ZELIRA THERAPEUTICS

Global biopharmaceutical company developing and marketing clinically validated cannabinoid-based medicines

US FDA New Drug Approval (NDA) Program

HOPE® 1 for treatment of irritability in Phelan McDermid Syndrome (PMS) comorbid with Autism Spectrum Disorder (ASD)

ASX: ZLD
OTCQB:ZLDAF
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Executive Summary

Proprietary platform of cannabinoid medicine

HOPE® 1 is a THC:CBD oral solid capsule

Large pipeline potential on the back of lead programs

Strong IP position

Drug candidates targeting cluster symptoms associated with Autism Spectrum Disorder (ASD)

Near-term development milestones

Initial focus - Phelan McDermid Syndrome (PMS) co-morbid with ASD per pre-IND meeting held Q2 2024

Multiple targets within the ASD indication

Progressed company in a capital-efficient manner

Phase 2 PoC trial to start immediately upon IND opening

Can proceed to Phase 3 pivotal trials as soon as Q2 2026

Aim for NDA submission as early as Q2 2027

Clinically validated, highly de-risked ASD treatment

Unique “Launch, Learn, Develop” model and approach to real-world data

Zelira has spent many years collecting real-world patient data to develop an optimized therapeutic and clinical plan for this population

Zelira is seeking US$35M to complete FDA clinical trials and registration for its HOPE® 1 drug candidate, targeting Autism Spectrum Disorder (ASD)

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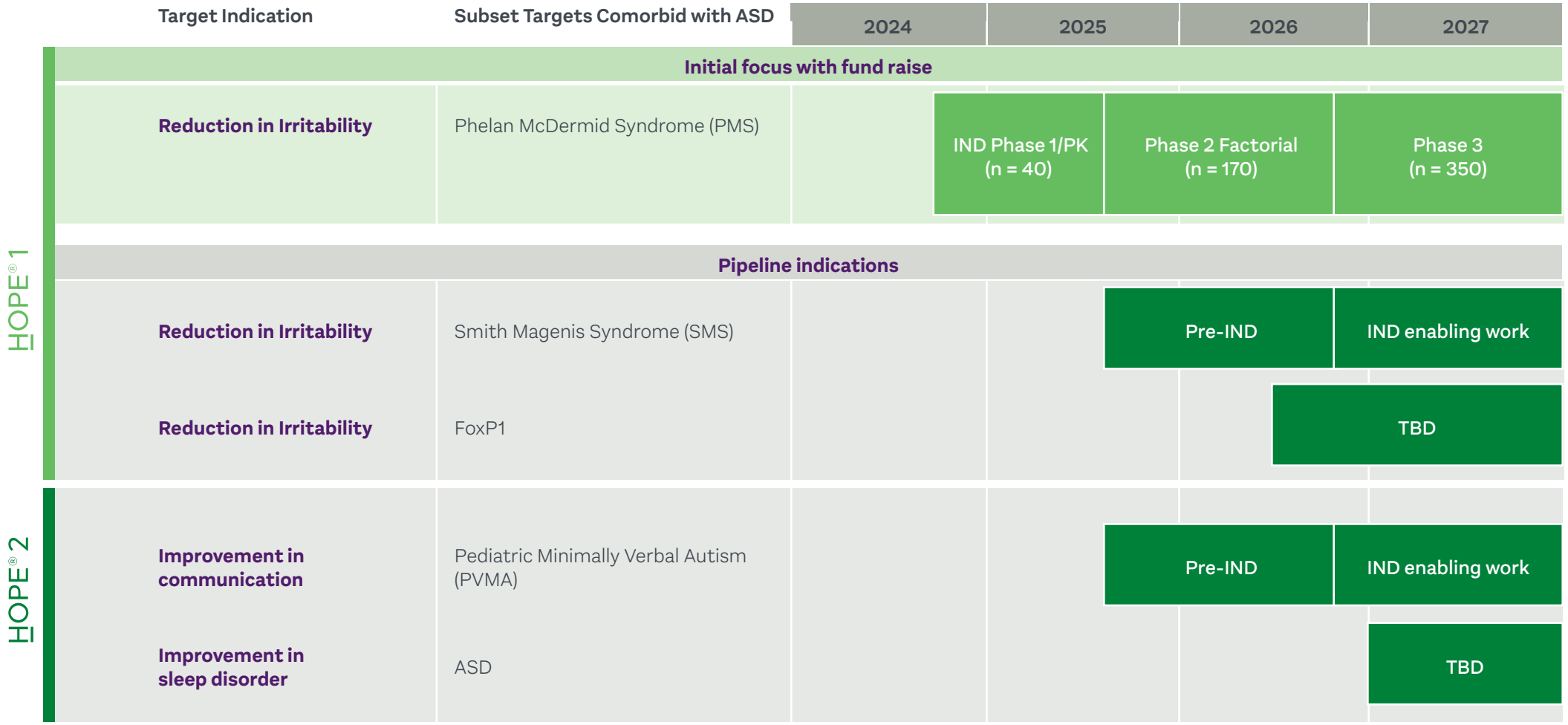
HOPE® 1 and HOPE® 2 development pathway for indications within Autism Spectrum Disorder (ASD) subset



