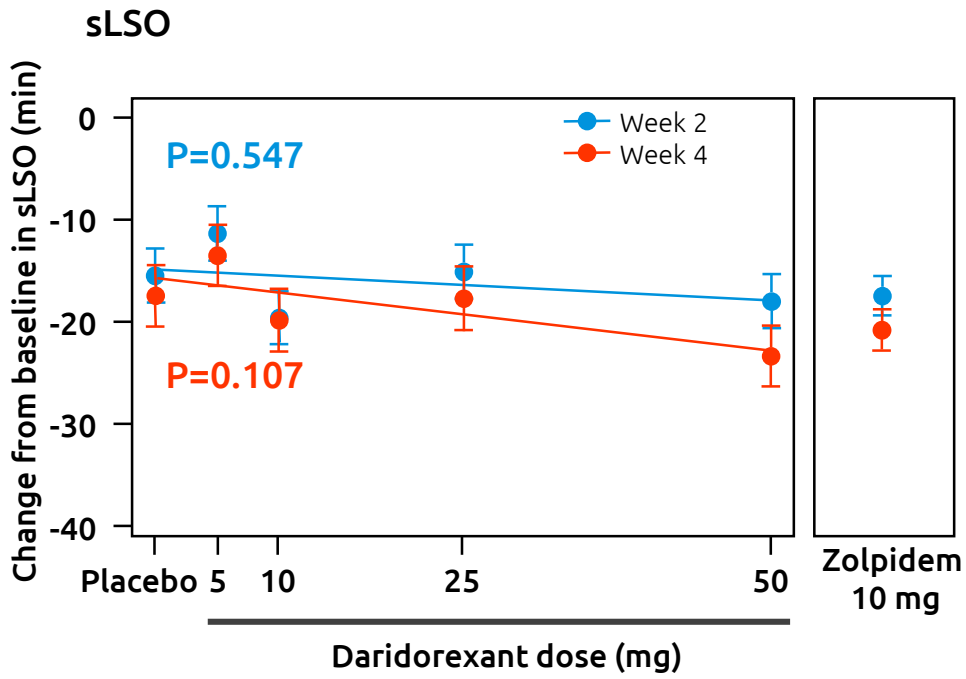
Subjective WASO & LSO

Adult study





Data shown as mean (SE)

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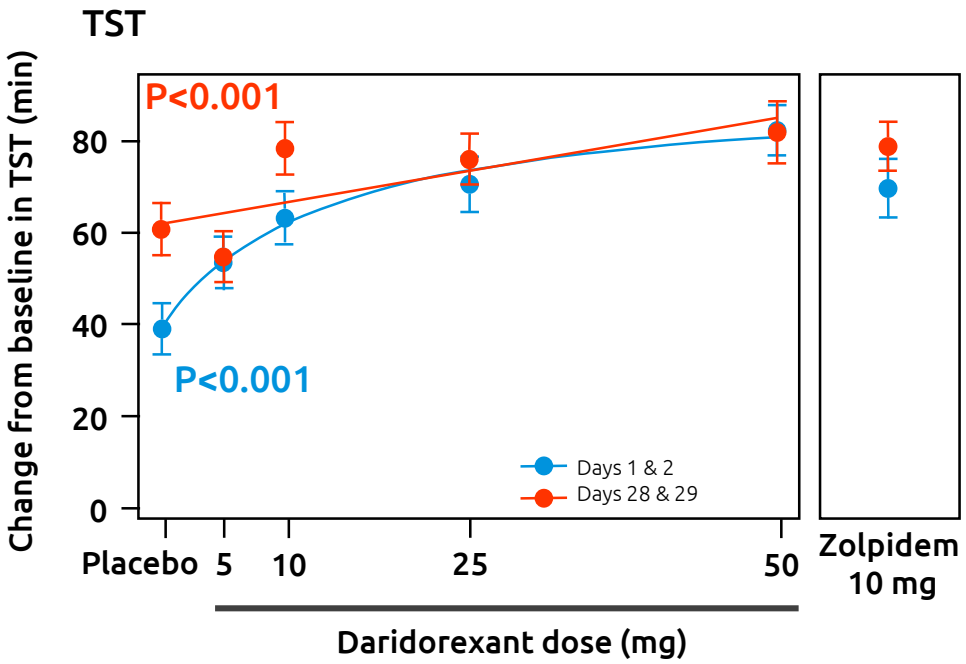
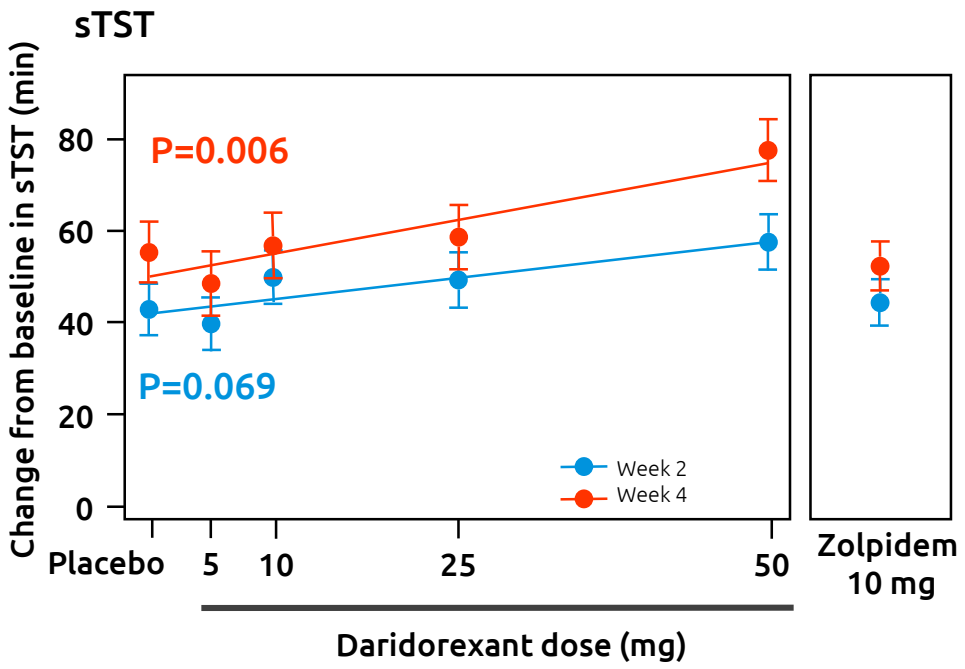
Total sleep time (TST) & subjective TST

