

20 July 2026

PRESENTATION AT 2026 PMS FOUNDATION FAMILY CONFERENCE

- **PYC is a precision medicine company dedicated to changing the lives of patients with genetic diseases who have no treatment options available**
- **The Company is developing a drug candidate (known as PYC-002) that addresses the underlying cause of a severe neurodevelopmental disorder known as Phelan-McDermid Syndrome (PMS)**
- **PMS affects 1 in every 7,300 children and there are no approved treatment options available for PMS patients¹**
- **The Company today announces that it is presenting at the PMS Foundation Family Conference held in Colorado, USA from 15-19 July 2026. The presentations include new data² generated in patient-derived models supporting the disease-modifying potential of PYC-002 - this updated data demonstrates that:**
 - **The increase in SHANK3 protein expression observed following treatment with PYC-002 maintains the natural isoform balance of the target gene³; and**
 - **Treatment with PYC-002 restores neuronal (brain cell) communication deficits in PMS patient-derived models to levels observed in models derived from unaffected individuals⁴**
- **PYC is currently completing IND-enabling⁵ studies of PYC-002 to support progression of the drug candidate into clinical studies in 2026⁶ and 2027⁷**

¹ Levy, T., D. Lapidus, K. Friedman, et. al. "Prevalence of Phelan McDermid syndrome Estimated To Be ~1:7300 Using a Multisource Model." *Autism Research*. 2026. <https://doi.org/10.1002/aur.70297>.

² "PYC-002, a disease modifying RNA therapeutic approach to treat Phelan-McDermid syndrome" presentation and poster attached to this ASX Announcement of 20 July 2026

³ SHANK3 shows a distinct protein isoform expression profile in each brain region implicated in PMS. Upregulation of the target gene in a manner that maintains the natural isoform balance of SHANK3 across the brain and supports region-specific neuronal function maximises the likelihood of functional correction of the deficits associated with PMS.

⁴ Multi-Electrode Array (also called microelectrode array) is a non-invasive electrophysiology platform in which neurons are cultured directly on top of a grid of microelectrodes embedded in the base of the culture plate. Those electrodes record the extracellular voltage changes that neurons generate as they fire, allowing real-time, longitudinal recording of electrical activity over hours, days, or weeks without disturbing the cells.

⁵ IND = Investigational New Drug

⁶ PYC expects to initiate a Natural History Study in PMS in 2026. Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026 and alignment with relevant regulatory authorities.

⁷ PYC expects to initiate first-in-human interventional trials in 2027. Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026 and alignment with relevant regulatory authorities.

PERTH, Australia and SAN FRANCISCO, California – 20 July 2026

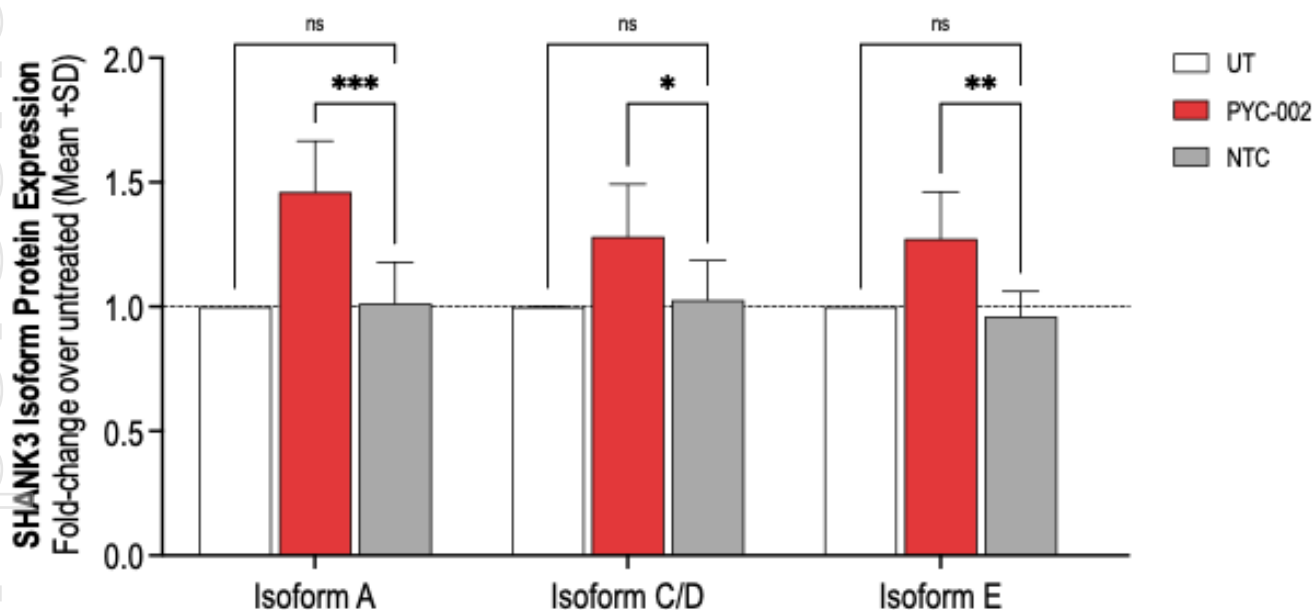
PYC Therapeutics Limited (ASX:PYC) (PYC or the Company) is a precision medicine Company dedicated to changing the lives of patients with genetic diseases who have no treatment options available.

The Company currently has three clinical-stage drug development programs in addition to a fourth drug candidate (known as PYC-002) that addresses the underlying cause of Phelan-McDermid Syndrome (PMS).

PYC today announces that it is presenting at the PMS Foundation Family Conference held in Colorado, USA from 15-19 July 2026. The Company's presentations will include new data generated in patient-derived models supporting the disease-modifying potential of PYC-002 – specifically, this updated data demonstrates that:

- The increase in SHANK3 protein expression observed following treatment with PYC-002 maintains the natural isoform balance of the target gene (See Figure 1)⁸; and
- Treatment with PYC-002 restores neuronal communication deficits in patient-derived models of the brain to 'unaffected' levels (See Figure 2)⁹

Figure 1. Treatment of PMS patient-derived neurons (brain cells) with PYC-002 increases all four isoforms of the SHANK3 protein in a manner not seen with the Non-Targeting Control (NTC) oligonucleotide¹⁰. Maintenance of the physiological isoform balance of the target gene supports the potential of PYC-002 to restore the function of the neurons affected by the insufficient levels of *SHANK3* in patients with PMS.



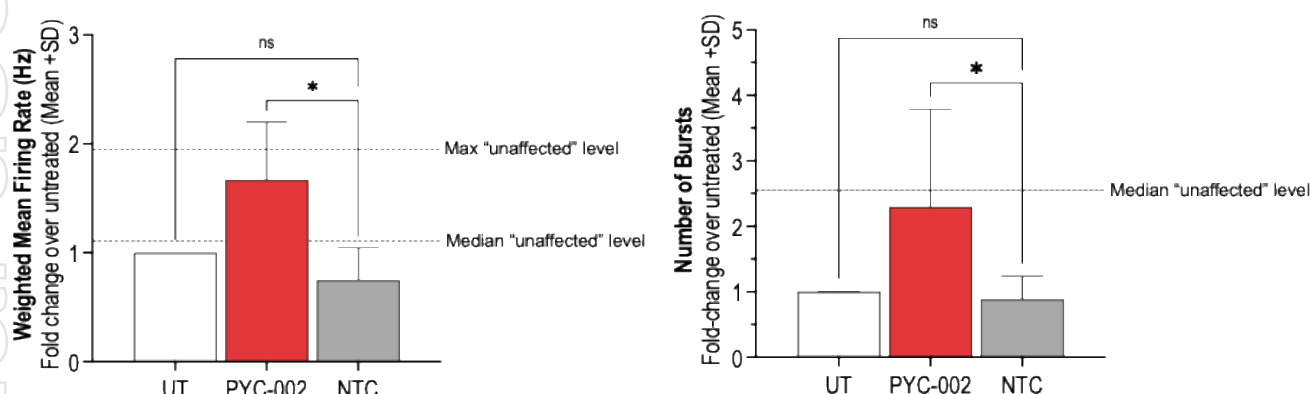
⁸ *SHANK3* shows a distinct protein isoform expression profile in each brain region implicated in PMS. Upregulation of the target gene in a manner that maintains the natural isoform balance of *SHANK3* across the brain and supports region-specific neuronal function maximises the likelihood of functional correction of the deficits associated with PMS.

⁹ Multi-Electrode Array (also called microelectrode array) is a non-invasive electrophysiology platform in which neurons are cultured directly on top of a grid of microelectrodes embedded in the base of the culture plate. Those electrodes record the extracellular voltage changes that neurons generate as they fire, allowing real-time, longitudinal recording of electrical activity over hours, days, or weeks without disturbing the cells.