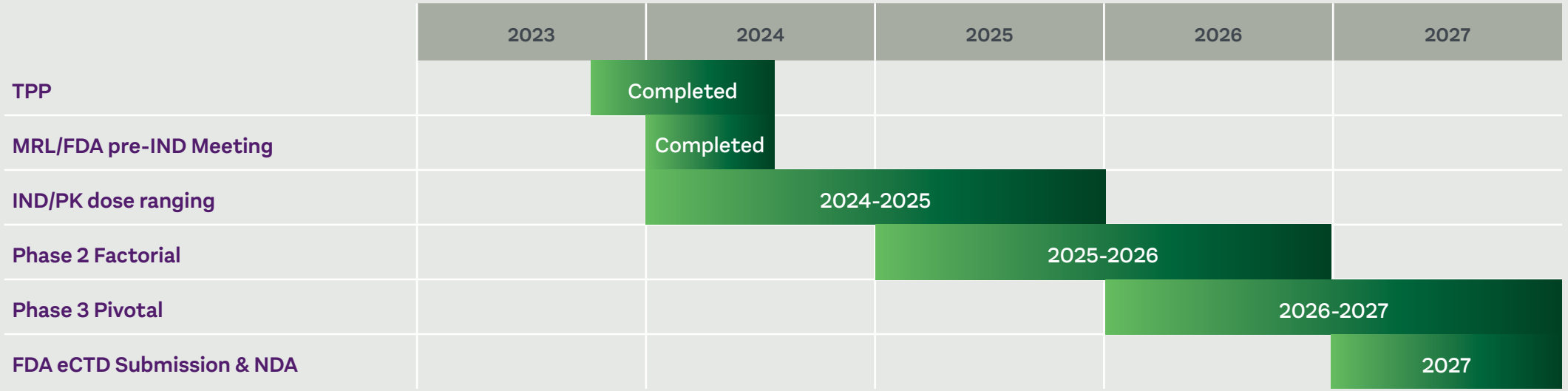
Development pathway for HOPE® 1 Phelan McDermid Syndrome (PMS) program

Phelan-McDermid Syndrome (PMS)

Ultra-rare genetic condition caused by a deletion or change of chromosome 22 in the 22q13 region or disease causing (pathogenic) variant of the SHANK3 gene. Most affected individuals have moderate to profound intellectual disability and a very high prevalence of ASD.

Regulatory Pathway

Accelerated regulatory pathway strategy utilizing existing pre-clinical, USDMF and CMC data sets already generated by Zelira through its Launch, Learn and Develop strategy and clinically-validated real-world patient data, using the FDA 505(b)(2) pathway.



Pre-IND meeting held in June 2024; feedback was to proceed in Autism Spectrum Disorder (ASD) subset indication, irritability associated with PMS patients

Zelira's unique rapid commercialisation strategy

Launch

Generate proprietary formulations

Launch products in global markets

Rapid path to revenues

Low Capex model

HOPE® 1 launched in Pennsylvania in 2020 and subsequently in Washington DC, Louisiana and Australia under the TGA Special Access Program

Learn

Collect real-world patient data

Refine product to meet patient needs

Real-time response to market

Over 11 Million doses of HOPE® 1 dispensed in Pennsylvania over the past five (5) years without any negative safety signal

