Pioneering personalized medicine
in epigenetics

ORYZON

Topline Results

Phase 2b PORTICO study

Efficacy of vafidemstat in
Borderline Personality Disorder

January 7, 2024

Legal Notice

DISCLAMER This document has been prepared by Oryzon Genomics, S.A. exclusively for use during the presentation. Oryzon Genomics, S.A. does not assume liability for this document if it is used with a purpose other than the above. The information and any opinions or statements made in this document have not been verified by independent third parties; therefore, no express or implied warranty is made as to the impartiality, accuracy, completeness or correctness of the information or the opinions or statements expressed herein. Oryzon Genomics, S.A. does not assume liability of any kind, whether for negligence or any other reason, for any damage or loss arising from any use of this document or its contents. Neither this document nor any part of it constitutes a contract, nor may it be used for incorporation into or construction of any contract or agreement. Information in this document about the price at which securities issued by Oryzon Genomics, S.A. have been bought or sold in the past or about the yield on securities issued by Oryzon Genomics, S.A. cannot be relied upon as a guide to future performance.

IMPORTANT INFORMATION This document does not constitute an offer or invitation to purchase or subscribe shares, in accordance with the provisions of Regulation (EU) 2017/1129 of the European Parliament and of the Council of 14 June 2017, the restated text of the Securities Market Law, approved by Royal Legislative Decree 4/2015, of 23 October, and/or Royal Decree 1310/2005, of 4 November, and its implementing regulations. In addition, this document does not constitute an offer of purchase, sale or exchange, nor a request for an offer of purchase, sale or exchange of securities, nor a request for any vote or approval in any other jurisdiction. The shares of Oryzon Genomics, S.A. may not be offered or sold in the United States of America except pursuant to an effective registration statement under the Securities Act of 1933 or pursuant to a valid exemption from registration. Any public offering of the Company's securities to be made in the United States will be made by means of a prospectus that may be obtained from the Company or the selling security holder, as applicable, that will contain detailed information about the Company and management, as well as financial statements.

FORWARD-LOOKING STATEMENTS This communication may contain forward-looking information and statements about Oryzon Genomics, S.A., including financial projections and estimates and their underlying assumptions, statements regarding plans, objectives and expectations with respect to future operations, capital expenditures, synergies, products and services, and statements regarding future performance. Forward-looking statements are statements that are not historical facts and are generally identified by the words "expects," "anticipates," "believes," "intends," "estimates" and similar expressions. Although Oryzon Genomics, S.A. believes that the expectations reflected in such forward-looking statements are reasonable, investors and holders of Oryzon Genomics, S.A. shares are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Oryzon Genomics, S.A., that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include those discussed or identified in the documents sent by Oryzon Genomics, S.A. to the Comisión Nacional del Mercado de Valores, which are accessible to the public. Forward-looking statements are not guarantees of future performance. They have not been reviewed by the auditors of Oryzon Genomics, S.A. You are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date they were made. All subsequent oral or written forward-looking statements attributable to Oryzon Genomics, S.A. or any of its members, directors, officers, employees or any persons acting on its behalf are expressly qualified in their entirety by the cautionary statement above. All forward-looking statements included herein are based on information available to Oryzon Genomics, S.A. on the date hereof. Except as required by applicable law, Oryzon Genomics, S.A. does not undertake any obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

Topline Results of VAFIDEMSTAT's Phase 2b PORTICO trial in Borderline Personality Disorder (BPD)

- **The primary endpoints improvement in *Borderline Personality Disorder Checklist (BPDCL)* and in aggression by CGI-S A/A did not reach statistical significance.**
- **Nominal statistically significant, and clinically meaningful, reduction was achieved in the secondary endpoint *Borderline Evaluation of Severity (BEST),* an overall measure of BPD disease severity, across weeks 8-12 (p = 0.042).**
- **Nominal statistically significant, and clinically meaningful, reduction was also achieved in the secondary endpoint *State-Trait Anger Expression Inventory 2 (STAXI-2) Trait Anger,* a measure of agitation and aggression, across weeks 8-12 (p=0.026).**
- **Results across all efficacy endpoints consistently favored vafidemstat over placebo.**
- **Global Statistical Test (GST) confirms consistent trend across efficacy endpoints.**
- **Vafidemstat was safe and well tolerated, consistent with the overall safety profile to date.**