¹⁰ Each bar represents the mean + standard deviation (SD) of 4 biological replicates of the *SHANK3* isoform protein fold-change over the untreated samples (white bars) assessed by Western Blot after 21 days post-gymnotic-treatment with PYC-002 (red bars) or non-targeting control (NTC, grey bars) in three PMS patient-derived induced pluripotent cell (iPSCs) derived glutamatergic neurons. Table shows the percentage of each *SHANK3* isoform normalised to the total *SHANK3* protein in each treatment group using a representative PMS patient-derived neuron. Note that isoforms C and D are measured together. Significance against the NTC group was calculated using two-way ANOVA. ns= non-significance; * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

Patient A	UT	Treated	NTC
Isoform A	~34%	~38%	~34%
Isoform C/D	~41%	~41%	~41%
Isoform E	~25%	~20%	~25%

Figure 2. PYC-002 restores neuronal communication deficits to ‘unaffected’ levels in PMS patient-derived neurons¹¹ in a manner not seen with the Non-Targeting Control (NTC) oligonucleotide.



A full copy of the materials presented at the conference is attached to this announcement.

Next Steps

PYC is currently completing IND-enabling studies for PYC-002 to enable progression into clinical trials in 2027¹².

¹¹The left plot shows the mean+SD of weighted mean firing rate (Hz), expressed as fold-change relative to untreated samples (white bar) measured by Multiple-Electrode Array (MEA) assay after 28 days post-gymnotic-treatment with PYC-002 (red bar) or non-targeting control (NTC, grey bar). Bars represent three biological replicates of iPSC-derived glutamatergic neurons from three different patients with PMS. The right plot shows the mean+SD of Number of Bursts fold-change over untreated samples (white bar) measured by MEA assay after 28 days post-gymnotic-treatment with PYC-002 (red bar) or NTC (grey bar). Bars represent three biological replicates of iPSC-derived glutamatergic neurons from three different patients with PMS. The median and maximum (Max) of unaffected levels were calculated using iPSCs glutamatergic neurons derived from eight unaffected lines. These values were compared as fold-change with untreated PMS measurements (white bar). Significance against the NTC group was calculated using Kruskal-Wallis and Dunnet test. ns = non-significance; * $p < 0.05$.

¹² Subject to the risks and uncertainties outlined in the Company's ASX disclosures of 2 February 2026 and alignment with relevant regulatory authorities.

About PYC Therapeutics

PYC Therapeutics (ASX: PYC) is a clinical-stage biotechnology company creating a new generation of RNA therapies to change the lives of patients with genetic diseases. The Company utilises its proprietary drug delivery platform to enhance the potency of precision medicines within the rapidly growing and commercially proven RNA therapeutic class. PYC's drug development programs target monogenic diseases – the indications with the highest likelihood of success in clinical development¹³.

For more information, visit pyctx.com, or follow us on [LinkedIn](#).

Forward looking statements

Any forward-looking statements in this ASX announcement have been prepared on the basis of a number of assumptions which may prove incorrect and the current intentions, plans, expectations, and beliefs about future events are subject to risks, uncertainties and other factors, many of which are outside the Company's control. Important factors that could cause actual results to differ materially from assumptions or expectations expressed or implied in this ASX announcement include known and unknown risks. Because actual results could differ materially to assumptions made and the Company's current intentions, plans, expectations, and beliefs about the future, you are urged to view all forward-looking statements contained in this ASX announcement with caution. The Company undertakes no obligation to publicly update any forward-looking statement whether as a result of new information, future events or otherwise.

This ASX announcement should not be relied on as a recommendation or forecast by the Company. Nothing in this ASX announcement should be construed as either an offer to sell or a solicitation of an offer to buy or sell shares in any jurisdiction.

This ASX announcement was approved and authorised for release by the Board of PYC Therapeutics Limited

CONTACT US

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¹³ Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank
<https://doi.org/10.1101/2020.11.02.2022232>



PYC Therapeutics

Life-changing science

PYC-002, a disease modifying RNA therapeutic approach
to treat Phelan-McDermid syndrome

2026 PMSF Family Conference



Disclaimer



The purpose of this presentation is to provide an update of the business of PYC Therapeutics Limited (ASX:PYC) ['PYC']. These slides have been prepared as a presentation aid only and the information they contain may require further explanation and/or clarification. Accordingly, these slides and the information they contain should be read in conjunction with past and future announcements made by PYC Therapeutics and should not be relied upon as an independent source of information. Please contact PYC and/or refer to the Company's website for further information.

The views expressed in this presentation contain information derived from publicly available sources that have not been independently verified. No representation or warranty is made as to the accuracy, completeness or reliability of the information.

Any forward looking statements in this presentation have been prepared on the basis of a number of assumptions which may prove incorrect and the current intentions, plans, expectations and beliefs about future events are subject to risks, uncertainties and other factors, many of which are outside PYC's control. Important factors that could cause actual results to differ materially from assumptions or expectations expressed or implied in this presentation include known and unknown risks. Because actual results could differ materially to assumptions made and PYC's current intentions, plans, expectations and beliefs

about the future, you are urged to view all forward looking statements contained in this presentation with caution.

This presentation includes information about PYC's drug development pipeline. PYC's drug candidates are investigational or under development and not approved by any regulatory authority in any jurisdiction. The safety, efficacy or other desirable attributes of our unapproved drug candidates have not been established in patients or determined by any regulatory authority. This presentation is for corporate communication purposes only and is not intended as promotion or advertising to any audience in any jurisdiction.

This presentation may also contain statistical data and drug information based on independent sources, industry publications or other publicly available information. We have not independently verified the accuracy or completeness of such data and information. Accordingly, we make no representations as to the accuracy or completeness of such data or information. You are cautioned not to give undue weight to such data.

This presentation should not be relied on as a recommendation or forecast by PYC. Nothing in this presentation should be construed as either an offer to sell or a solicitation of an offer to buy or sell shares in any jurisdiction.

PYC-002 is a disease modifying approach that targets SHANK3 upregulation to treat Phelan-McDermid syndrome



- PYC is developing PYC-002, an antisense oligonucleotide for the treatment of Phelan-McDermid syndrome (PMS).
- PYC-002 is designed to target the underlying cause of PMS by increasing SHANK3 expression towards healthy levels.
- By restoring SHANK3, our goal is to help rebuild neuronal connections and improve communication between brain cells.
- The drug is administered via a lower back (IT) injection to deliver the medicine to the brain.
- PYC-002 is currently in the IND-enabling stage, with a natural history study launching in Q4 2026 and first clinical trials planned to begin in 2027.[#]

[#] Timelines are estimated and may change as studies progress

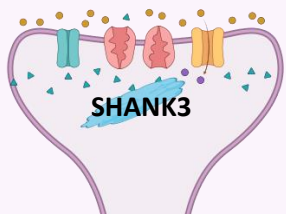
PYC-002 targeting the root cause of PMS to restore neuronal structure and improve connection between brain cells



PMS BIOLOGY: WHAT HAPPENS

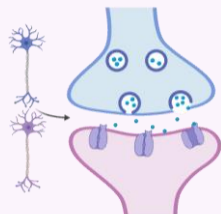
1 Reduced SHANK3

SHANK3 helps brain cells build and maintain healthy connections.



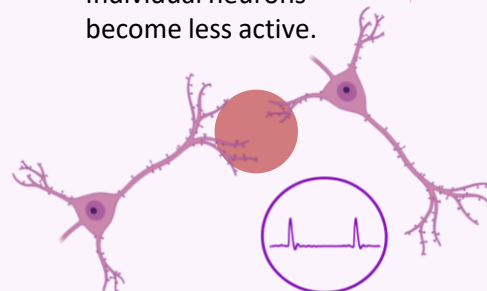
2 Fewer healthy connections

Brain cells are less well connected.



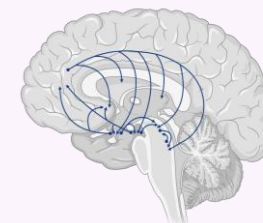
3 Reduced brain cell activity

Individual neurons become less active.



4 Less effective communication

Neural networks communicate less effectively.



5 Challenges in daily life

Impaired learning, communication and behavioral challenges.



Learning Communication Behavior

HOW PYC-002 IS DESIGNED TO HELP

PYC-002 is designed to restore SHANK3 – the underlying biology of PMS.



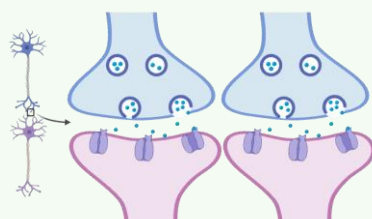
1 Increase SHANK3

PYC-002 is designed to increase the cell's own SHANK3 protein.



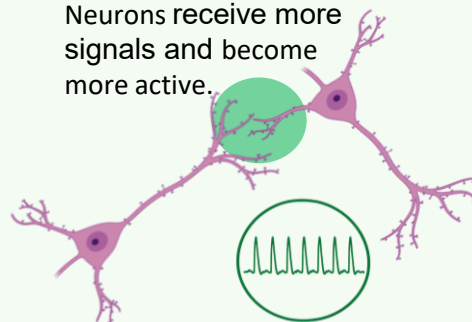
2 Restore brain cell connections

More SHANK3 helps rebuild and strength connection.