All sales in the US are out of pocket payments by parents that buy HOPE® 1 to administer to their children with ASD, on a consistent, repeated, monthly basis

Develop

Patient data informs and de-risks design of clinical trial

Supports path to registration

Proprietary HOPE® 1 product currently on the market as a tincture, reformulated into a free-flowing powder and pharmaceutical grade capsule using Zelira's proprietary, patent protected ZYRAYDI™ technology

The formal FDA trials for HOPE® 1 represents the third and final stage of our Launch, Learn, Develop strategy for validation and commercialization

ZYRAYDI™ (Enhanced Cannabinoid Capture and Dissolution Matrix)

- Breakthrough technology developed by Zelira
- Solves the problem of developing solid oral dosage forms from cannabinoid distillate
- Zelira's unique, proprietary matrix prevents cannabinoid separation from the powder providing a free flow powder base for tablets and capsules
- This technology allows development of standardised pharmaceutical grade, cannabinoid-based medicines in solid oral dosage
- A move from extracts (oils) to capsules and tablets enhances patient and HCP familiarity and increased acceptance of cannabinoid-based medicines

The ZYRAYDI™ matrix contains pharmaceutical grade excipients that are on the FDA-approved list of GRAS (Generally Recognized As Safe) ingredients

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US FDA Clinical Trials

HOPE® 1 – Treatment of Irritability in PMS Comorbid with Autism Spectrum Disorder (ASD)

HOPE® 1 - Target Product Profile (TPP)

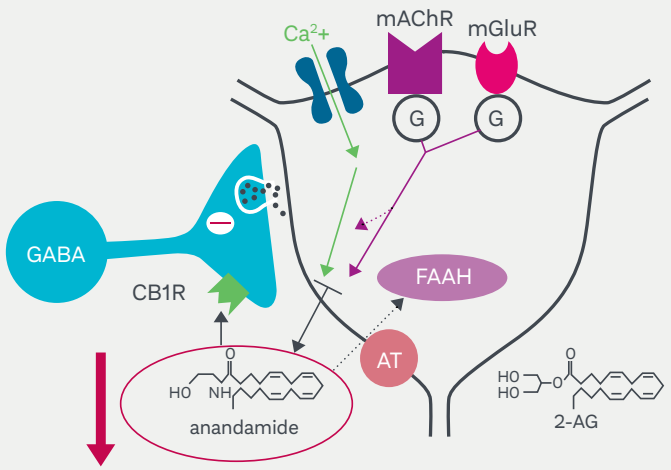
Drug Substances	HOPE® 1
Drug Product	CBD:THC (1:1)
Clinical Phase	1, 2 & 3 with PK/BE
Endpoint Strategy	Reduction in the Aberrant Behavior Checklist - Irritability Subscale (ABC-I)
Regulatory Authority for Product Registration	US FDA

Route of Administration	Oral solid capsule (size 2) - 1.25mg and 2.5mg THC/CBD capsules
Indication	Monotherapy - Treatment of irritability and ASD symptoms in adolescents with Phelan McDermid Syndrome (PMS) co-morbid with ASD
Study Population	Adult/Pediatrics
Location(s) (Jurisdiction) of Clinical Trial	Australia (TGA) /US (FDA)

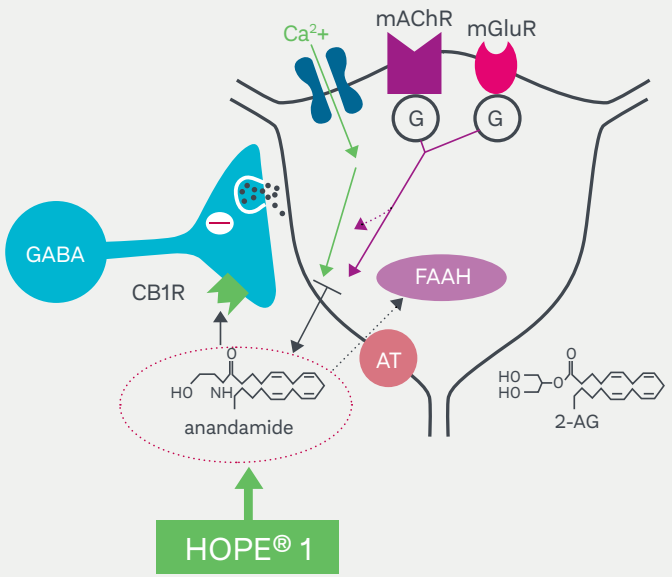
HOPE® 1 CBD:THC (1:1) targets anandamide signal and activity to improve Autism Spectrum Disorder (ASD) cluster symptoms in PMS population