ORYZON

Borderline personality disorder: A serious and prevalent disease with no approved drugs

Two main types of symptoms

Unstable-extreme interpersonal relationships

+

Agitation and Aggression*

*Including self-directed aggression

+ 9 million affected in US+EU

- Frantic efforts to avoid real or imagined **abandonment**
- Pattern of **unstable and intense interpersonal relationships** alternating between extremes of idealization and devaluation
- **Identity disturbance:** markedly and persistently **unstable self-image** or sense of self
- **Affective instability** due to a marked reactivity of mood
- **Chronic feelings of emptiness**
- **Impulsivity** with **self-damage** (spending, sex, substance abuse, reckless driving, binge eating)
- Recurrent threats, or **suicidal / self-harming behavior**
- Inappropriate, **intense anger** or **difficulty controlling anger** (e.g., frequent displays of temper, recurrent fights)
- **Transient**, stress-related **paranoid ideation** or **severe dissociative symptoms**

ORYZON

Borderline Personality Disorder (BPD). Multifactorial etiology

BPD etiology is multifactorial, but LSD1i effects are coherent with a potential therapeutic benefit.

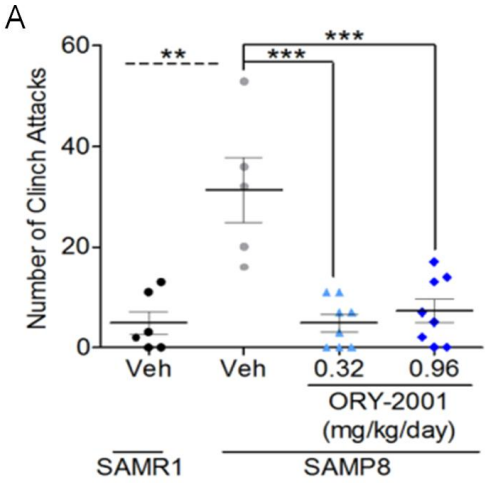
- A growing body of data indicates that the glutamatergic system, particularly the *N*-methyl-D-aspartate (NMDA) subtype receptor, plays a major role in neuronal plasticity and other functions and may underlie the pathophysiology of multiple psychiatric disorders[1]
- Prefrontal glutamatergic emotion regulation is disturbed in cluster B (BPD) and C personality disorders[2]
- **LSD1 inhibition rescues/restores NMDA deficiencies in different preclinical models**

ORYZON

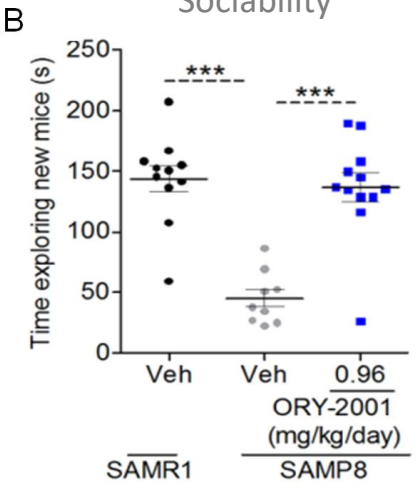
[1] Grosjean B, Tsai GE. NMDA neurotransmission as a critical mediator of borderline personality disorder. J Psychiatry Neurosci. 2007 Mar;32(2):103-15. PMID: 17353939; PMCID: PMC1810584.
[2] Smesny S. et al., 2018 https://doi.org/10.1016/j.jad.2017.10.044)

Vafidemstat's unique MoA and pharmacology supports use in different mental diseases

Aggression



Sociability



Vafidemstat (aka ORY-2001) and other LSD1i induce expression of genes involved in neuronal plasticity, restoring neuronal morphology, branching and axonal navigation