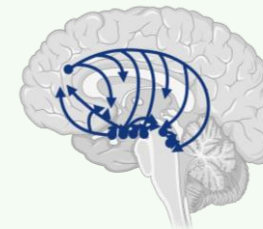
3 Restore brain cell activity

Neurons receive more signals and become more active.



4 Improve communication between brain cells

Neural networks communicate more effectively.



Potential to improve the symptoms of PMS

By targeting the root cause of PMS, PYC-002 has the potential to be a disease-modifying therapy.

PYC-002 is a precision ASO designed to restore SHANK3

What is an ASO?

An ASO is synthetic, short strings of RNA/DNA designed to target the disease at the RNA level—the direct middle step between our DNA blueprint and the protein itself.



- Designed to be highly specific to target
- Optimized for stability to support durable benefits
- Several ASO drugs are already approved and have been used in the clinic

Why this approach?



Specifically target SHANK3 – the root cause of PMS



Uses the cell's good copy of the SHANK3 gene to make more SHANK3 protein



Maintains the cell's natural control and balance



Designed to increase SHANK3 where it is needed



Built on a clinically validated ASO technology

PYC-002 is delivered by intrathecal (IT) injection, allowing it to reach target brain regions to restore SHANK3 towards healthy levels

What is an IT injection?

A small amount of drug is gently injected into the cerebrospinal fluid through the lower back.

Why IT injection

Allows the transport and delivery of the drug to the brain for an efficient targeting of SHANK3 in neurons.

Our goal

To deliver the right amount of drug to the right place, to help make the biggest possible difference.



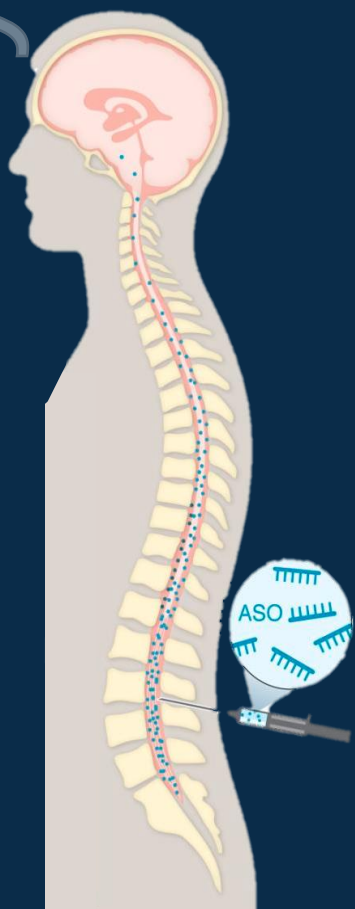
Safety is our priority

IT injection are commonly used in patients for several approved ASOs (>10 years) and late-stage clinical studies; and are generally considered safe.



How often will the drug be given?

Intrathecal delivery of ASOs has supported durable brain drug exposure. Dosing is given a few times per year (as determined by the study).



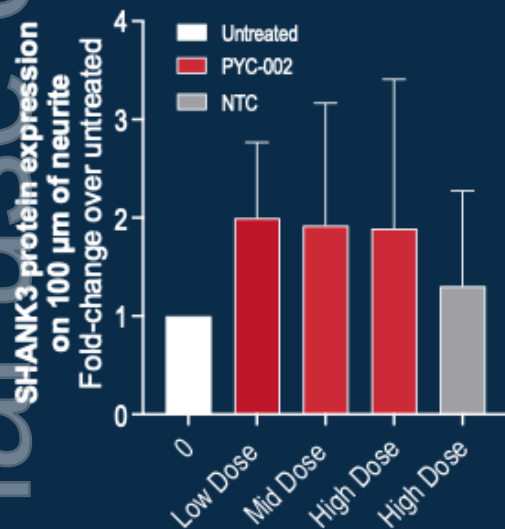
Encouraging evidence in pre-clinical studies supports PYC-002 moving towards clinical studies



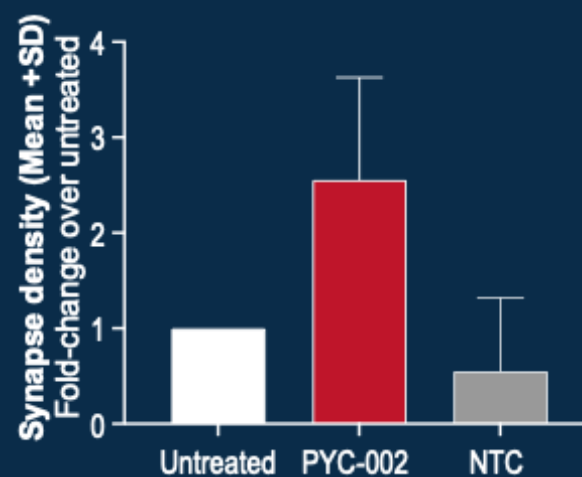
- ✓ In studies using PMS patient-derived cells, PYC-002 restored SHANK3 protein expression toward healthy levels; and
- ✓ Restoring SHANK3 protein helps brain cells form healthier connections and communicate more effectively; and
- ✓ In animal studies, PYC-002 reached the target brain cells and increased SHANK3 protein at well-tolerated doses.



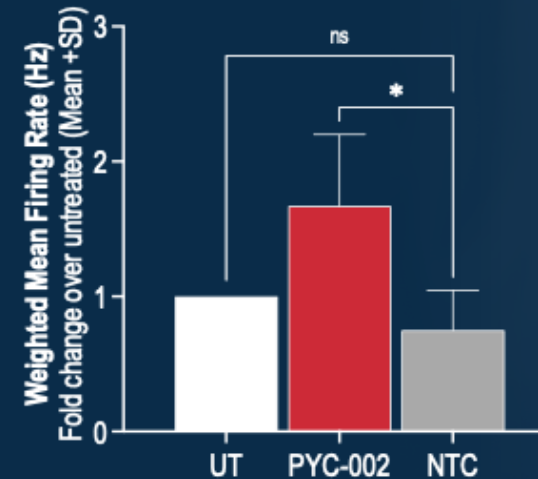
Preclinical studies support the potential of PYC-002 to address the underlying cause of PMS



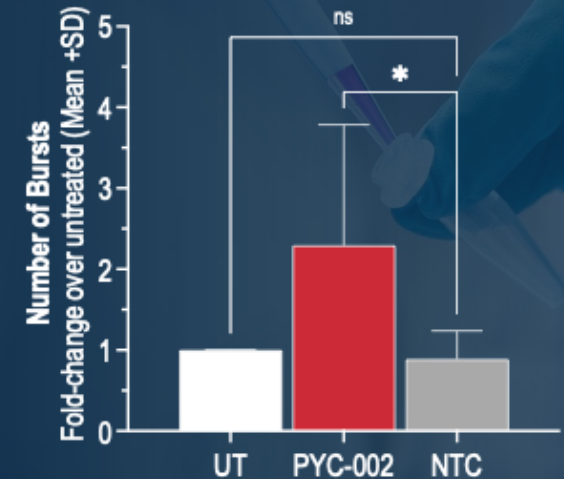
✓ SHANK3 protein increase



✓ Rebuilds connections between brain cells



✓ More brain cells are active



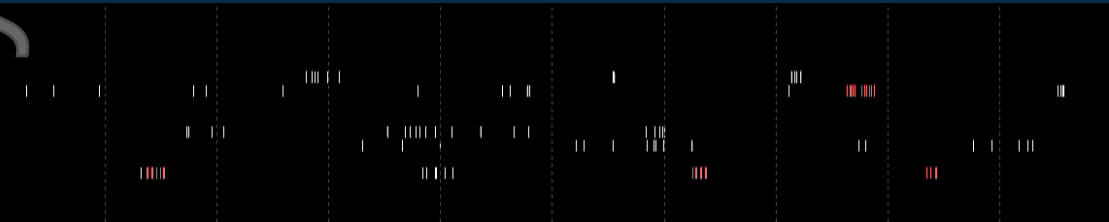
✓ Stronger communication between neurons

Each plot represents the effect in one or more PMS patient-derived induced pluripotent cells (iPSCs) glutamatergic neurons on the parameter measured treated gymnotically with vehicle (untreated, white bars), PYC-002 (red bars) or with a non-targeting control ASO (NTC gray bars) for 21 days for protein and synapse density and for 28 days for Weighted Mean Firing rate and number of bursts. Dose # are indicated when different doses were tested and matched in the NTC group. Each bar represents the mean + standard deviation (SD) of 2, 2, 3 and 3 biological replicates (N), respectively in plots from left to right. Each N is the representative of the mean of 5-12, 3-15, 4 and 4 technical replicates, respectively in plots from left to right. SHANK3 on neurite and synapse density were assessed by high content imaging (HCI), Weighted Mean Firing Rate and number of burst by multi-electrode array (MEA) assay. Significance against the NTC group was calculated using Kruskal-Wallis and Dunnet test. ns = non-significance; * $p < 0.05$.