Anandamide is an endogenous cannabinoid that mimics the effects of THC by interacting with the same receptors

Blocking CB1 receptors, which are neuronal targets of anandamide decreased anandamide signal and activity that correlates with decreased neuronal integrity



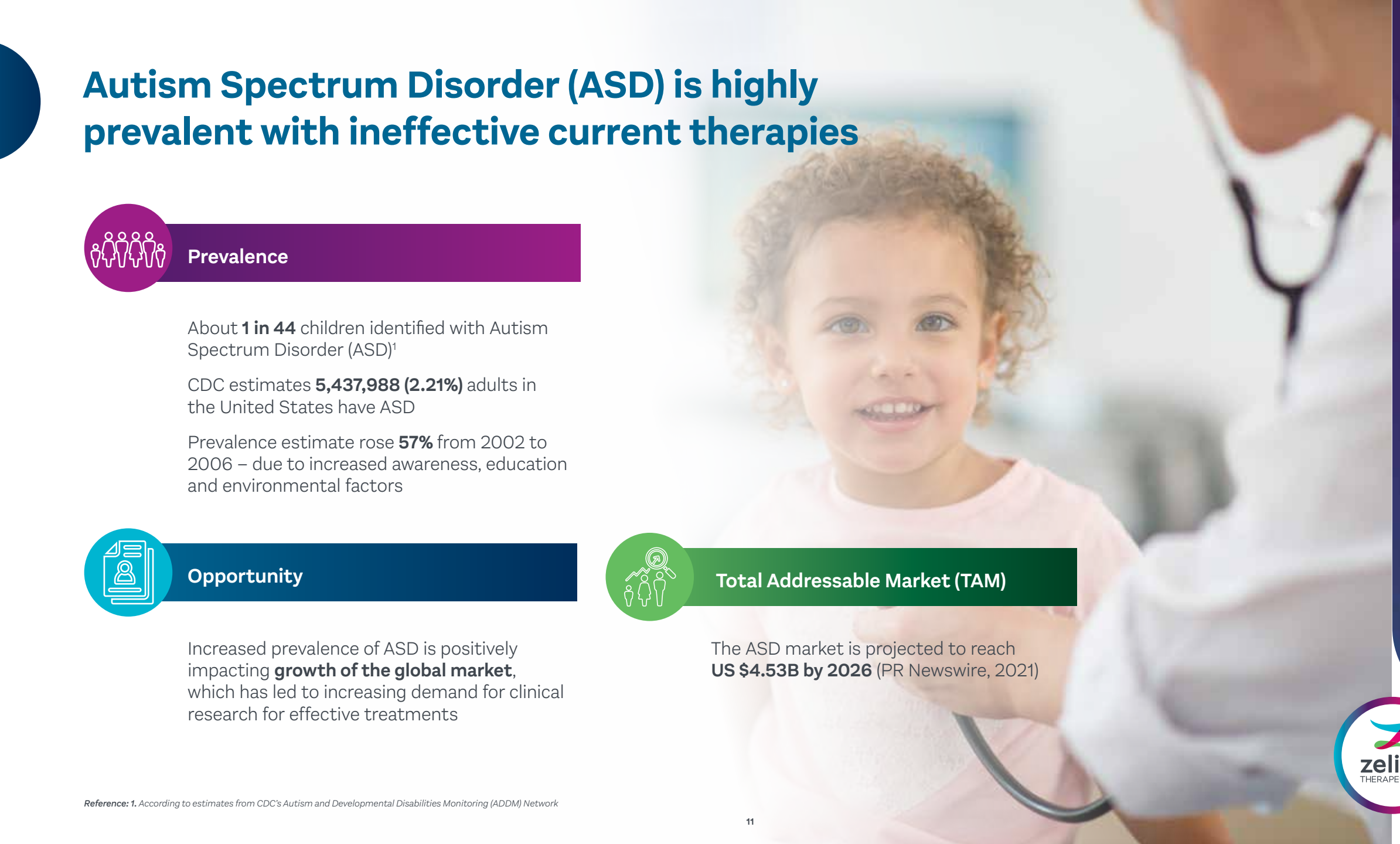
HOPE® 1 modulates enhancement of anandamide signal and activity toward typical neuronal integrity by increasing activity at CB1 receptors may improve social impairment related to ASD