Vafidemstat restores the response to stress by regulating genes involved in control of stress cues in the PFC-amygdala axis, as IEG, SRF, and others

LSD1i is able to rescue glutamatergic NMDA-R hypofunction in prefrontal cortex in different ASD and SCZ models

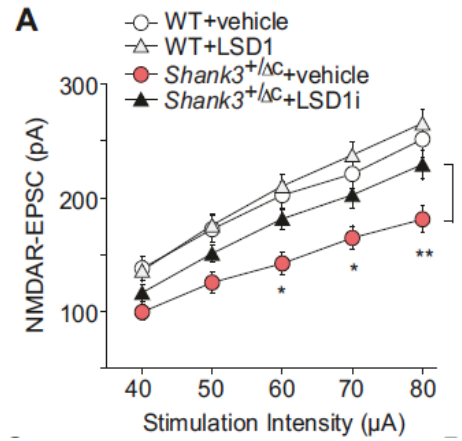
Vafidemstat improves sociability

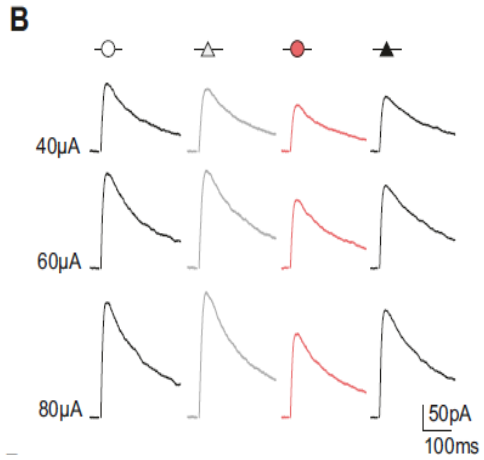
Vafidemstat reduces aggression

Vafidemstat improves memory

Borderline Personality Disorder, Schizophrenia, Autism, ADHD, others

NMDAR rescue





Maes et al, 2020 PLoS ONE
Rapanelli et al. 2022 Mol Psychiatry, Shank3-deficient mice

ORYZON

Vafidemstat is safe and well tolerated

A very robust safety package. +430 treated subjects

Brain Penetrant

An optimal CSF : plasma ratio of 0.9

Safe, No DDIs

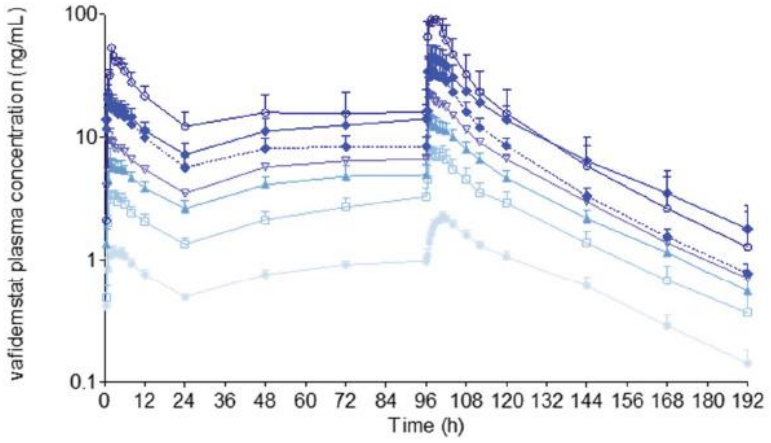
Comparable SARs between placebo and vafidemstat arms in 6 Phase II trials: 1.0% vafidemstat vs 1.0% placebo