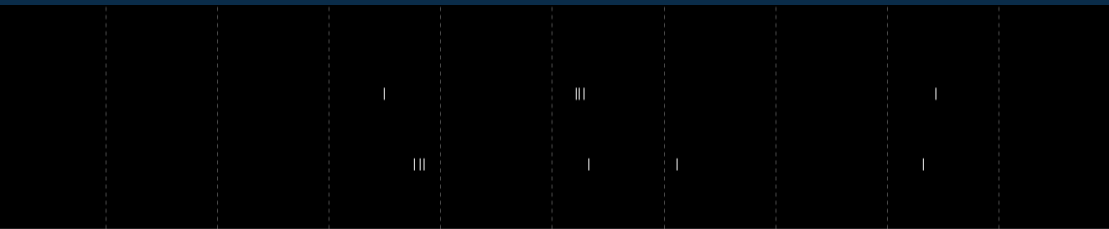
Restoring SHANK3 protein helps patient-derived brain cells communicate more effectively



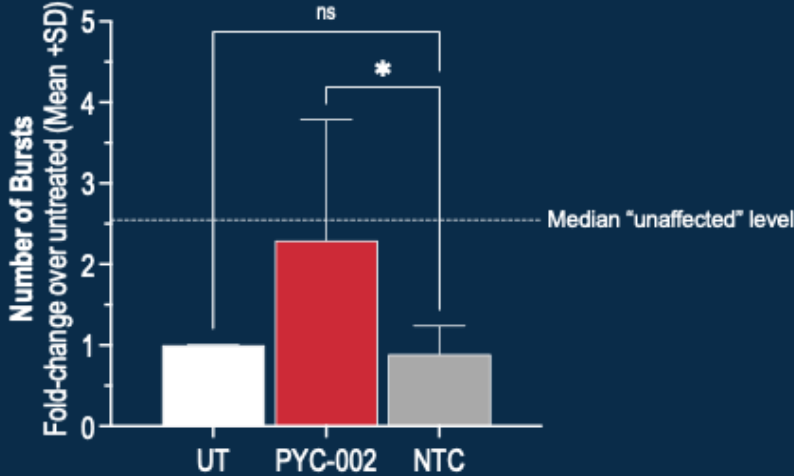
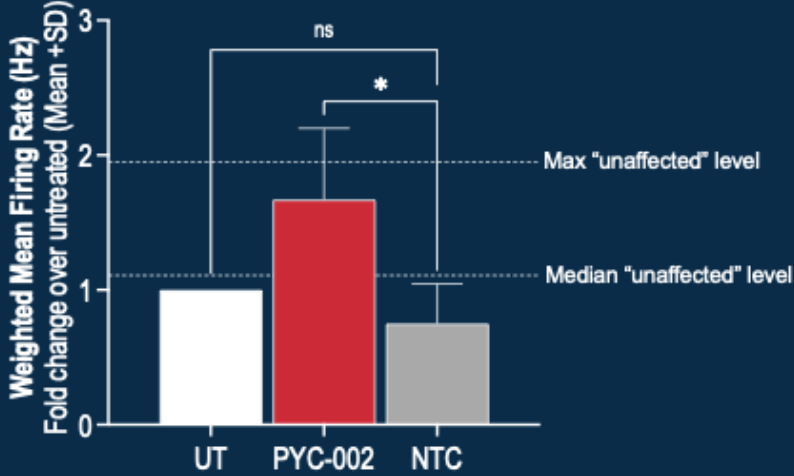
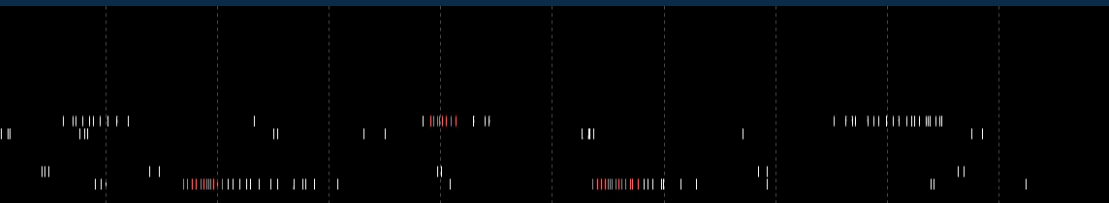
Untreated Healthy control-derived neurons



Untreated PMS patient-derived neurons

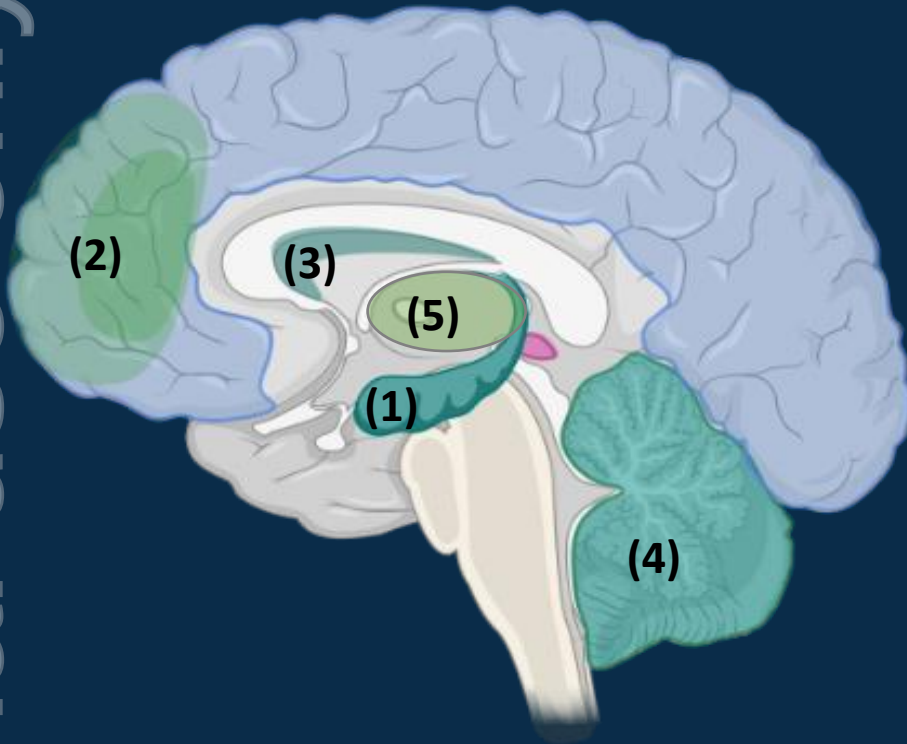


PYC-002 + PMS patient-derived neurons



The upper plot shows the mean+SD of weighted mean firing rate (Hz), expressed as fold-change relative to untreated samples (white bar) measured by Multiple-Electrode Array (MEA) assay after 28 days post-gymnotic-treatment with PYC-002 (red bar) or non-targeting control (NTC, grey bar). Bars represent three biological replicates of iPSC-derived glutamatergic neurons from three different patients with PMS. The lower plot shows the mean+SD of Number of Bursts fold-change over untreated samples (white bar) measured by MEA assay after 28 days post-gymnotic-treatment with PYC-002 (red bar) or NTC (grey bar). Bars represent three biological replicates of iPSC-derived glutamatergic neurons from three different patients with PMS. The median and maximum (Max) of unaffected levels were calculated using iPSCs glutamatergic neurons derived from eight unaffected lines. These values were compared as fold-change with untreated PMS measurements (white bar). Significance against the NTC group was calculated using Kruskal-Wallis and Dunnet test. ns = non-significance; *p<0.05.

Deficient SHANK3 levels in multiple brain regions disrupts neuronal communication contributing to the PMS phenotype¹⁻³



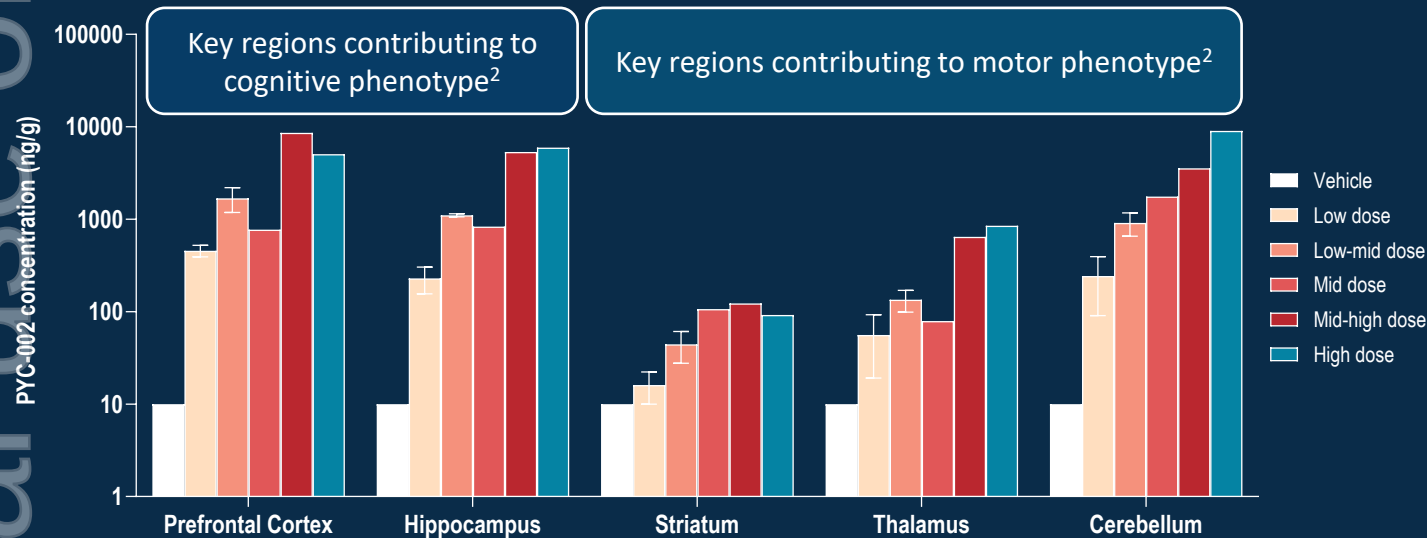
Brain regions implicated in PMS and impact on phenotype