Adult study





Data shown as mean (SE)

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Treatment emergent adverse events

Adult study

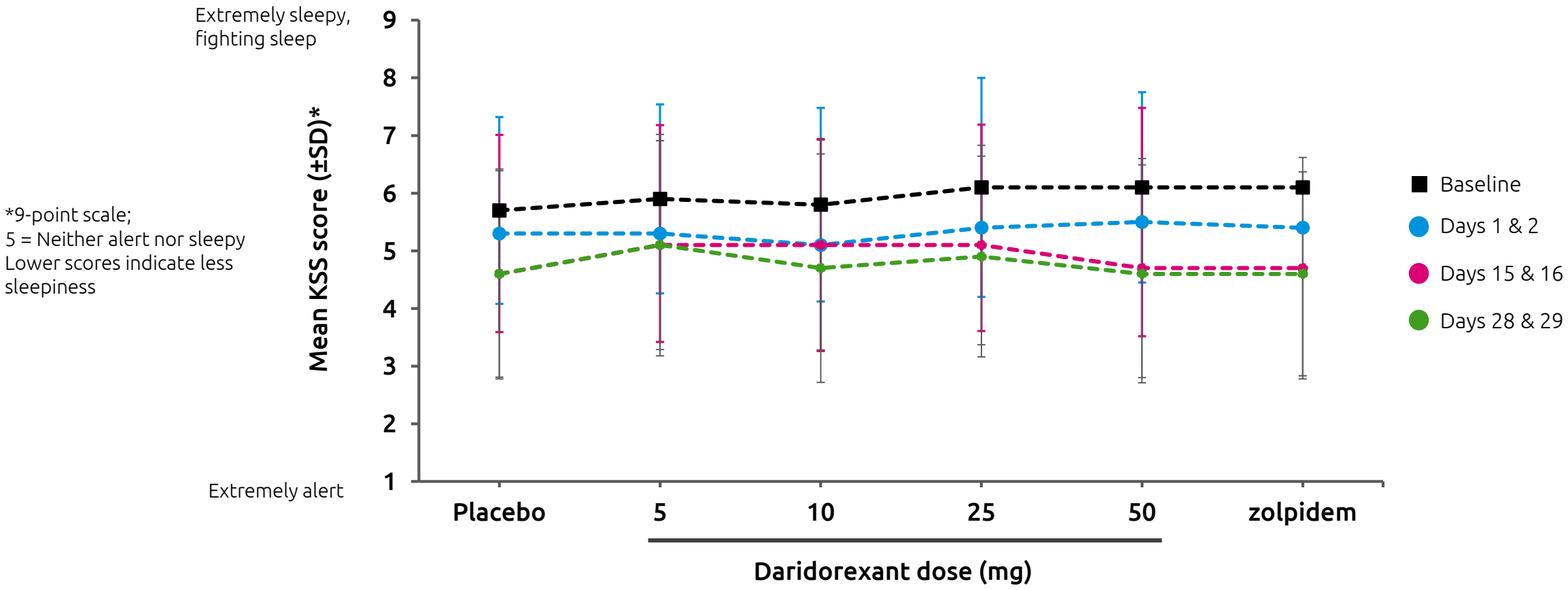
n (%)	Placebo (n=60)	Daridorexant 5 mg (n=60)	Daridorexant 10 mg (n=58)	Daridorexant 25 mg (n=60)	Daridorexant 50 mg (n=61)	Zolpidem 10 mg (n=60)
Participants with ≥1 TEAE	18	21	22	23	21	24
AEs leading to treatment discontinuation						
Angioedema	0	0	0	0	1	0
Anxiety	0	0	0	0	0	1
Arthralgia	0	0	1	0	0	0
Headache	0	0	1	0	0	0
Pain in extremity	0	0	1	0	0	0
Renal pain	0	0	1	0	0	0
Tooth infection	0	0	1	0	0	0
Participants with ≥1 serious AE	0	0	2	0	1	0
Participants with ≥1 AE of special interest						
Somnolence	0	0	1	1	2	0
Hypersomnia	0	0	0	1	0	0

- Treatment with daridorexant was well tolerated
- There was no evidence of rebound insomnia or withdrawal syndrome

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

Karolinska sleepiness scale (morning assessment)

Adult study



*9-point scale;
5 = Neither alert nor sleepy
Lower scores indicate less sleepiness

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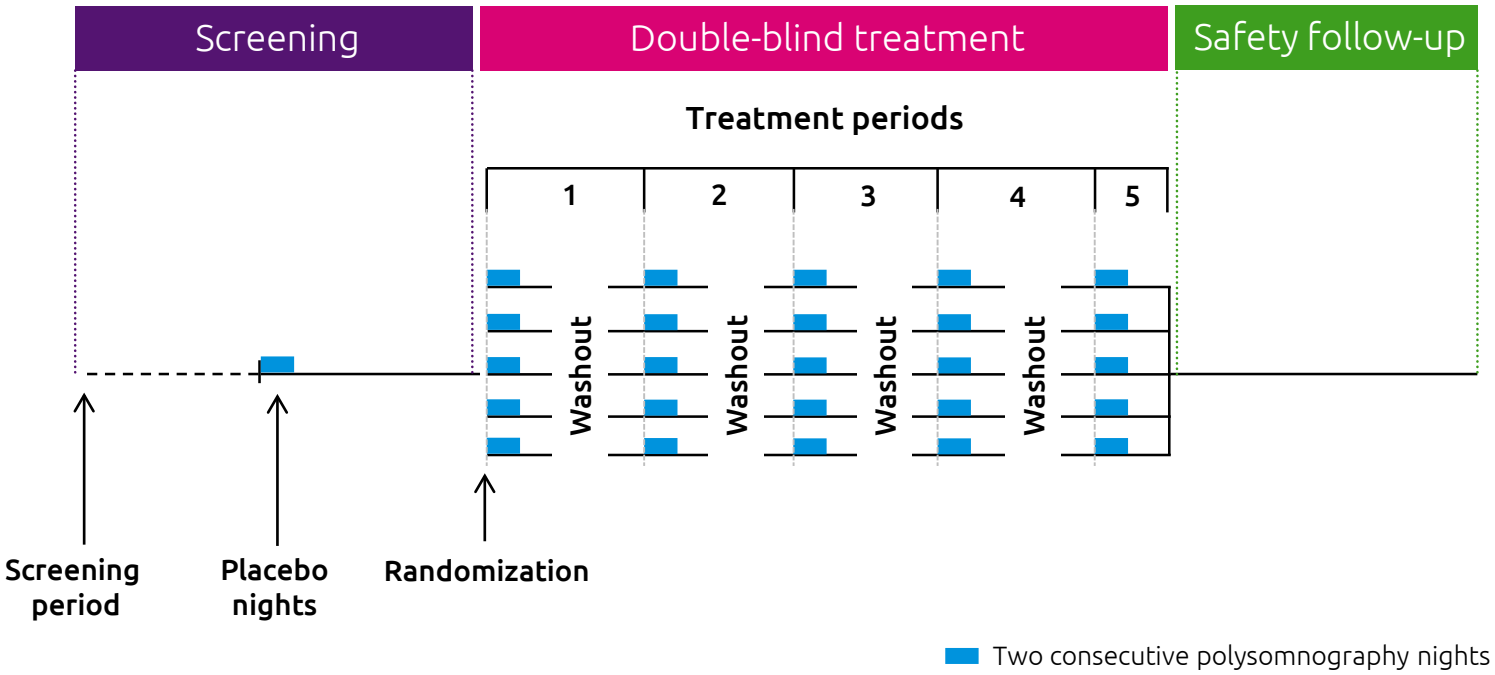
Elderly study design