The fatty acid amide arachidonylethanolamide (anandamide) is the prototypical endocannabinoid, i.e., an endogenous ligand of the G protein coupled cannabinoid receptor in the brain, CB1, which binds the main psychoactive component of marijuana and other derivatives of Cannabis sativa.[1] N-Acetylaspartic acid (NAA), the highly abundant neurochemical in the brain correlates with neuronal integrity.[2]

References: 1. *Devane, W. A., Hanus, L., Breuer, A., Pertwee, R. G., Stevenson, L. A., Griffin, G., Gibson, D., Mandelbaum, A., Etinger, A. & Mechoulam, R. (1992) Science 258, 1946–1949.* ***2.*** *Kleinhans NM, Schweinsburg BC, Cohen DN, et al. N-acetyl aspartate in Autism Spectrum Disorders: regional effects and relationship to fMRI activation. Brain Res. 2007;1162:85–97.*

Autism Spectrum Disorder (ASD) is highly prevalent with ineffective current therapies



Prevalence

About **1 in 44** children identified with Autism Spectrum Disorder (ASD)[1]

CDC estimates **5,437,988 (2.21%)** adults in the United States have ASD

Prevalence estimate rose **57%** from 2002 to 2006 – due to increased awareness, education and environmental factors

Opportunity

Increased prevalence of ASD is positively impacting **growth of the global market**, which has led to increasing demand for clinical research for effective treatments

Total Addressable Market (TAM)

The ASD market is projected to reach **US $4.53B by 2026** (PR Newswire, 2021)

Reference: 1. *According to estimates from CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network*

Current Antipsychotic and Antidepressant drugs are ineffective and carry significant safety risks in children

Existing Therapies

Global market is segmented into antipsychotic drugs, SSRIs/antidepressants, stimulants and sleep medications

Aripiprazole®, Risperidone®, and Melatonin® are FDA approved drugs targeting ASD behaviors. Bumetanide® and Balovaptan® are under clinical trial to evaluate safety and efficacy for the treatment of ASD. (Coherent Market Insights, 2021)

Safety Profile

- Increased fracture risk
- Weight grain/Increased appetite/increased anxiety and fatigue
- Sedation/Somnolence
- Hormonal Imbalance
- Extrapyramidal symptoms/Worsening akathisia
- Emesis

Warnings and Precautions

- Potential for cognitive impairment
- Motor skills impairment
- Cerebrovascular events
- GI Disturbances/Dysphagia/Emesis

HOPE® 1 Initial indication presents Orphan Drug Designation (ODD) Opportunity – Treatment of irritability in Phelan McDermid Syndrome (PMS) co-morbid with ASD

Phelan-McDermid Syndrome (PMS)

Ultra-rare genetic condition caused by a deletion or other structural change of the terminal end of chromosome 22 in the 22q13 region or a disease-causing (pathogenic) variant of the SHANK3 gene.

Most affected individuals have moderate to profound intellectual disability and a very high prevalence of ASD.

Zelira has an opportunity to register HOPE® 1 as an Orphan Indication within the Autism Spectrum Disorder with unmet need, Phelan-McDermid Syndrome (PMS) meets the FDA orphan status.

Achieving Orphan Drug Designation Status for HOPE® 1 will allow Zelira to secure 7 Years of Market Exclusivity in the USA and will allow for fast-tracked hybrid registration across other global markets such as the EMA in Europe. This opportunity also presents a strong potential for Priority Review Voucher (PRV)

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Real world evidence – HOPE® 1 improved Clinical Global Impression (CGI) and Efficacy Score in ASD patients