1. **Hippocampus:** critical for learning and memory processes
2. **Prefrontal cortex:** important for decision making, social behaviours and cognitive functions
3. **Striatum:** plays a crucial role in synaptic function and plasticity, essential for decision making, emotion and motor control
4. **Cerebellum:** functions in balance and motor/movement control
5. **Thalamus:** receiving incoming sensory and motor information

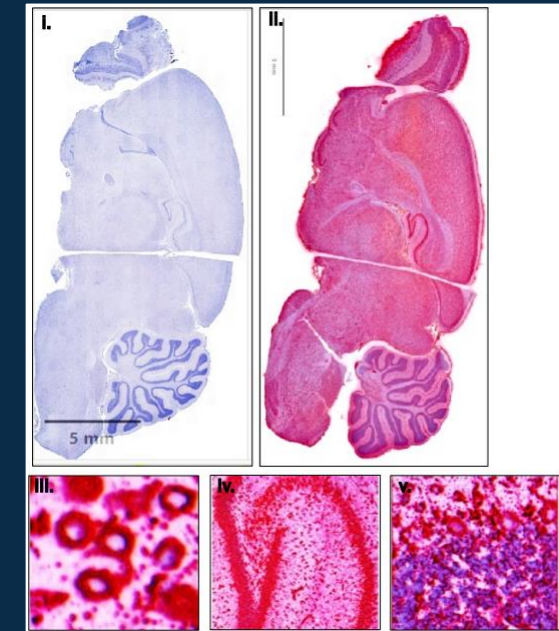
PYC-002 distributes to all key brain regions implicated in PMS at safe and well-tolerated doses¹



Concentration of PYC-002 in the NHP brain after single dose²



Distribution of PYC-002 in the rat brain after single dose³



PYC-002 demonstrates broad distribution to regions of the NHP and rat brain that are implicated in PMS

The prefrontal cortex and hippocampus in particular are responsible for many of the key functions that form part of the PMS phenotype

1. Refer ASX Announcement 13 October 2025

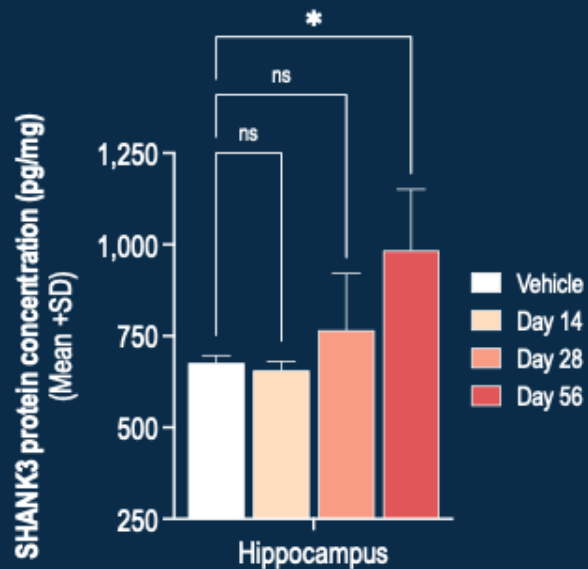
2. Concentration of PYC-002 (ng drug per g tissue, mean $\pm$ SEM) in brain tissue samples from Cynomolgus monkeys (*Macaca fascicularis*) 28 days after treatment with a single intrathecal injection, assessed by hy-ELISA. (n=3 for vehicle, low dose, low-mid dose, n=1 for mid dose, mid-high dose and high dose).

3. Distribution of PYC-002 in brains from Sprague-Dawley rats (*Rattus norvegicus*) treated with i. vehicle control or ii-v. low dose PYC-002 for 14 days. Samples stained with in situ hybridisation probe targeting PYC-002 ASO (red) and counter-stained with hematoxylin. i. and ii. Whole Brain, iii. Cortex, iv. Hippocampus, v. Cerebellum

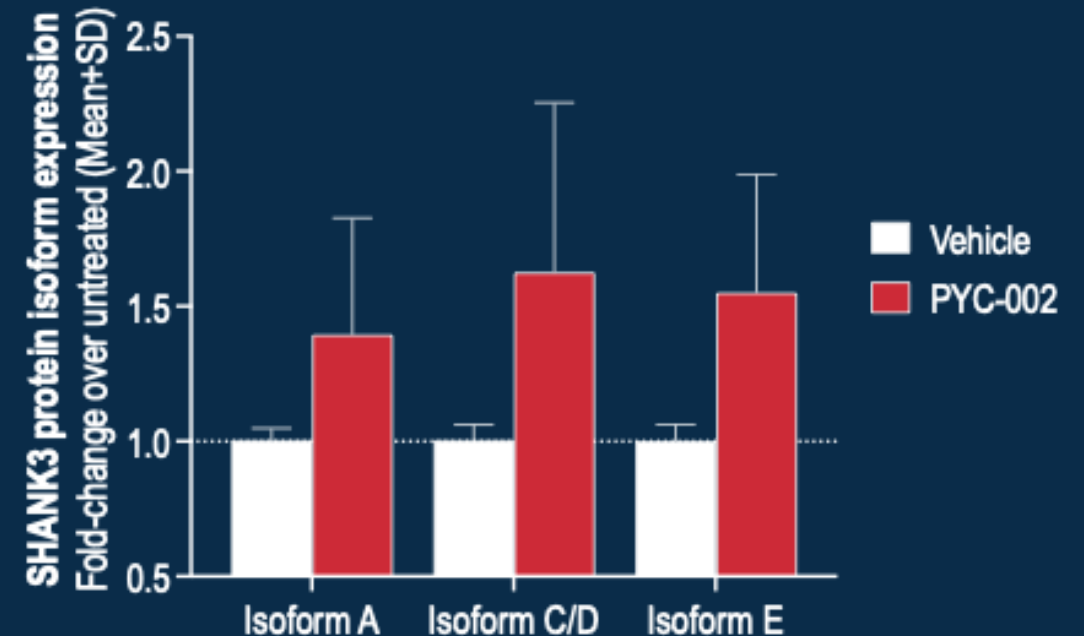
PYC-002 increases SHANK3 protein at safe and well-tolerated doses



SHANK3 protein increased up to 1.5-fold in monkey brain following a single IT injection¹