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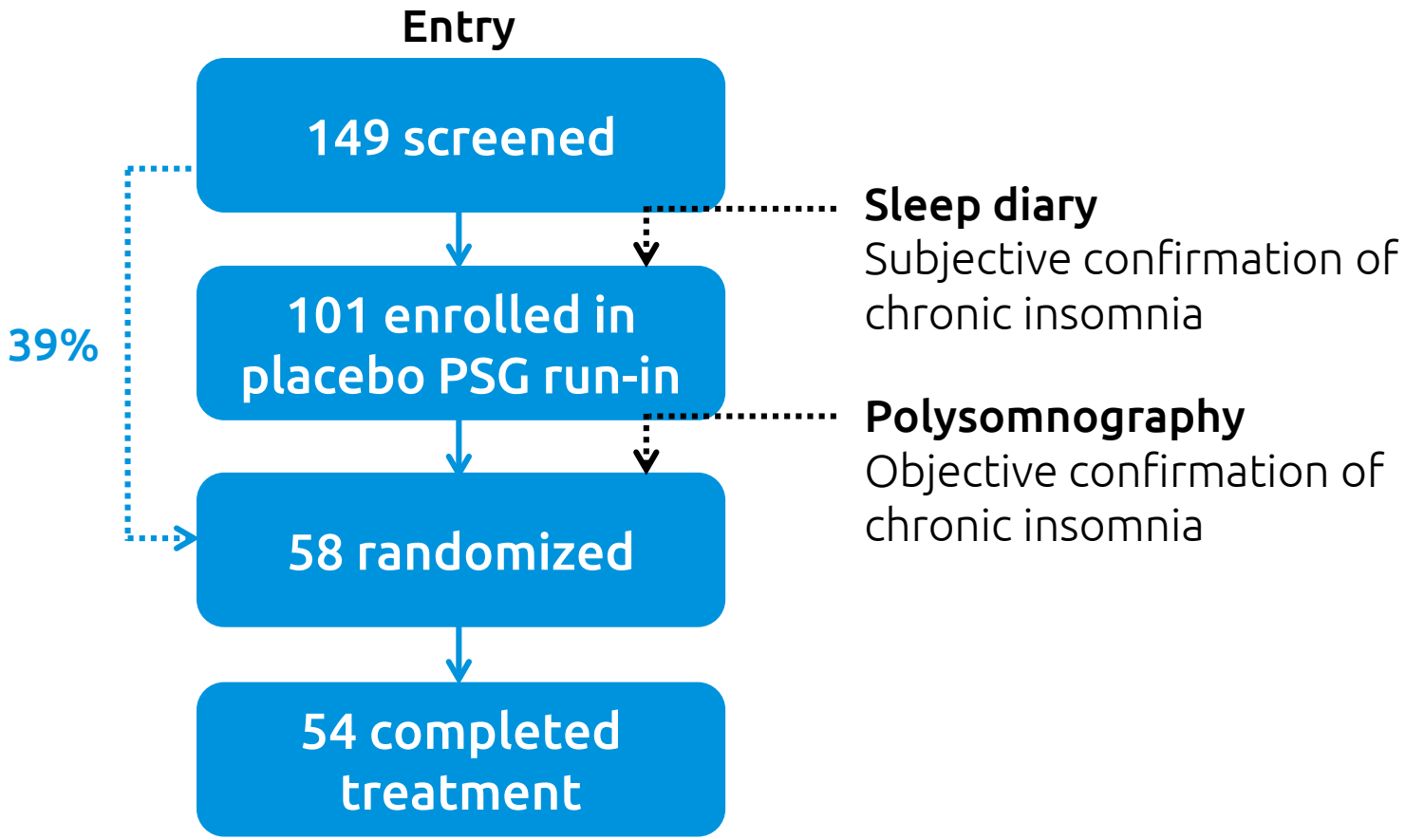
Elderly study patient disposition



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Demographics and baseline characteristics

Elderly study (N = 58)

