Ovid Therapeutics
PAVING THE WAY FOR MORE IN ANGELMAN SYNDROME (AS)

Angelman Society of Israel, December 5th, 2019

ד"ר ג'רמי לוין

יו"ר ומנכ"ל

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THE NUMBERS ARE IN: SEE THE PROGRESS IN ANGELMAN SYNDROME

How many people were at this event three years ago?

600

How many AS therapies were in development five years ago?

0

How many people are at this event today?

900+

How many promising AS therapies are in development today?

5

AT THE DOORSTEP OF PHASE 3 CLINICAL RESULTS: OV101

We are proud to see OV101 (gabadoxol) progress into Phase 3 studies with the NEPTUNE study.

But OV101 is just the beginning for AS therapies—**we couldn’t be more excited to see what else other companies have in store.**

THERE WAS LESS TO THE STORY NOT TOO LONG AGO…

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ANGELMAN SYNDROME (AS) - A CONDITION PAVING A NEW PATH

1

DRUG DISCOVERY WAS ONLY BEGINNING

2

RESOURCES JUST DIDN'T EXIST

3

AS WAS RELATIVELY UNKNOWN

WE WERE INSPIRED TO MAKE A DIFFERENCE IN ANGELMAN SYNDROME

OVID THERAPEUTICS INC. WAS FOUNDED TO ADDRESS NEUROLOGICAL ORPHAN DISEASES TO BRING NOVEL APPROACHES—WHERE THE UNMET MEDICAL NEED FOR PATIENTS AND FAMILY IS GREAT.

AND BY ENGAGING WITH ADVOCACY, FAMILIES, AND PATIENTS WITH ANGELMAN SYNDROME, WE MET A COMMUNITY EMPOWERED AND MOTIVATED TO MAKE A MEANINGFUL DIFFERENCE AND

THE ROAD TO GABADOXOL: EXPLORING TONIC INHIBITION

ABOUT TONIC INHIBITION

Tonic inhibition is an important physiological process in the brain that is key to the brain's ability to discriminate signal from noise.

EXCITATORY SIGNAL OVERLOAD

Decreased tonic inhibition causes the brain to become overloaded with excitatory signals, resulting in a wide range of symptoms in AS patients.

WAS RESTORATION THE WAY FORWARD?

Restoring tonic inhibition may improve several symptoms of AS, such as motor function, sleep, and behavioral aspects.

THE ROAD TO GABOXADOL: PROMISING PRECLINICAL LEARNINGS

The ideal $GABA_A$ inhibitor was gaboxadol—which was initially explored for other neurological conditions

In AS mouse model, OV101 (gaboxadol):

- Restored tonic inhibition
- Corrected motor activity
- Improved gait and balance
- Improved cognition and memory

CONTROL | **AS MOUSE MODEL (UBE3A DEFICIENT)** | **TREATED WITH OV1010**

Source: Egawa et al., Decreased tonic inhibition in cerebellar granule cells causes motor dysfunction in a mouse model of Angelman Syndrome. *Science Translational Medicine* **4,** 163ra157, 5 December 2012

ENTERING THE CLINICAL STAGE

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ALIGNING THE STARS …

ENTER THE PHASE 2 STARS STUDY WITH OV101

- The first industry-sponsored, international, randomized, double-blind, placebo-controlled clinical trial in adults and adolescents with Angelman syndrome.
- 88 individuals with AS were enrolled
- Investigated safety parameters as well as exploratory efficacy endpoints