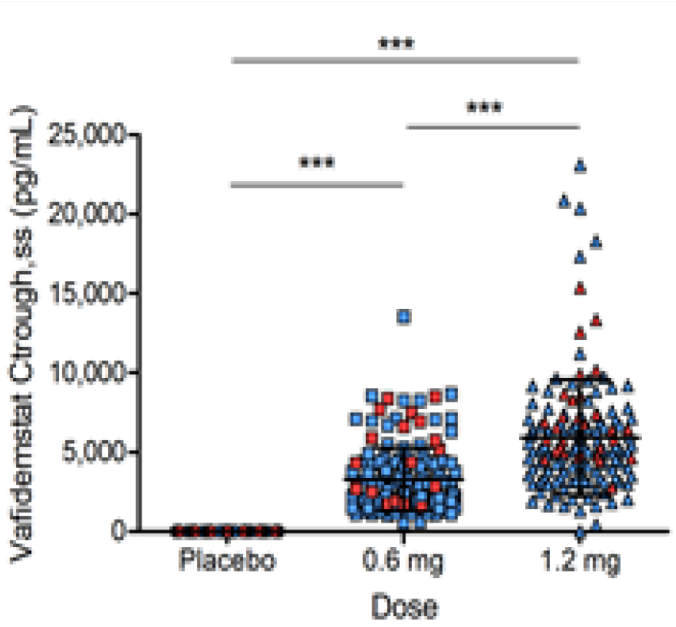
No side effects

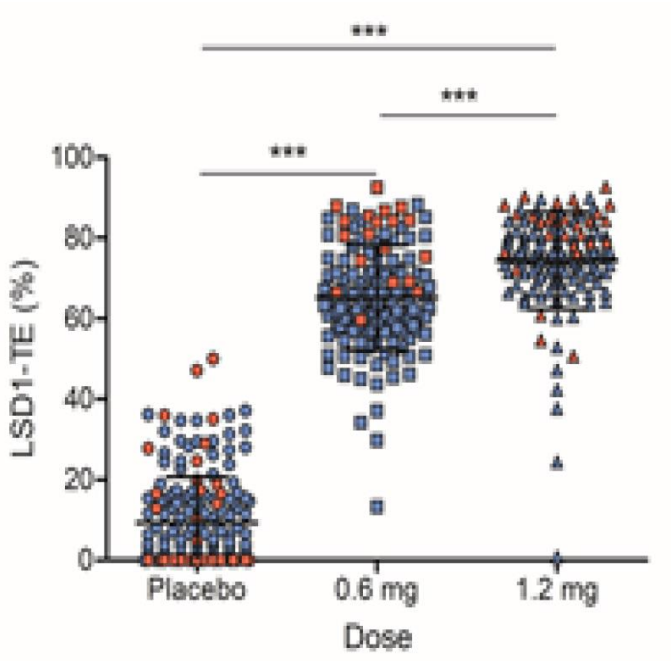
- No weight gain
- No sedation / somnolence
- No sexual dysfunction
- No extrapyramidal signs

Vafidemstat: Excellent pharmacology & established RP2D in previous trials

Oral, once a day







PK data supports once daily dosing in both adult and elder subjects

Full LSD1 occupancy at 1.2 mg/day

ORYZON

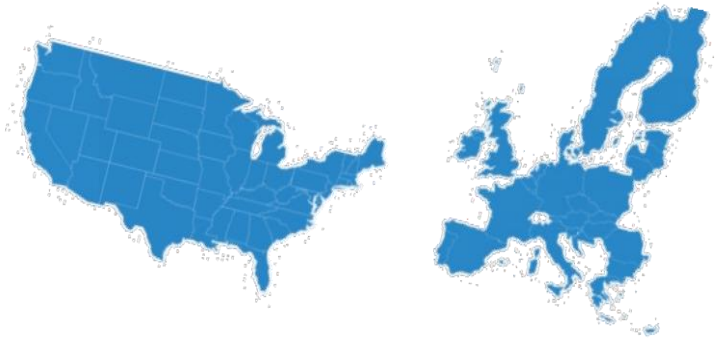
Multiple Shots on goal & main investment thesis in the short-mid term

