A Clinical Study with KP1077 in Adults with Idiopathic Hypersomnia

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Speakers

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Principal Investigator, Zevra Study KP1077.D01

Presentation Outline

• Zevra Company Overview	Dr Rene Braeckman
• Idiopathic Hypersomnia (IH) Disease Background	Dr Chris Drake
• New Treatment Option for IH (KP1077)	Dr Rene Braeckman
• Zevra's Phase 2 Study in IH	Dr Chris Drake

Zevra's Mission

- Zevra is a rare disease therapeutics company driven by science, data and patients' unmet need to create transformational therapies for diseases with limited or no treatment options.
- Zevra pushes boundaries beyond what is possible to advance new therapies that meaningfully improve patients' lives.

Approach

- Driven by a ***patient-centric*** approach coupled with outside-the-box strategies to develop promising product candidates for rare diseases.
- Expert and skillful team of scientists, patient advocates, development strategists, medical and commercialization specialists, and business development leaders with a proven record of bringing new therapies to patients.
- Specialized in a data driven approach to advance therapies and to find solutions to overcome complex clinical and regulatory challenges.

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IH Disease Background

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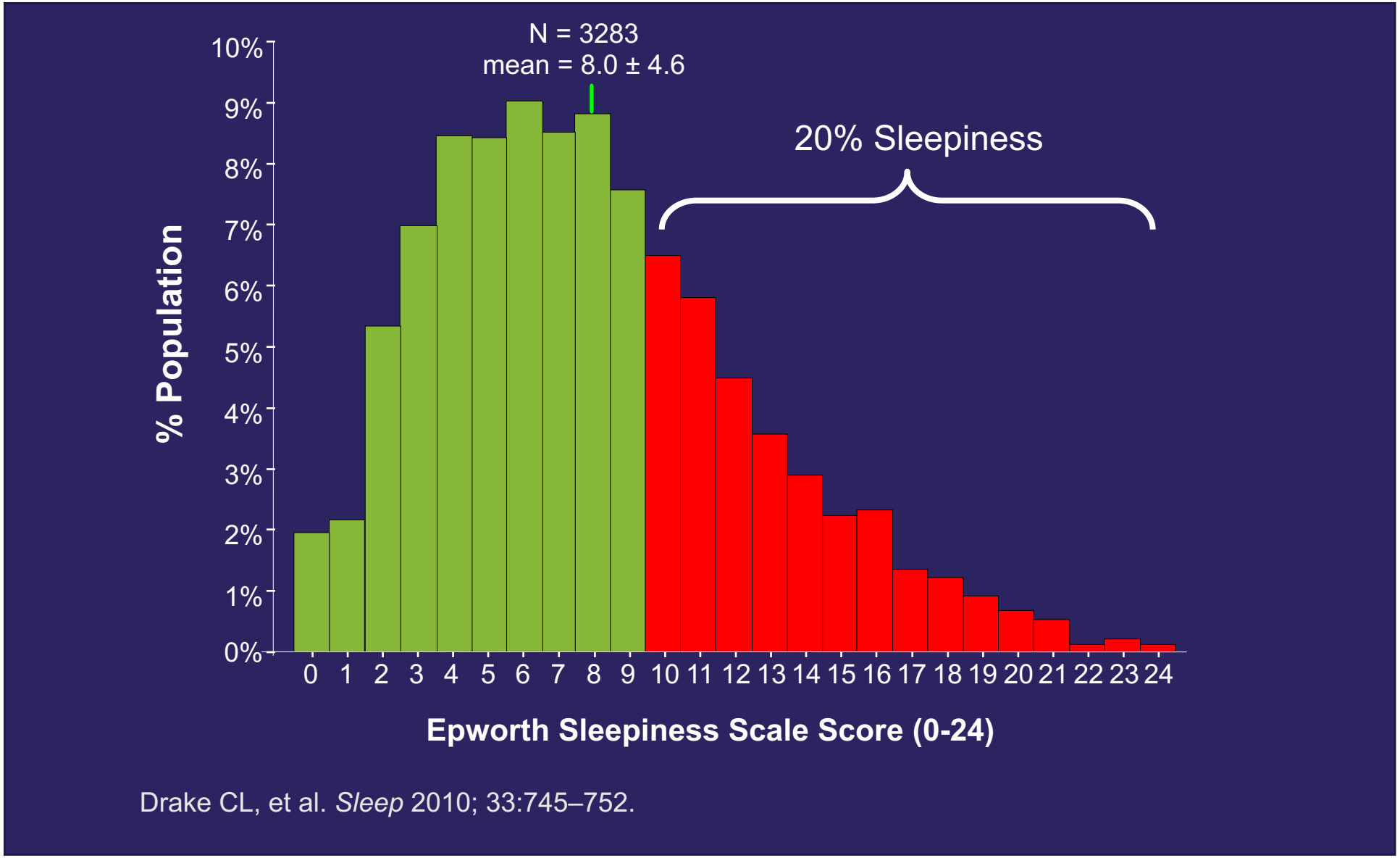
Still Sleepy After All These Years