Background on HOPE® 1	• HOPE® 1 tincture launched under the TGA's Special Access Scheme B in Australia • Administered sublingually, optimal dosage not yet established at the start of the study • Targeting Autism Spectrum Disorder (ASD) • This study focused on real-world patient data to assess the product's impact on CGI scores.
Dataset & Analysis	• Data derived from Emyria's Emerald Clinics in Western Australia, Victoria, and New South Wales • Analyzed 45 initial dispensations of HOPE® 1, focusing on active, lapsed, and new patients. Additional data on 19 patients from Emerald Clinics
CGI Assessment	• Clinicians used the CGI scale to assess: • Severity of Illness • Global Improvement • Therapeutic Effect • Side Effects • Derived CGI Efficacy Index, CGI Improvement, and CGI Severity scores from these assessments
Patient Demographics	• Majority of patients prescribed HOPE® 1 were children, with a mean age of 14.1 years • Active patients had a mean treatment time of 4.8 months; lapsed patients averaged 1.8 dispenses
Dosing Information	• Patients underwent a 2-3 month dose escalation phase before reaching maintenance doses
	• Younger patients averaged 12.6mg THC: 12.6mg CBD per day
	• Older patients averaged 17.9mg THC: 17.9mg CBD per day
Adverse Events	• 25 adverse events reported in 9 patients: sedation, changes in appetite, neurological changes, slurred speech, gastrointestinal issues, eye redness, and mood changes. 7 patients were on concomitant medications • Clinicians reported that AE's were generally transient and resolved within 24 hours
Dosing Recommendations	• Recommended a structured approach to dose escalation over 2-4 weeks, followed by maintenance dosing
	• Suggested dosing schedule included morning, afternoon, evening, and bedtime doses
A Patient Case Study	• A young male with ASD showed marked behavioral improvements, reduced aggression, and better impulse control after two weeks on HOPE® 1. His family noted a significant positive change, considering HOPE® 1 as providing "hope for a future"

After 1 month, 56% showed minimal improvement

After 3 months, 50% showed moderate improvement

After 4 months, 60% showed marked improvement

By 5 months, 100% of patients showed improvement

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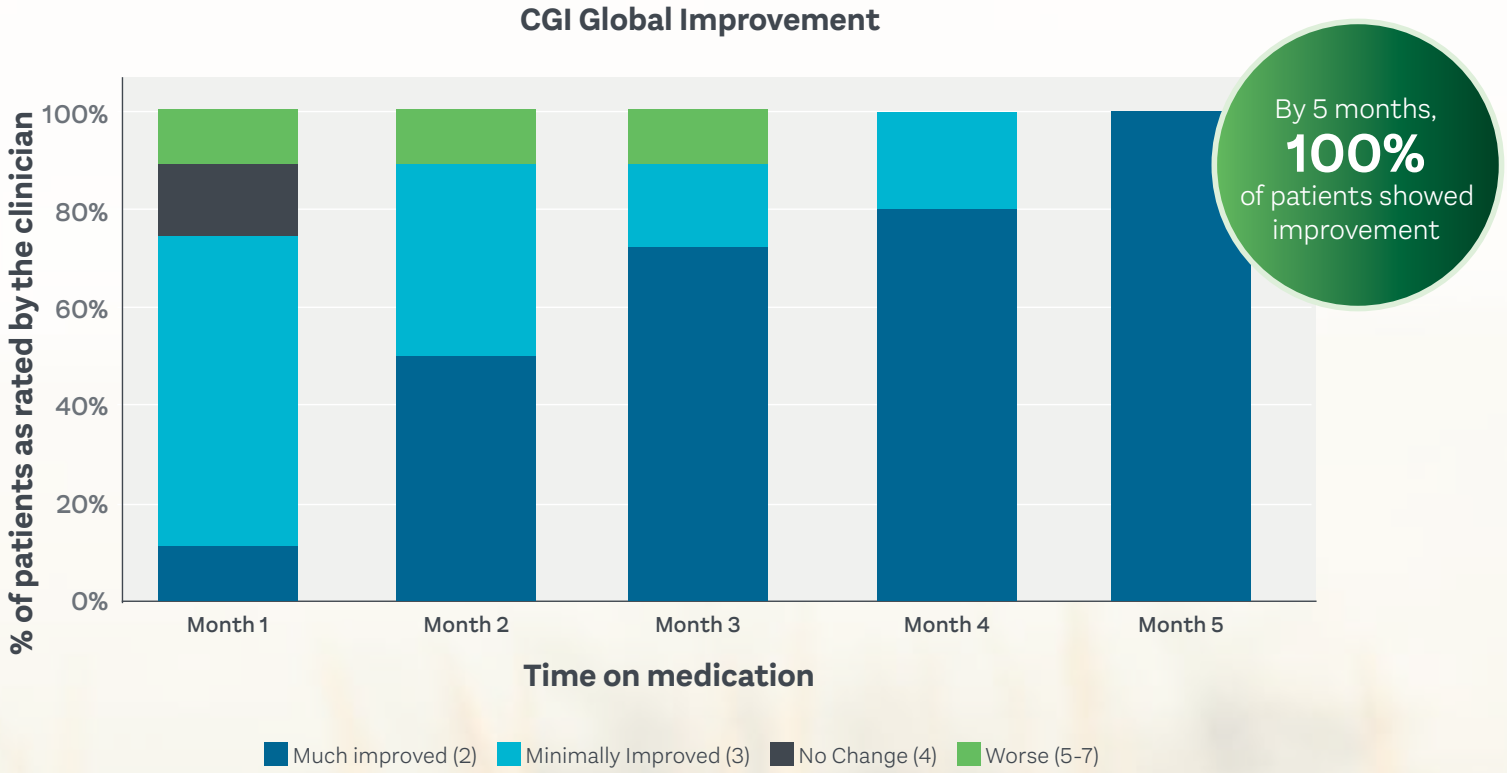
Real world evidence – HOPE® 1 improved Clinical Global Impression (CGI) and Efficacy Score in ASD patients