Program	Study	Preclinical Phase	Phase I		Phase II		Status	Expected Milestone(s)
			Phase Ia	Phase Ib	Phase IIa	Phase IIb		
CNS: Vafidemstat (ORY-2001) - CNS optimized LSD1 inhibitor								
Borderline personality disorder Agitation/Aggression & Overall Improvement	PORTICO						Completed. Study has results	Top line data in January 2024 BioMks & Final Data 2Q2024 EoP2 FDA meeting in 2024
Schizophrenia Negative Symptoms & Cognition	EVOLUTION						Recruiting	Timeline updates 2024
Kabuki Syndrome	HOPE			Phase Ib / II			IND in preparation	IND 2024
Oncology: Iadademstat (ORY-1001) - Selective LSD1 inhibitor								
AML 1L Unfit Patients Combination with azactidine	ALICE						Completed. Study has results	Final positive results presented at ASH2022
AML 1L Unfit Patients Combination with azactidine and venetoclax	IIS-X002			Phase Ib			IND Approved Led by OSHU	FPI 1Q2024
AML R/R-Flt3mut+ Combination with gilteritinib	FRIDA			Phase Ib			Recruiting	EHA-2024, ASH-2024
Neuroendocrine High Grade R/R Combination with paclitaxel	C-X001 NET Basket						Recruiting Collab. Study with FCCC	Study updates 2H24
ED-SCLC 1L Combination with ICI	CRADA-IIS						IND in preparation Led by MSKCC	IND 1Q2024
ED-SCLC 1L Combination with ICI	STELLAR						IND in preparation Company sponsored	IND 2024
Other Programs								
ORY-3001 (LSD1i) Sickle Cell Disease	--						IND enabling tox completed	
ORY-4001(HDAC6i) CMT, ALS	--						IND enabling tox ongoing	2023 PNS Annual Meeting June 2023

Borderline personality disorder: an unmet medical need & a vast commercial opportunity

A Prevalent & impairing disease

9 million in US & EU

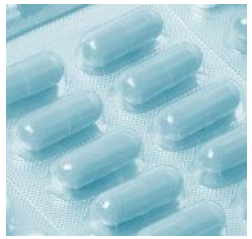


Two main types of symptoms

Unstable-extreme interpersonal relationships
+
Aggression & self-aggression

No approved drugs yet

Patients in off-label anti-psychotics



Vafi improves these symptoms in:
- **BPD patients**
- **in PC models**

Vafidemstat commercial opportunity

- **BPD multi-symptom treatment** represents a substantial peak revenue opportunity of **+$3.5B**
- **Aggression.** Positive results, only in BPD, would still represent a meaningful business opportunity with peak sales of **~$1.4B.** Additional market opportunities, e.g. **Aggression in AD,** would increase this figure
- **Schizophrenia negative symptoms** treatment also represents a big commercial opportunity, where global net revenues could reach **~$2.5B at peak**

PORTICO: Phase IIb randomized, placebo-controlled, double blinded trial in BPD

Key Inclusion criteria

Men and women **18-65 years of age**

DSM-5 BPD diagnostic criteria, at least 3 months before the Screening visit.

Agitation-Aggression Psychiatric Inventory-Clinician Report (AAPI-CR) Agitation & Aggression (A/A) subscale score of ≥ 16 (severity x frequency) summed across the 4-items comprising the A/A subscale, and the sum of the A/A subscale severity scores ≥ 6

Stable regimen of background pharmacotherapy at Screening, Baseline and throughout the trial

Maintenance of pre-screening psychotherapy schedule throughout the trial

Willing and able to adhere to the protocol prohibitions, restrictions and requirements

N = 210
Randomized
1:1

Vafidemstat, 1.2mg
Once daily (5 ON, 2 PBO),
N = 106

Placebo
Once daily,
N = 104

14-week trial

Primary Endpoints

Improvement in Clinical Global Impression-Severity by **Agitation/Aggression** (**CGI-S A/A**) from baseline to weeks 8-12

Improvement in Borderline Personality Disorder Checklist (**BPDCL**) from baseline to weeks 8-12

Secondary Endpoints (efficacy)