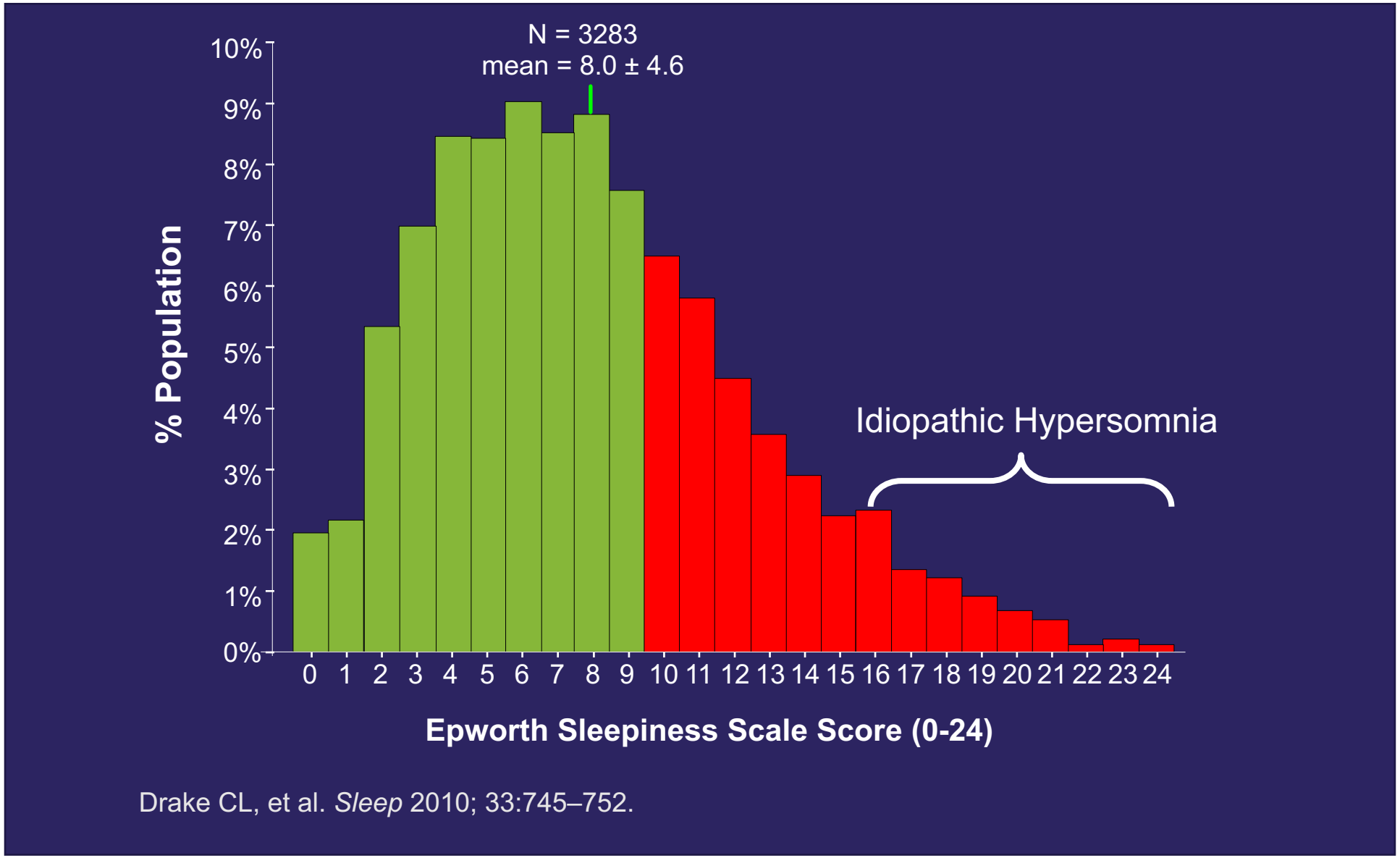
A New Approach to the Treatment of Idiopathic Hypersomnia

Sleepiness is Common



Drake CL, et al. *Sleep* 2010; 33:745–752.