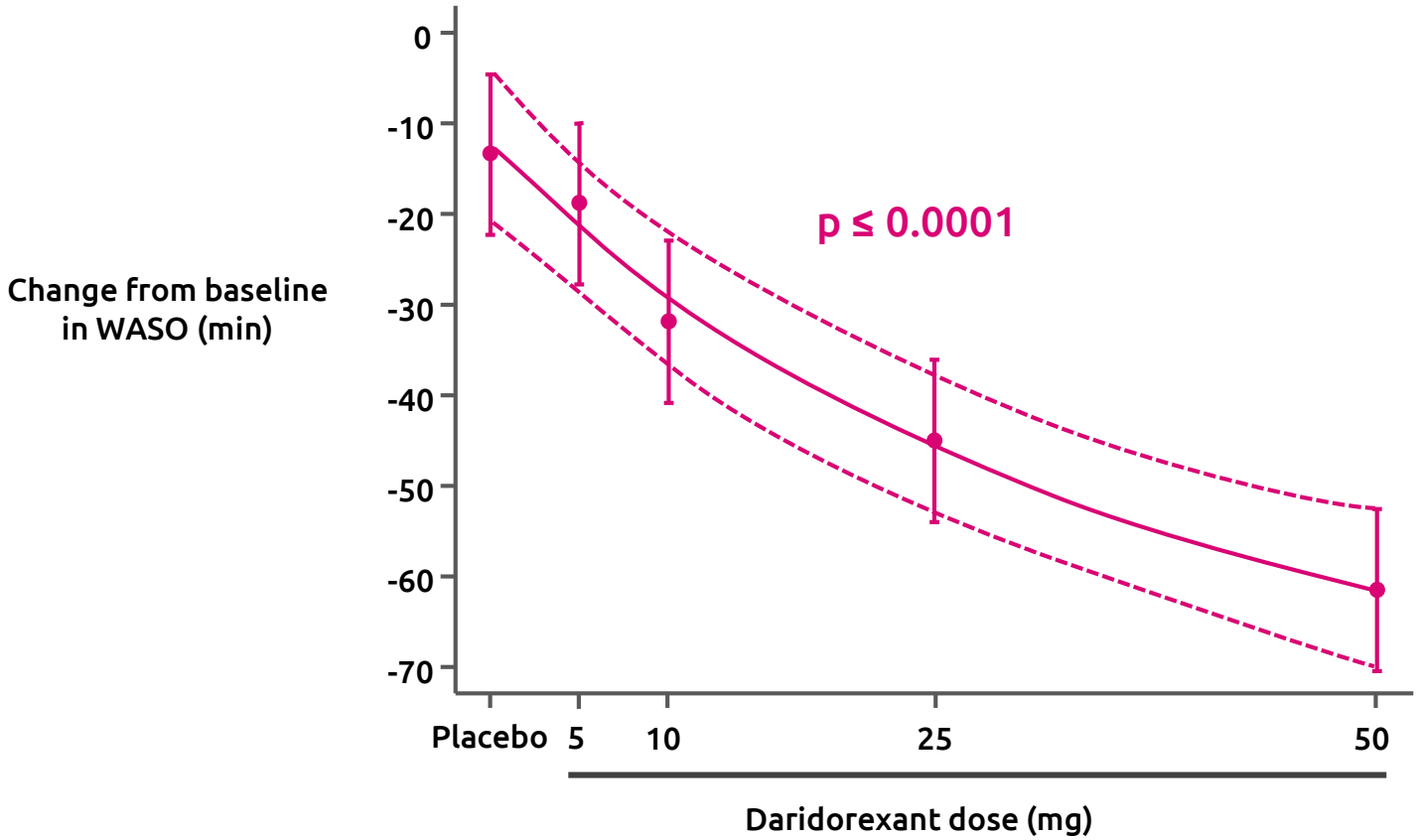
Demographic characteristic	
Median age (range), years	69 (65-85)
Sex, n (%) – Male	19 (33)
– Female	39 (67)
Mean BMI (SD), kg/m^2	25.8 (2.9)
Race, n(%) – White	54 (93)
– Black or African American	3 (5)
– American Indian or Alaska Native	1 (2)

Baseline sleep parameters Mean (SD)	
WASO, min	116.9 (40.2)
LPS, min	75.1 (50.0)
TST, min	295.8 (57.6)
sWASO, min	99.6 (65.7)
sLSO, min	65.7 (43.2)
sTST, min	301.7 (64.5)
KSS	5.1 (1.8)
ISI©	20.5 (3.0)

BMI, body mass index ; ISI©, insomnia severity index©; KSS, Karolinska sleepiness scale; LPS, latency to persistent sleep; SD, standard deviation; sLSO, subjective latency to sleep onset; sTST, self-reported TST; sWASO, subjective WASO; WASO, wake after sleep onset

Wake after sleep onset (WASO)

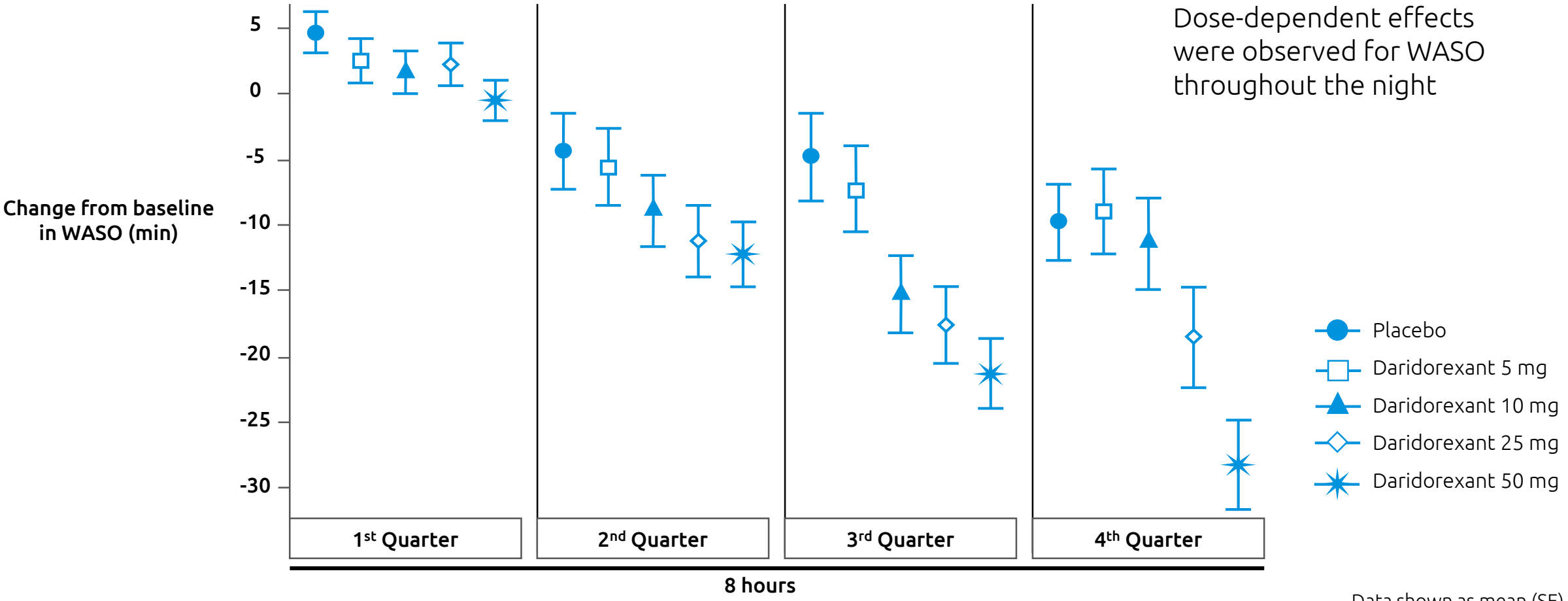
Elderly study



Dots: LSMean changes from baseline; bars: 95% CIs; dotted line = 95% CI of curve

WASO by quarter of the night

Elderly study



Data shown as mean (SE)