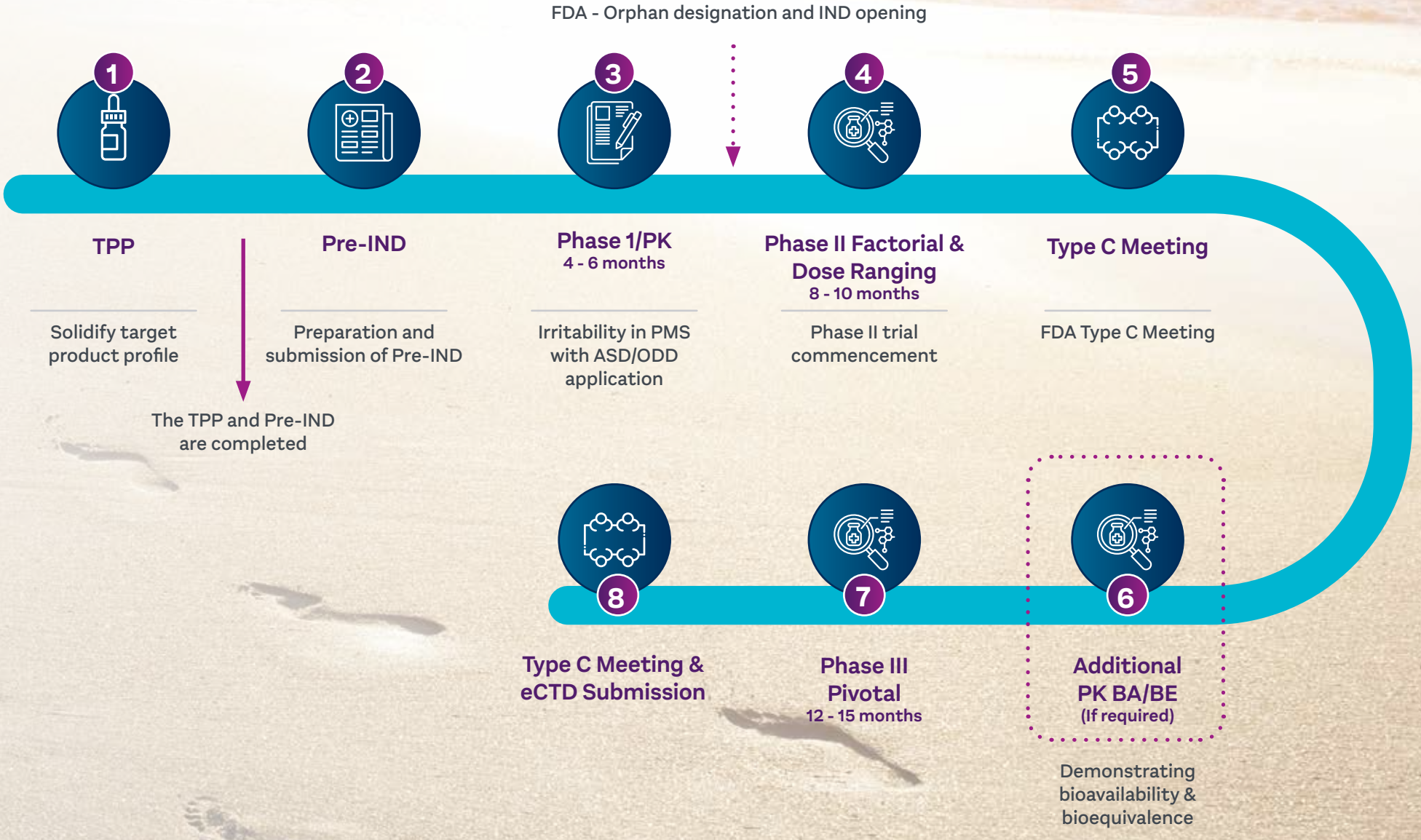
By 5 months, **100%** of patients showed improvement