Excessive Sleepiness is a Medical Symptom



Drake CL, et al. *Sleep* 2010; 33:745–752.

What is Idiopathic Hypersomnia

- ***Excessive Daytime Sleepiness (EDS)***
  Irrepressible need to sleep or daytime lapses into sleep

- ***"Sleep Drunkenness" / Sleep Inertia***
  Prolonged difficulty waking, with frequent reentries into sleep, confusion, automatic behavior, and irritability

- ***Unrefreshing Nighttime Sleep***
  Main sleep period of 10+ hours, often unrefreshing in nature

- ***Long, Unrefreshing Naps***
  Daytime naps lasting >1 hour that are unrefreshing; no benefit from prescribed or scheduled naps

- ***Impaired Cognitive Dysfunction***
  Brain fog, problems with memory and attention, a feeling of one's mind going blank, or making a mistake in a habitual activity

Drowsy Driving Is a Serious Health and Safety Risk

- **The National Highway Traffic Safety Administration estimates that between 2005 and 2009 drowsy driving was responsible for an annual average of[1]:**
  - **83,000 crashes**
  - **37,000 injury crashes**
  - **At least 800 fatal crashes**
- **Up to 6,000 fatal crashes each year may be caused by drowsy drivers.[2-4]**

Estimate **1.35** million

US drivers involved in a drowsy driving related crash in five-year period ending in 2002

National Survey of Distracted and Drowsy Driving Attitudes and Behavior: 2002

1. National Highway Traffic Safety Administration. Research on Drowsy Driving. http://www.nhtsa.gov/Driving+Safety/Drowsy+Driving. Accessed October 20, 2015.
2. Masten SV, Stutts JC, Martell CA. Predicting daytime and nighttime drowsy driving crashes based on crash characteristic models. 50th Annual Proceedings, Association for the Advancement of Automotive Medicine; October 2006; Chicago, IL.
3. Klauer SG, Dingus TA, Neale VL, Sudweeks JD, Ramsey DJ. *The Impact of Driver Inattention on Near-Crash/Crash Risk: An Analysis Using the 100-Car Naturalistic Study Data, 2006*. Springfield, VA: DOT; year. DOT HS 810 594.
4. Tefft BC, AAA Foundation for Traffic Safety. Prevalence of Motor Vehicle Crashes Involving Drowsy Drivers, United States, 2009 – 2013.Washington, DC: AAA Foundation for Traffic Safety; 2014. https://www.aaafoundation.org/sites/default/files/AAAFoundation-DrowsyDriving-Nov2014.pdf. October 19, 2015.

Treatment of Excessive Sleepiness

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New Treatment Option for IH

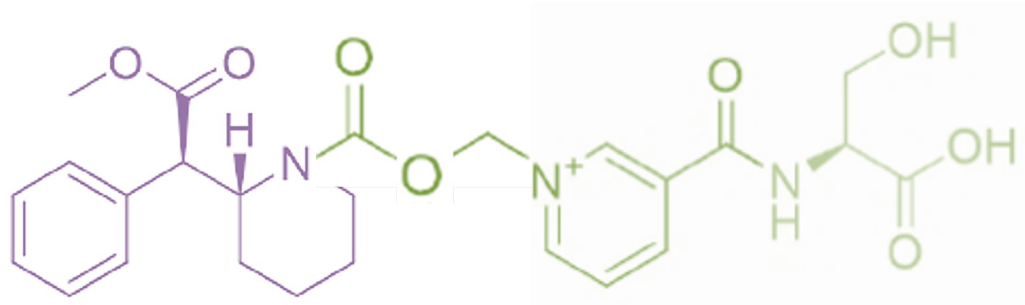
Zevra's KP1077 Product

Prodrug Technology

Following ingestion, normal human metabolic processes cleave the ligand and release the active drug

Serdexmethylphenidate (SDX)

Prodrug: Serdexmethylphenidate (SDX)