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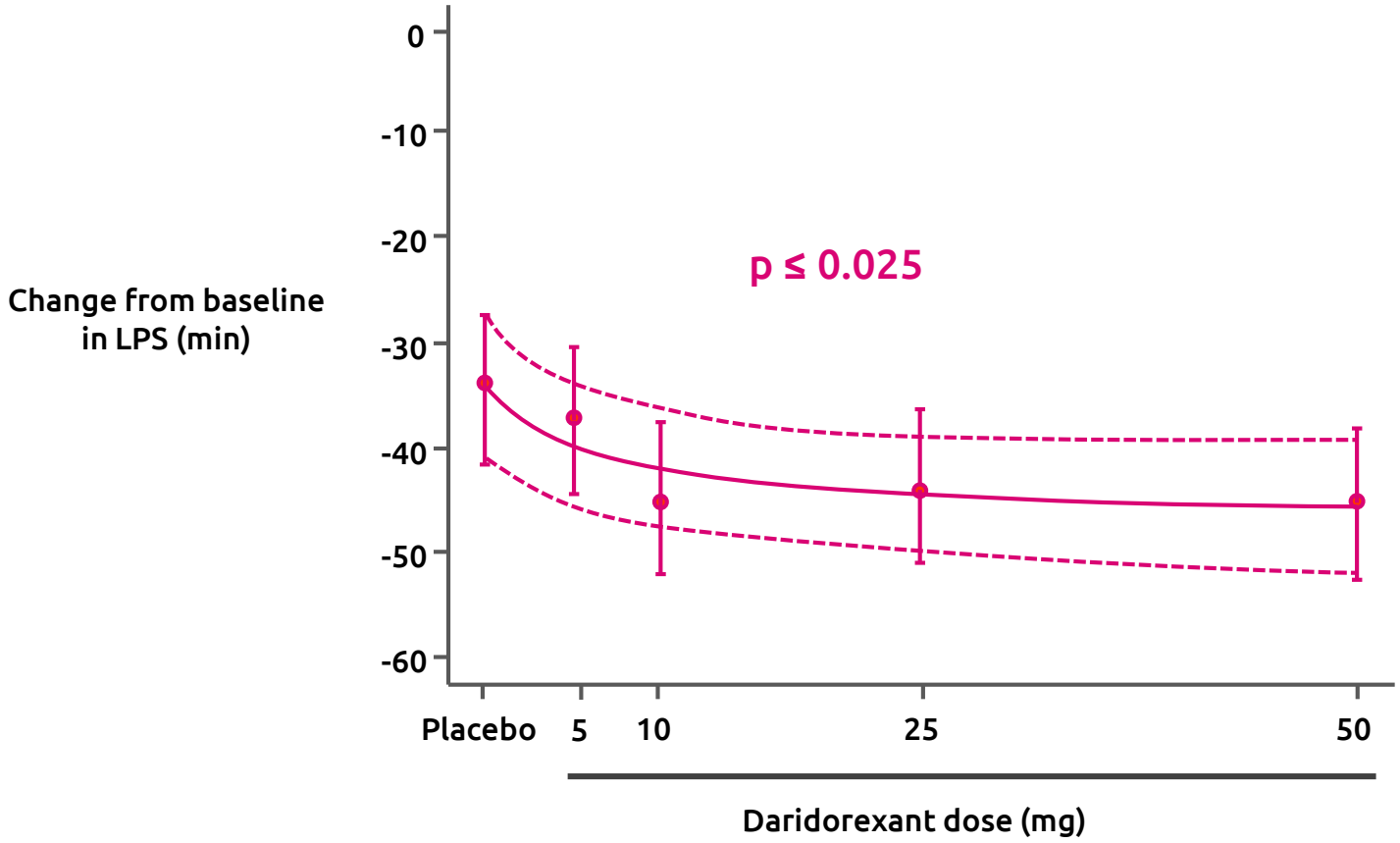
Latency to persistent sleep (LPS)