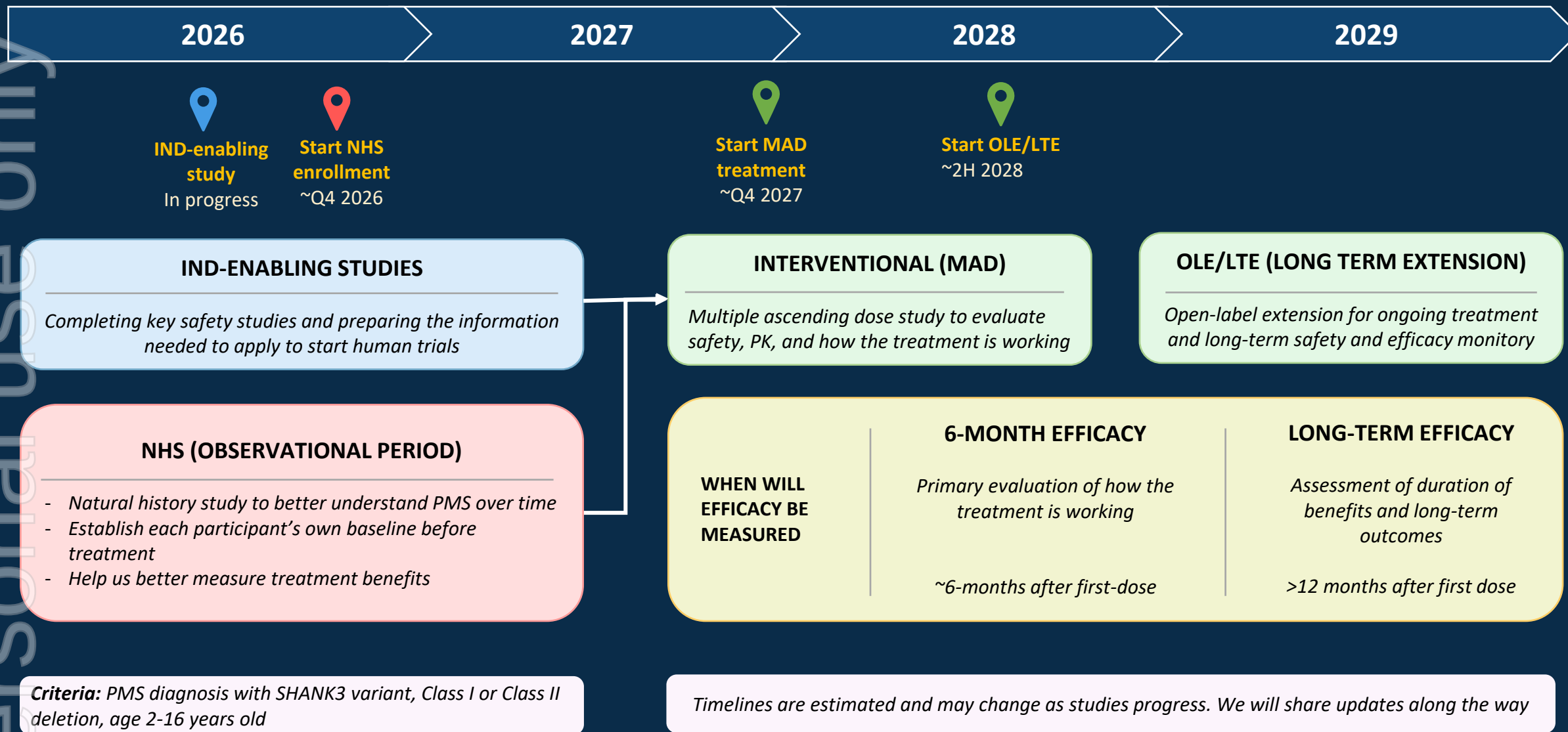


A single dose of PYC-002 increases SHANK3 protein up to 2-fold in rat brains²



1. Concentration of SHANK3 protein (pg protein per mg tissue, mean ± SD) in brain tissue samples from Cynomolgus monkeys (*Macaca fascicularis*) 15, 28, 56 days after treatment with a single intrathecal injection, assessed by ELISA. (n=3 for vehicle, n=2 for day 14, n=4 for day 28 and n=4 for day 56). Significance tested with one-way ANOVA and Dunnett's, ns= non-significant, * = $p < 0.05$
2. SHANK3 expression in wild-type Sprague Dawley rats with and without treatment with PYC-002. Rats received a single intrathecal dose of vehicle control or PYC-002 (900 µg). Assessment of SHANK3 protein levels in key brain regions was completed 14 days post-treatment (n=3 treated with PYC-002 and n=6 vehicle). ** $p < 0.01$ determined using two-way ANOVA comparing PYC-002 treated to vehicle group in each brain region.

Where we are today – and what's next





HIPPOCAMPUS An Observational Study

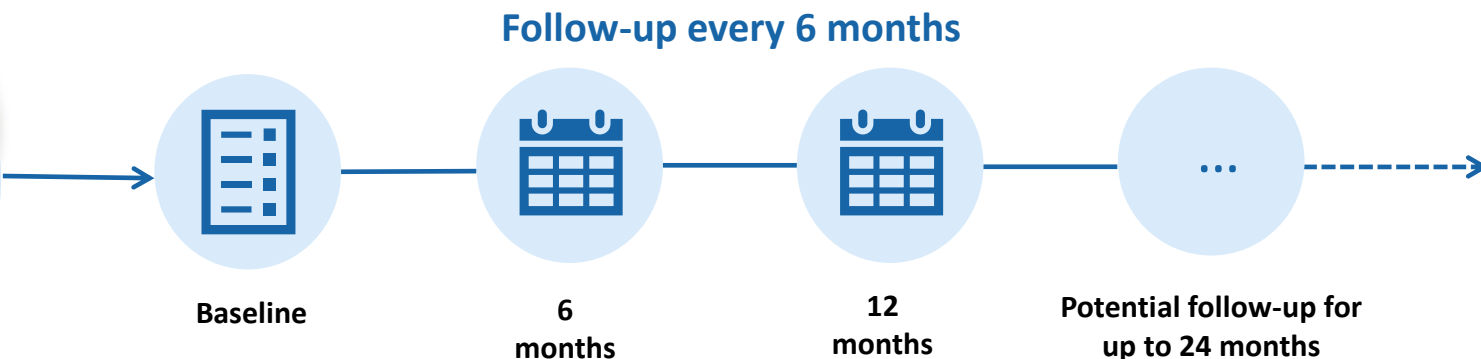
History of **P**rogression in **P**helan-McDermid: **O**bservational **C**haracterization and
Assessment of **M**apped **P**henotypes **U**nderlying **S**HANK3 Deficiency



Understanding PMS today to inform future clinical studies



Natural History Study



Eligibility



Age 2-16 years



Confirmed PMS



English questionnaires
(completed by participant
or care givers)



Key Endpoint Analysis



Cognition



Language and
Communication

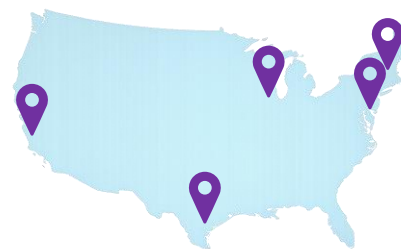


Behavior



Biomarkers

Study sites



Study sites are in the US.
To be announced.

Study initiation



Q4 2026

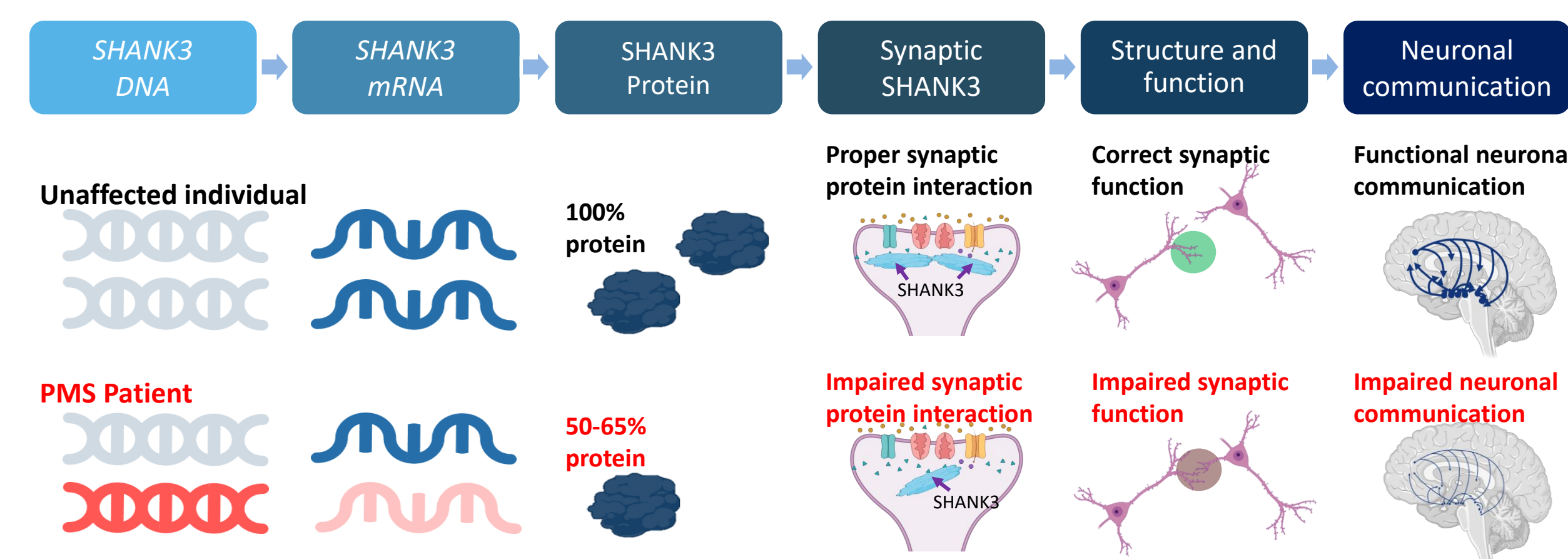
PYC-002: an RNA drug candidate for the treatment of Phelan-McDermid syndrome

Dulce B. Vargas-Landin, Abbie Francis, Sasiwimon “Fern” Utama, Donna Bezner, Wontaek Oh, Priyanka Sain, Rungtiwa Nutalai, Tracy Chai, Tanisha Verma, Dean De Alvis, Linda de Castro, Laura Florez, Philipp Bayer, Alexander de Bont, Jeremy Ash, George Mitchell, Adam D. Martin, Maria Kerfoot, Janya Grainok
All authors from PYC Therapeutics, Harry Perkins Institute of Medical Research, Nedlands, Western Australia, Australia