Active Drug: d-methylphenidate

Ligand: Carboxymethylene linker + niacin + L-serine

SDX – Improved Attributes

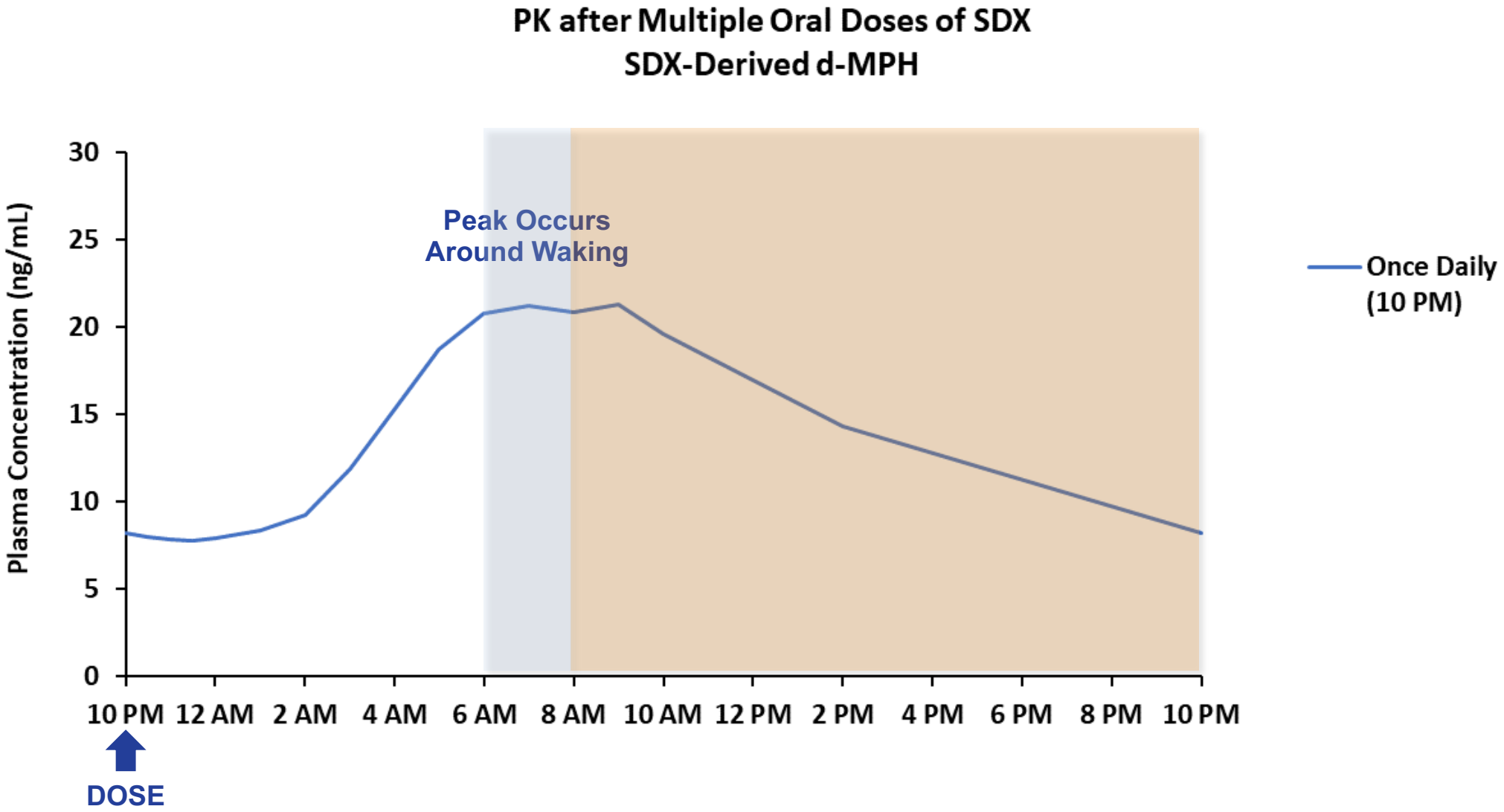
- Less abuse potential
- Unique ***Pharmacokinetic*** Profile

  Pharmacokinetics *is the study of a drug's journey through a person's body, including examining the amount of drug in a person's plasma. The total amount of drug, the peak level of the drug, and the time it takes to reach the peak level in person's plasma are important to understand the drug's safety and effectiveness.*