Elderly study



Dots: LSMean changes from baseline; bars: 95% CIs; dotted line = 95% CI of curve

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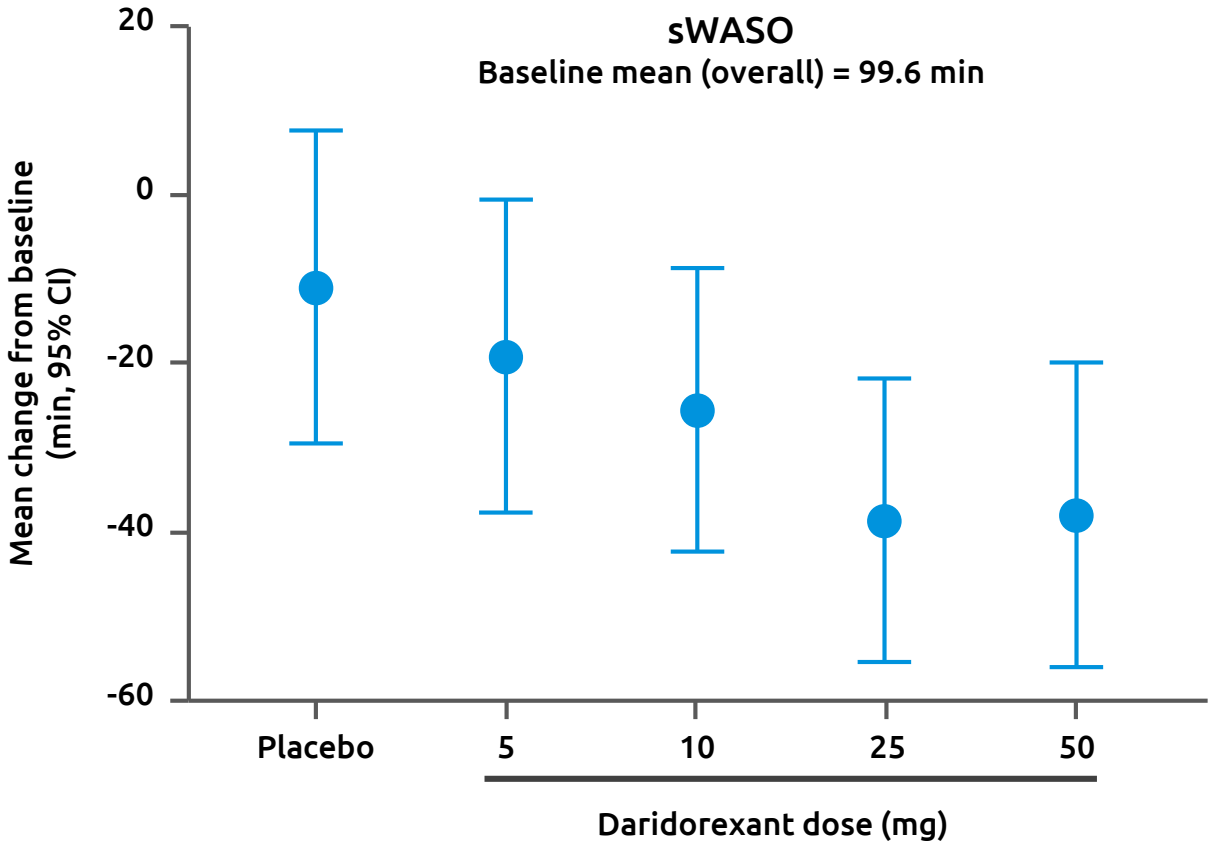
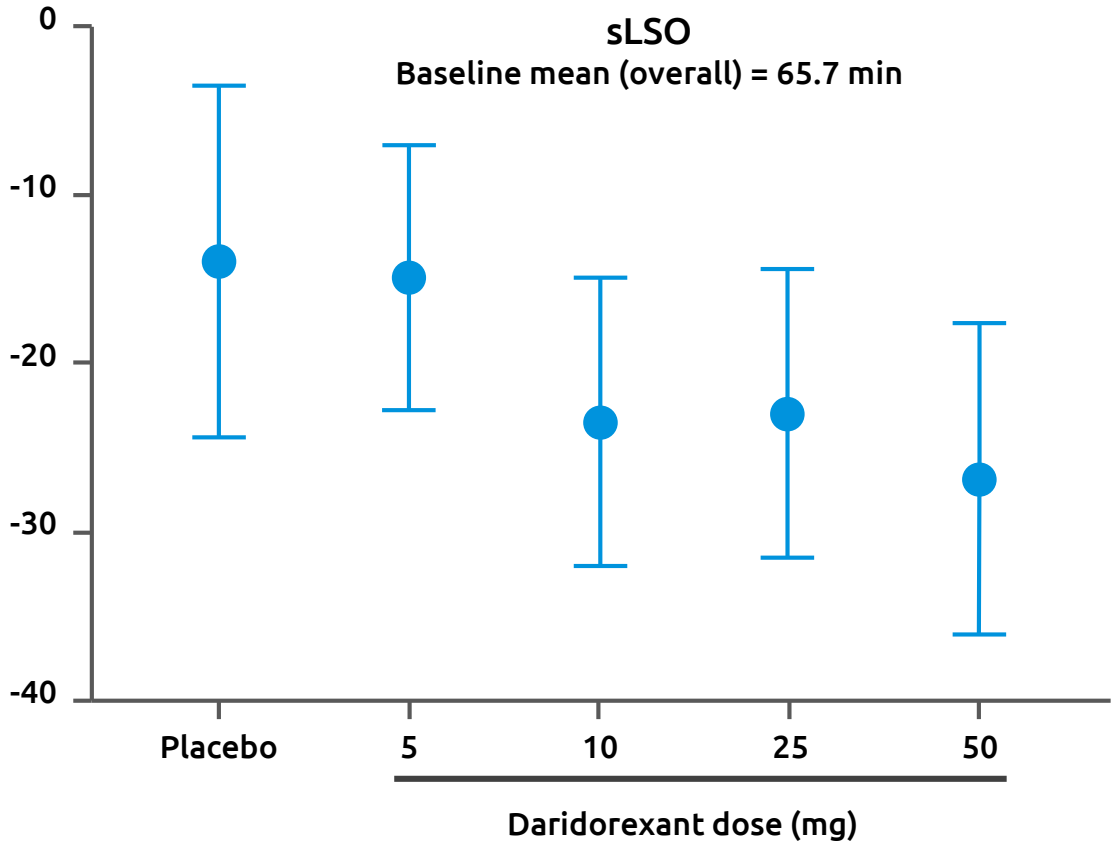
Subjective WASO & LSO