Understanding the disease

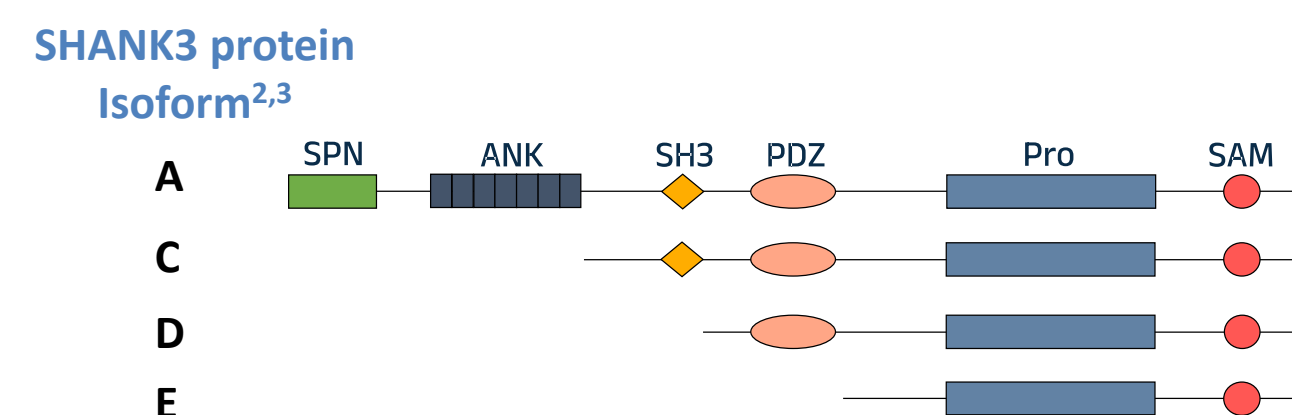
Phelan-McDermid syndrome (PMS) is a severe neurodevelopmental disorder caused by the deletion of, or a pathogenic sequence variant in, one copy of the *SHANK3* gene leading to an insufficiency of the SHANK3 protein¹. SHANK3 is a scaffolding protein critical for the structure, integrity and function of neuronal communication across the brain.



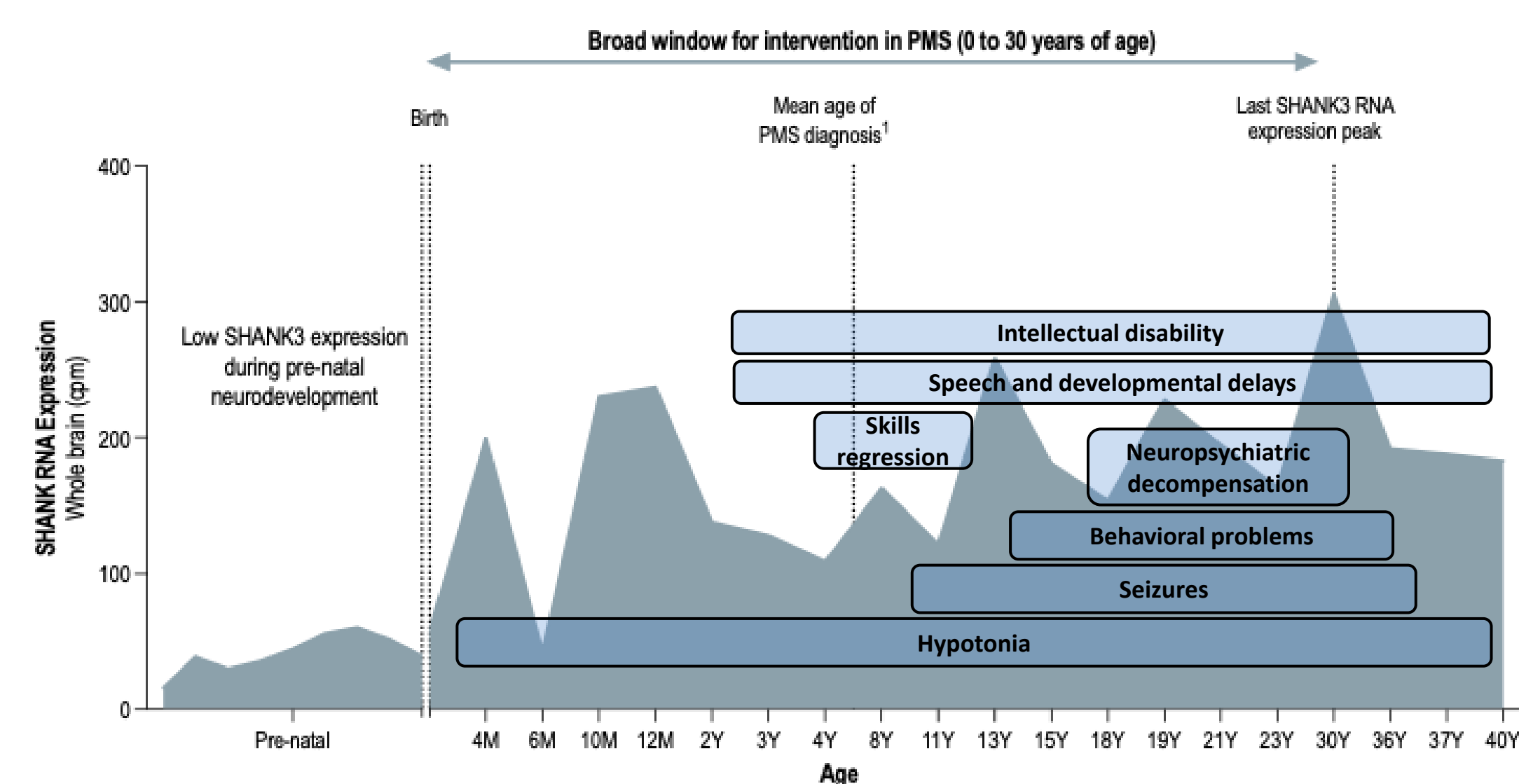
SHANK3 protein is expressed in brain regions essential for memory and cognition, such as the hippocampus and prefrontal cortex, where alternative SHANK3 protein forms, called isoforms, are present².

Relative expression of SHANK3 protein isoforms in the brain^{2,3}

Region	Isoform A	Isoform C	Isoform D	Isoform E
1. Hippocampus	~50%	~25%	~25%	<10%
2. Prefrontal Cortex	~30%	~30%	~30%	10%
3. Striatum	~70%			30%
4. Cerebellum		~50%	~50%	
5. Thalamus	~70%		~20%	10%



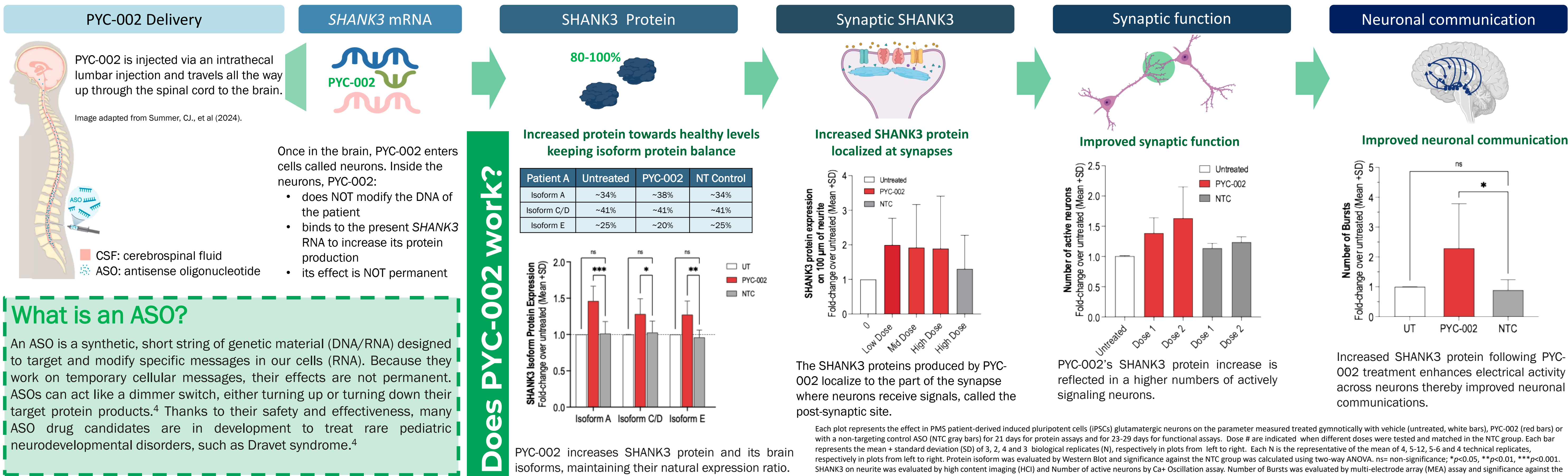
SHANK3 postnatal and lifelong expression³ provides a broad window for therapeutic intervention, from early childhood to adulthood.