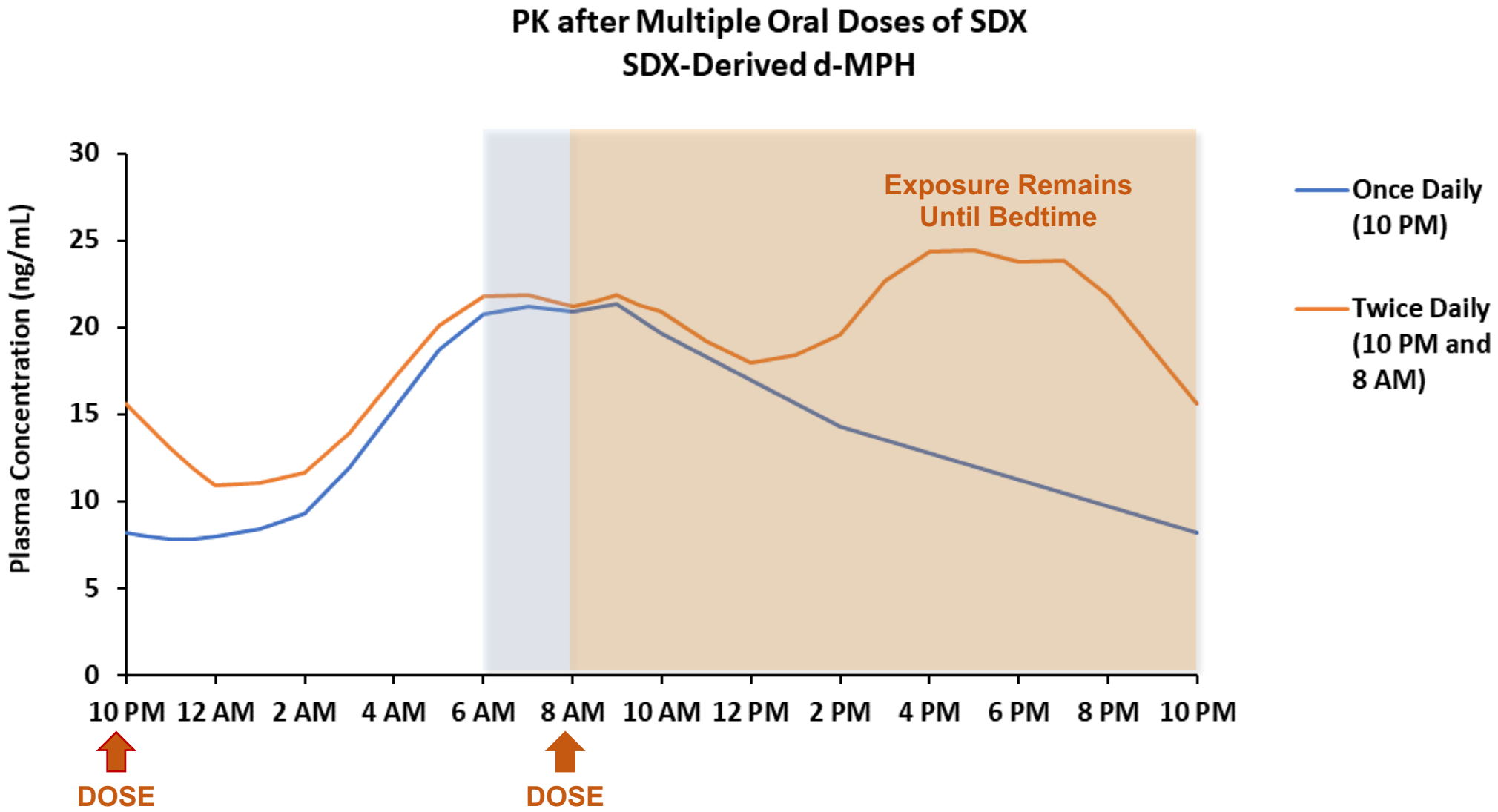
SDX is in Clinical Development for:

- Idiopathic Hypersomnia (IH)
- Narcolepsy

Pharmacokinetics (PK)



Pharmacokinetics (PK)