Elderly study





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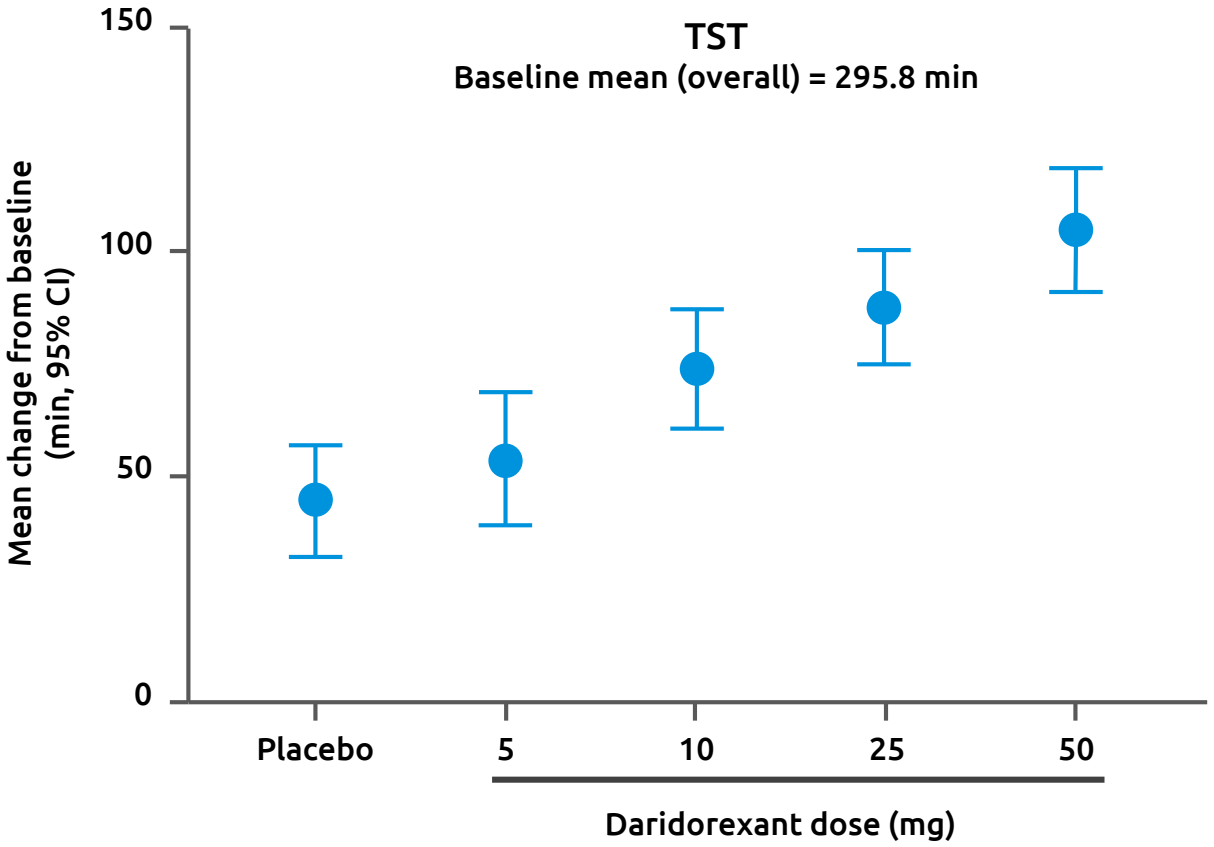
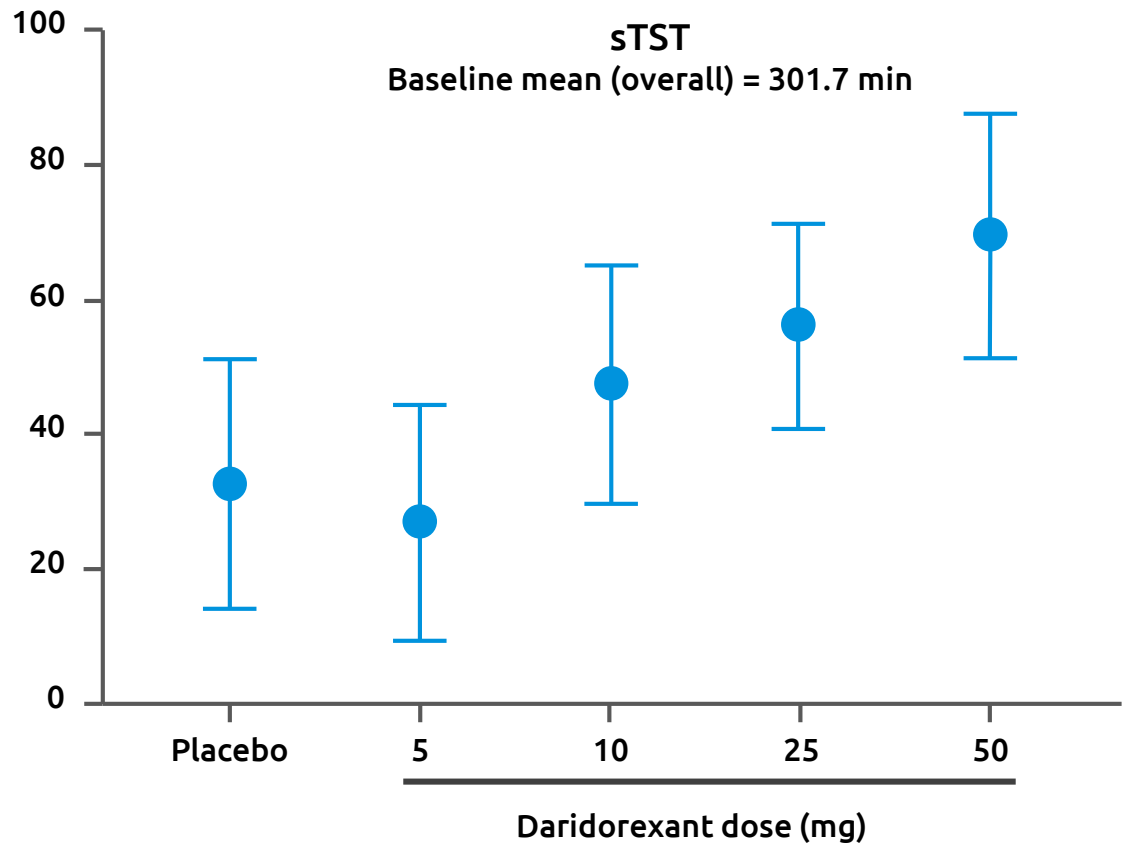
Total sleep time (TST) & subjective TST

Elderly study





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Safety results

Elderly study

n, (%)	SB-Placebo (N=58)	Placebo (N=54)	Daridorexant 5 mg (N=56)	Daridorexant 10 mg (N=54)	Daridorexant 25 mg (N=55)	Daridorexant 50 mg (N=56)
Participants with ≥1 adverse event	6	8	13	12	10	16
Adverse event for ≥2 participants in any dose group						
Fatigue	0	1	0	1	0	4
Nasopharyngitis	0	0	0	1	0	2
Gait disturbance	1	0	2	1	1	1
Headache	2	1	2	0	1	1