Improvements in CGI Global were observed with generally increasing improvements the longer the patient was on treatment

OBJECTIVE	Investigate the effect of HOPE® 1 on behavioural symptoms in people with ASD
ENDPOINTS	Improvement in CGI scores (Clinician and Caregiver)
PATIENTS	N=45
PATIENT AGE	Mean age of patients was 14.1 years of age; the youngest patient was 5.1 years
DURATION	Mean time on treatment was 4.8 months; maximum treatment time to-date was 8.9 months

Meghan Thomas and Christopher Frampton, "HOPE® 1 Demonstrates Improvements in Clinical Global Impression (CGI) in Patients with Autism Spectrum Disorder," Zelira Therapeutics, March 2022.

Full pathway to US-FDA in 36 months



iNGENū CRO

- Global Contract Research Organization (CRO) working exclusively in the cannabinoid and psychedelic space
- Zelira HOPE® 1 SPV appointed iNGENū as its CRO to lead clinical validation and US FDA registration
- iNGENū will drive clinical trials and pivotal studies for approval and licenses required for commercialization
- iNGENū and its US based affiliate, Purysis, hold Schedule 1 licenses and the DEA and FDA licenses required to conduct the HOPE® 1 trials in Australia and the United States
- iNGENū and its US based affiliate, Halo, have a US based manufacturing facility fully licensed to provide clinical trial and commercial product for HOPE® 1

Successful and positive FDA Pre-IND meeting

Prompt FDA response	U.S. FDA responded quickly to Zelira's Pre-IND meeting request, demonstrating the Agency's engagement in advancing the HOPE® 1 program
Positive feedback on study design	The FDA provided valuable guidance on the design of the IND-opening Phase 1 study, reinforcing the scientific rigor of Zelira's proposed clinical development plan
Support for target population	The FDA acknowledged the potential link between Phelan-McDermid Syndrome (PMS) and Autism Spectrum Disorder (ASD), supporting our rationale for targeting these populations in the clinical trials
Clear direction on bridging studies	The FDA accepted Zelira's justification for the low CBD dose in ZEL-HOP1 compared to Epidiolex® and provided clear guidance on the design of bridging studies, including the possibility of single-dose studies with Marinol®
Flexibility on study components	The FDA agreed that omitting the Single Ascending Dose (SAD) component from the Phase 1 study was reasonable, allowing us to streamline the study design
Guidance on dosing and ratios	The FDA provided insights on optimizing the ratio of THC and CBD in ZEL-HOP1, which will help us fine-tune the formulation for maximum efficacy and safety
Confirmation on PK sampling	The FDA recommended longer pharmacokinetic (PK) sampling periods to adequately characterize the terminal elimination phase of CBD, aligning with the pharmacological profile of oral CBD products
Ethical considerations supported	The FDA supported Zelira's approach to limiting PK sampling when drug levels are no longer measurable, aligning with our ethical considerations in study design

Zelira has made significant progress in its HOPE® 1 program following a successful Pre-IND meeting with the FDA, setting the stage for the IND submission and the launch of Phase 1 clinical trials.

Thank You

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