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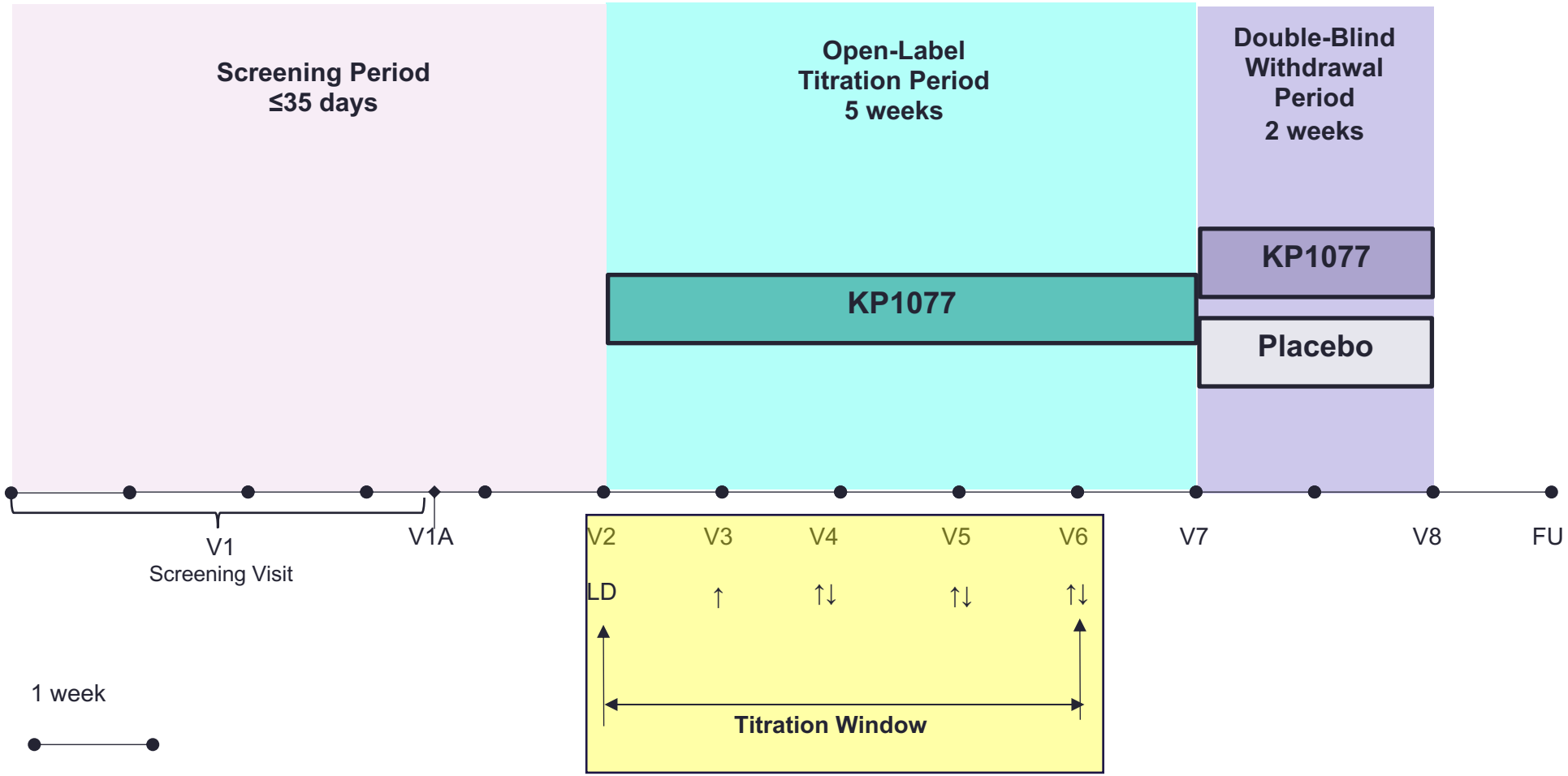
Zevra's Ongoing Phase 2 Trial in IH

Study KP1077.D01

Study Design



V = Visit; FU = Follow-Up Phone Call; LD = Low Dose (Starting Dose)

Eligibility Criteria for Study Participation

Adults (18 years of age or older) who meet the following criteria may be eligible to participate:

- Previously diagnosed with IH or not yet diagnosed with IH.
  - Patients with symptoms of IH but not yet diagnosed will be diagnosed in the screening period of the trial.
- Able to give informed consent.
- Have excessive daytime sleepiness as measured by sleepiness questionnaires.
- Agree to wash out all current medications that may affect daytime sleepiness or nighttime sleep.
- Are not pregnant, or do not plan to get pregnant or breastfeed during the study.

This is not a complete list of eligibility criteria. The study doctor will review all the requirements with potential participants.

Study Participation

If you have Idiopathic Hypersomnia and are interested in participating in the study:

Visit the Zevra booth at the conference to get a list of clinical sites in the US, with location and contact information of a site near you.

Assistance to Participants in the Study

- No cost for patients to participate in the study
- Payment for sleep & nap studies in a sleep lab, needed for new IH diagnosis
- Reimbursement of travel expenses to/from study site

For more information about study design and qualification criteria, visit

www.hypersomniafoundation.org/research-studies/

clinicaltrials.gov (NCT05668754)

Or email:

medicalaffairs@zevra.com

Questions?