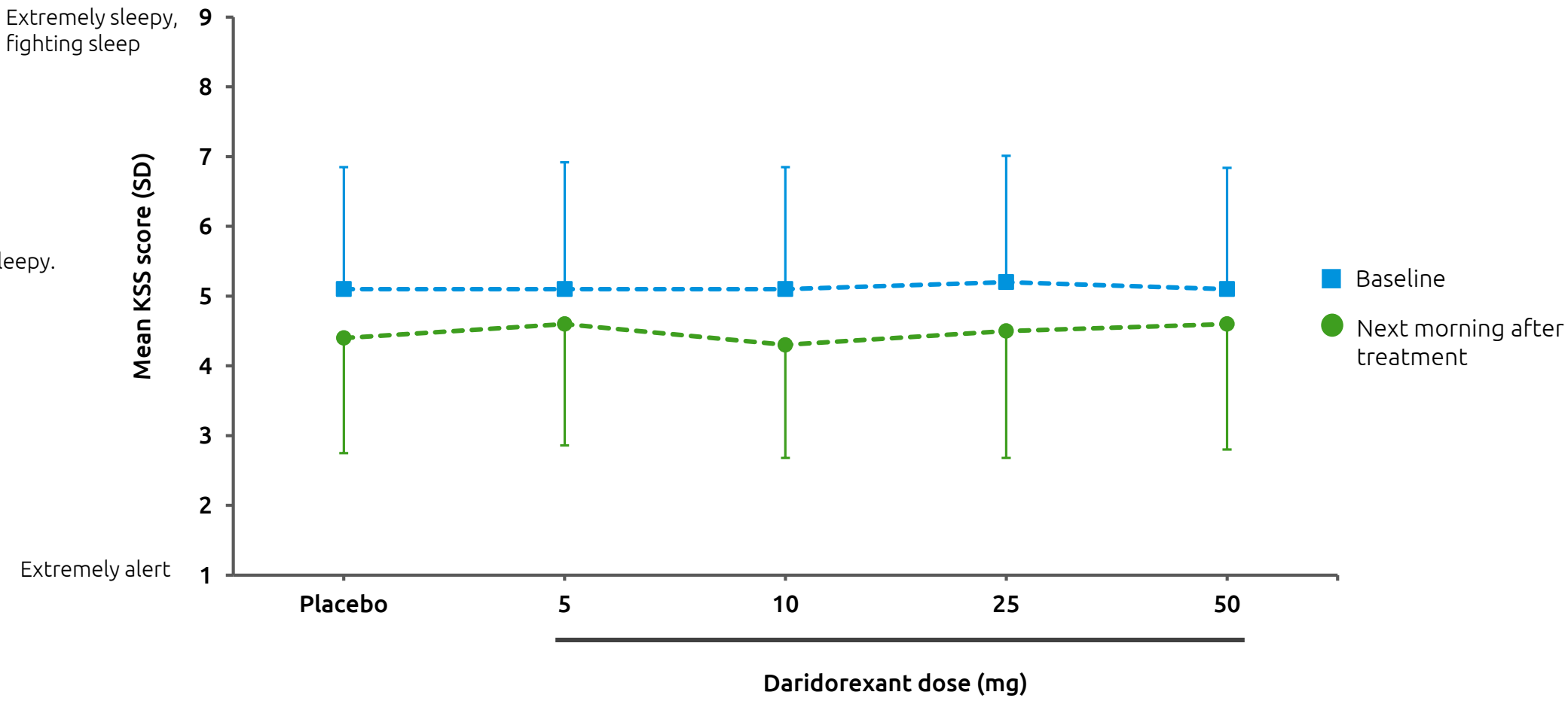
- No SAE, no deaths
- No narcolepsy-like events
- No suicidal ideation
- No complex sleep behaviors
- Four participants discontinued due to adverse events

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

Karolinska sleepiness score (morning assessment)

Elderly study

9-point scale:
5 = Neither alert nor sleepy.
Lower score indicates improvement.



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Conclusion from Phase 2

- In adult and elderly patients with chronic insomnia
  - daridorexant dose-dependently improved sleep onset, sleep maintenance, and total sleep time
  - daridorexant was well tolerated
  - no residual next-morning effect was observed at any dose

- Three doses were selected for Phase 3: 10 mg, 25 mg, and 50 mg

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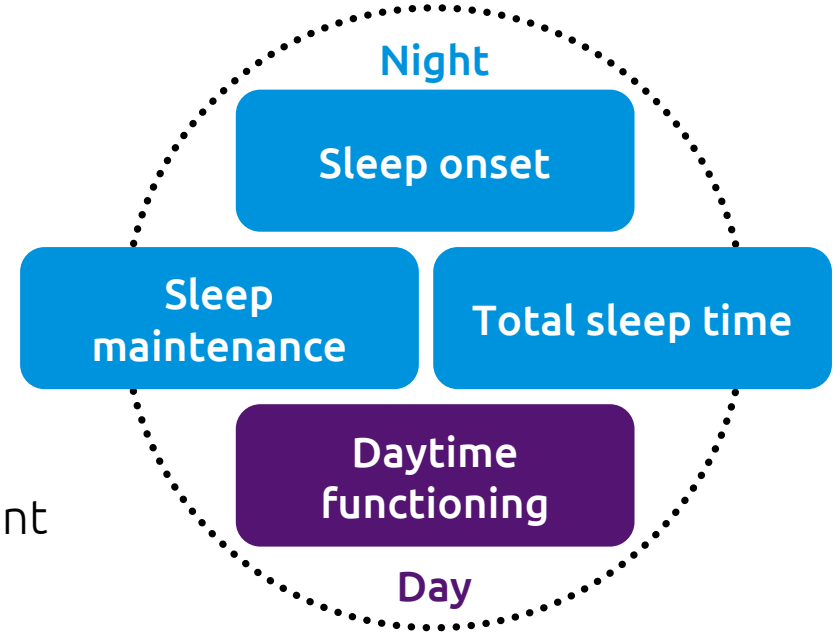
From Phase 2 to Phase 3



Concept

- 1,800 adult and elderly chronic insomnia patients in 2 studies
- Objective and subjective sleep assessment
- Assessment of impact on patient's functioning during the day
- Long-term efficacy and safety (up to 12 months), including assessment of residual "hang-over" effect, withdrawal symptoms, and rebound
- Comprehensive clinical pharmacology program in parallel
  e.g. driving performance, interaction (drugs, alcohol), abuse potential

Main studies (12 weeks)

301: placebo, 25 mg & 50 mg

302: placebo, 10 mg & 25 mg

Extension study (40 weeks)

303: placebo, 10 mg, 25 mg & 50 mg daridorexant

- On track to report 3-month efficacy results in the first half of 2020 and long-term efficacy and safety results later in the same year

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Be prepared for more