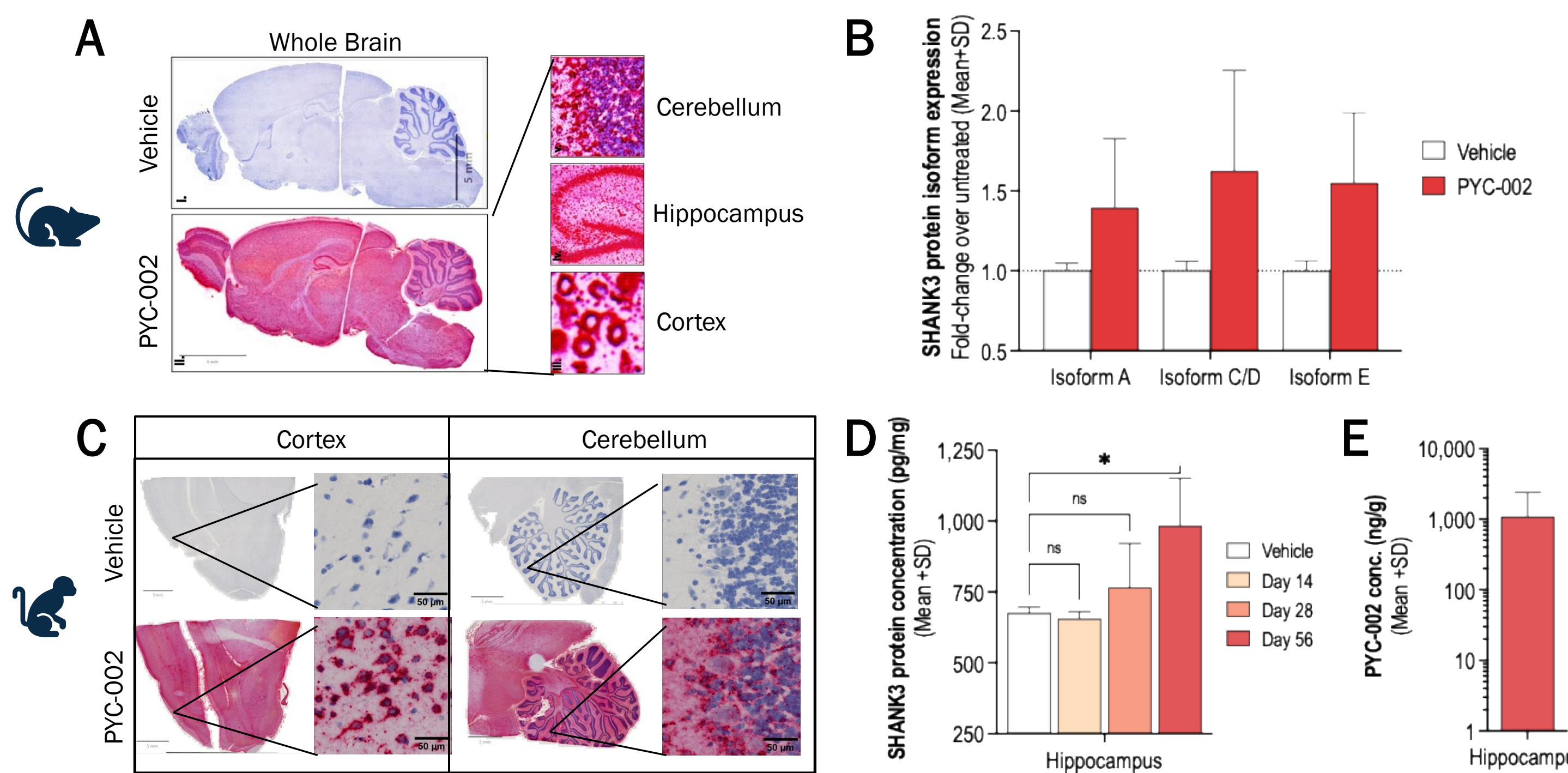
The plot shows in a gray shade the SHANK3 RNA expression levels in the brain³ throughout the life of a person, highlighting its postnatal expression and changes through development. Key symptoms in PMS⁴ are overlaid with their approximate time of onset.

PYC-002, an RNA drug candidate for PMS

How does PYC-002 work?



Where does PYC-002 go in the brain?

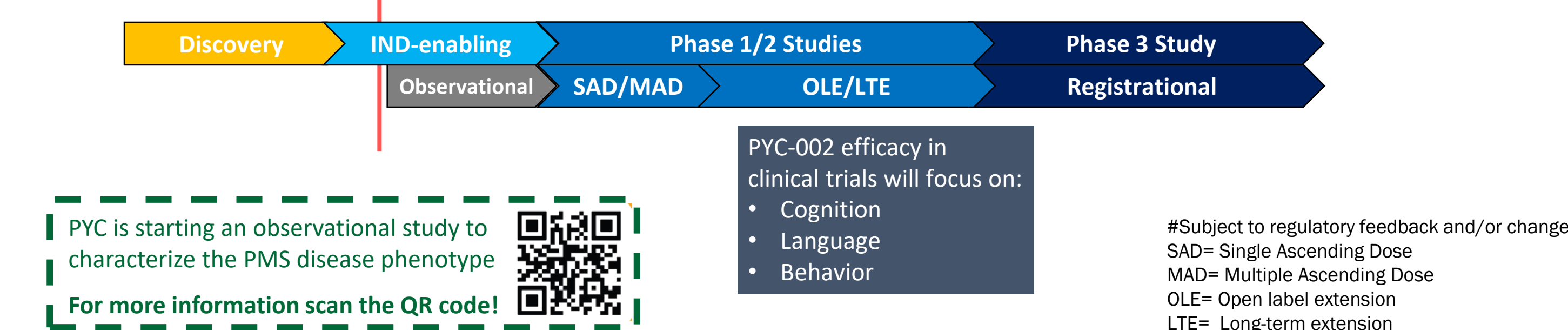


- ✓ PYC-002 shows broad and even distribution in rat and monkey brains (A and C).
- ✓ A single intrathecal injection of PYC-002 increases expression of several SHANK3 isoforms in rat brain after 14 days post-treatment (B).
- ✓ A single intrathecal injection of PYC-002 significantly increases the expression of SHANK3 in the hippocampus of monkeys at Day 56 (D), which is enabled by an effective and sustained ASO concentration (E).

Panels A and C show the distribution of PYC-002 in brains from adult Sprague-Dawley rats (*Rattus norvegicus*) and cynomolgus monkeys (*Macaca fascicularis*) treated with vehicle control or low dose PYC-002 for 14 days in rats, or high dose in monkeys for 28 days. Samples are stained with in situ hybridization probe targeting PYC-002 ASO (red) and counter-stained with hematoxylin (blue). Panel B shows SHANK3 protein isoform expression (mean ± SD) in prefrontal cortex of rats (n=2 per group) assessed using western blot at day 14 post-treatment. Panel D shows SHANK3 protein increase (mean ± SD) in hippocampus of cynomolgus monkeys (n=3-4 per timepoint/treatment group) assessed by ELISA at day 14, 28 or 56 post-treatment. Significance of the effect of treatment against vehicle was tested with one-way ANOVA with Dunnett's. (* p-value < 0.05; ns non-significant) Panel E shows the concentration of PYC-002 (ng drug per g tissue, mean ± SD) in hippocampus tissue samples (n=4) from cynomolgus monkeys 56 days after treatment, assessed by hy-ELISA.

What is next for PYC-002?

PYC-002 plans to progress to human trials in 2027[#]
We are here



References

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Is PYC-002 safe?

PYC-002 uses a drug class chemistry and route of administration that have been used in the clinic for >10 years in another pediatric disorder, proving their safety and efficacy. To evaluate the safety profile of PYC-002, exploratory (non-GLP) studies in juvenile rats and monkeys have been performed and resulted in no adverse findings related to the PYC-002 treatment at the end of the study. More safety studies are currently ongoing to support our clinical trial design.

Juvenile Sprague-Dawley Rat (<i>Rattus norvegicus</i>), 56 days after first injection			Juvenile Cynomolgus Monkey (<i>Macaca fascicularis</i>), 85 days after first injection		
Dose Regimen	Dose	Number of animals	Dose Regimen	Dose	Number of animals
Single	Low	6	Single	Mid	3
Single	Mid-high	6	Single	Very High	1
Single	High	4	Double	Mid-High	3
Single	Very High	2	Double	High	2
Double	Low	6			
Double	Mid-high	6			
Double	High	6			

All animals were dosed via intrathecal lumbar injection.

Conclusion

- ✂ PYC-002 drug candidate targets the root cause of Phelan-McDermid syndrome, the insufficiency of SHANK3 protein.
- ✂ PYC's mutation agnostic PYC-002 drug candidate:
 - increases SHANK3 protein expression level and maintains the balance of SHANK3 protein isoforms
 - increases the synaptic SHANK3 protein, needed for neuronal communication
 - improves synaptic structure and function in human iPSC-derived PMS neurons
 - improves neuronal communication in human iPSC-derived PMS neurons
- ✂ PYC-002 shows a broad distribution throughout the brain including in disease-relevant regions in rats and monkeys after single intrathecal injection.
- ✂ PYC-002 has a favorable safety profile in rats and monkeys following single and repeat intrathecal administration.
- ✂ A single, safe dose of PYC-002 upregulated multiple natural isoforms of SHANK3 critical for neuronal function in rats and PYC-002 caused upregulation in the hippocampus of monkeys.
- ✂ PYC is progressing through preclinical testing and is anticipated to enter human clinical trials in 2027[#].

For more information visit:
<https://pyctx.com/phelan-mcdermid-syndrome/>