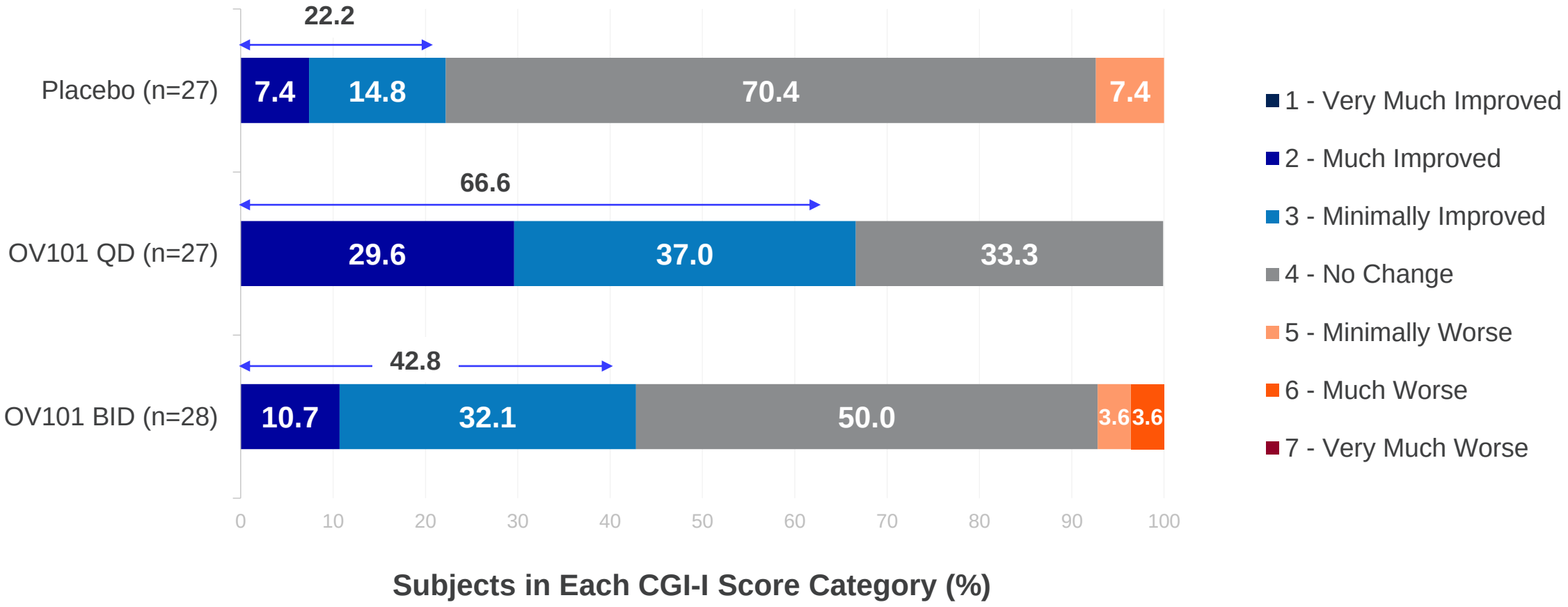
STARS CLINICAL TRIAL

FDA FAST TRACK DESIGNATION

AMERICAN ACADEMY OF NEUROLOGY® TOP SCIENCE PROGRAM

European Commission ORPHAN DRUG DESIGNATION

STARS PHASE 2 STUDY MET SAFETY AND TOLERABILITY ENDPOINT AND ALSO SHOWED EFFICACY



FOLLOWING THE LIGHT WITH NEPTUNE

IT'S TIME FOR PHASE 3

- Phase 3 NEPTUNE trial, a randomized, double-blind, placebo-controlled, 12-week trial of OV101 in pediatric patients with Angelman syndrome
- CGI-I-AS as a primary endpoint

THE DETAILS

- Study began in Sept 2019
- Last enrollments expected early 2020
- Anticipated data by mid 2020

NEPTUNE INCLUSION AND EXCLUSION CRITERIA SIMILAR TO PHASE 2 STARS STUDY

Key Inclusion Criteria

- Genetic diagnosis of AS
- Ages 4-12yr, plus age 2-3yr safety only
- Has a CGI-S-AS score of 3 or more
- Meets the following age-appropriate body weight criteria:
  - Subjects 2 to 3 years old must have a minimum body weight of 9 kg
  - Subjects 4 years and older must be between 17 kg and 64 kg (inclusive)

Key Exclusion Criteria

- Has poorly controlled seizures
- Cannot tolerate wearing the actigraph during the 28-day screening period of the study
- Use of benzodiazepines, zolpidem, zaleplon, zopiclone, eszopiclone, barbiturates, or ramelteon for sleep, or minocycline or levodopa within the 4 weeks prior to Day 1 or during the study

NEPTUNE STUDY DESIGN

THE CGI-I-AS ENDPOINT IN NEPTUNE

THE WHAT

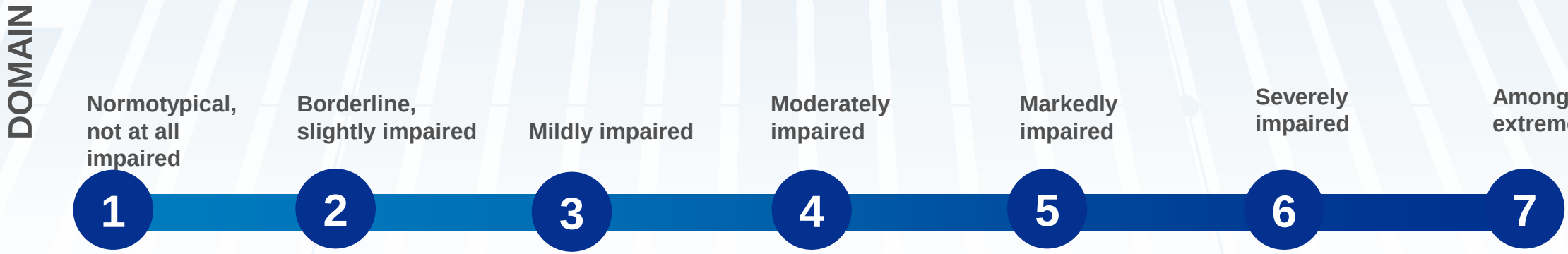
CGI-I-AS measures the change (i.e. clinical improvement/worsening) after an individual with AS has started treatment

THE HOW

Clinicians ask the caregiver of the individual with AS **to recall symptoms during the last of 4 weeks**

- For NEPTUNE, CGI-I-AS will be observed at Week 6 and Week 12 visits

A CLOSER LOOK AT THE CGI-S-AS SEVERITY SCALE



BEHAVIOR						
Normotypical typical child	**May interfere** with day-to-day functioning	**Mildly interferes** with day-to-day functioning May start to impact outings to community	**Moderately interferes** with day-to-day functioning Community outings **may** require preparation	**Markedly interferes** with day-to-day functioning Community outings are only possible with **moderate** preparation	**Severely interferes** with day-to-day functioning Community outings are only possible with **extensive** preparation	**Profoundly interferes** with day-to-day functioning Outings to community are **rare**

WHAT MEASURED CHANGE MEANS FOR PATIENTS AND FAMILIES

Physician and parent observations illustrating CGI-I from STARS trial

> *For the first time ever, she could walk down stairs without assistance, open screw tops, and purposely use a garage opener*

> *She could for the first time help with activities of daily living like undressing, she independently went to the fridge to obtain the medicine, it was unconceivable before that she could do such a thing*

> *It was like a veil was lifted, and for the first time there was social and cognitive awareness and engagement*

> *It was as if a light bulb was turned on in the brain*

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WE WERE NEVER IN THE FIGHT ALONE

AS ADVOCACY IS HELPING TO BRING NOVEL TREATMENT TO PATIENTS—FASTER AND SOONER THAN WE EVER THOUGHT POSSIBLE

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THE AS COMMUNITY IS POISED FOR POTENTIAL TREATMENTS TO CHANGE MEDICAL PRACTICE

CAN'T STOP

- Advancing new thinking to the treatment landscape
- Redefining clinical measures that are more patient-centric

WON'T STOP

- Being the innovation advocate thousands are depending upon
- Our commitment to the AS community

תודה.
שאלות?


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