To evaluate the change over time on the **CGI-S A/A**

To evaluate the change over time on the **BPDCL**

To evaluate the difference on the following measures, from baseline to weeks 8-12, as well as change over time, between the active treatment arm and the placebo arm:

- **Borderline Evaluation of Severity over Time (BEST)**
- **Beck Depression Inventory – II (BDI-II)**
- **State-Trait Anger Expression Inventory 2 (STAXI-2)**
- **State-Trait Anxiety Inventory (STAI)**

ORYZON

DEMOGRAPHICS

PORTICO enrolled a representative **real-world BPD population** allowing common comorbidities and concomitant medications that are typically exclusionary in other BPD trials, as well as allowed subjects to receive psychotherapy during the trial

	Vafidemstat (n = 106)	Placebo (n = 104)
Psychotherapy at Baseline: No (n) / Yes (n)	84/22	82/22
Age (years, Mean (SD))	32.4 (10.68)	31.8 (10.89)
Female n (%)	78 (73.6)	79 (76.0%)
Male n (%)	28 (26.4%)	25 (24.0%)
Race, n (%) White	87 (82.1%)	86 (82.7%)
Black/African American	9 (8.5%)	7 (6.7%)
Other	10 (9.4%)	11 (10.6%)
Height Mean (SD)	167.4 (9.09)	168.4 (10.36)
Weight Mean (SD)	73.0 (15.91)	75.8 (16.05)
BMI Mean (SD)	26.0 (4.89)	26.6 (4.48)

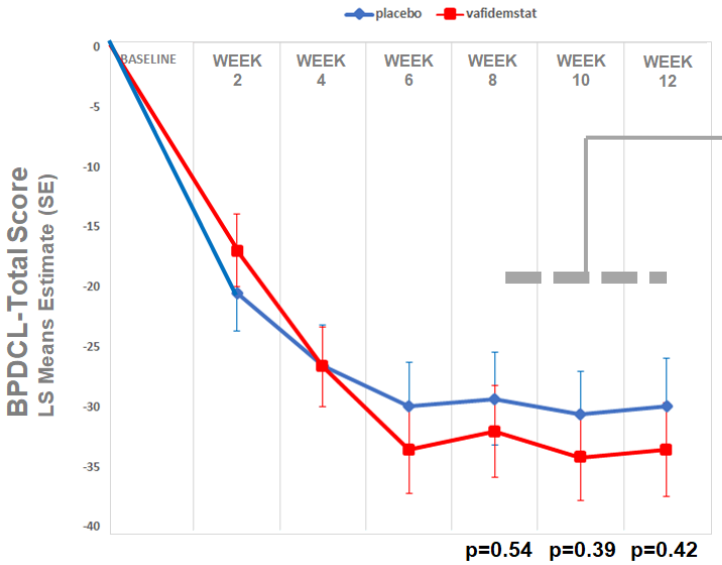
ORYZON

BASELINE CHARACTERISTICS

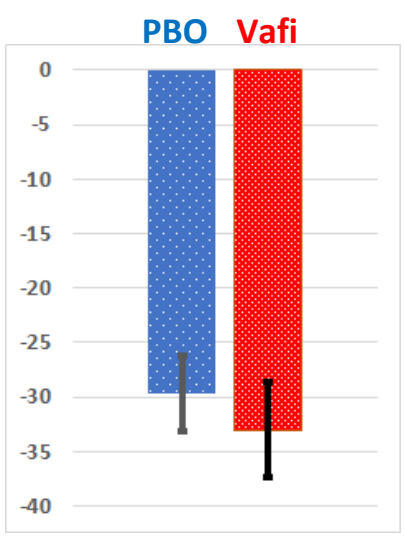
There were no statistically significant group differences across endpoints at Baseline

	Vafidemstat (n = 106)	Placebo (n = 104)
AAPI-CR Total	74.1 (22.51)	78.0 (22.30)
BPDCL Total	141.7 (36.96)	144.6 (34.08)
CGI-Severity A/A	4.8 (0.82)	4.7 (0.82)
BEST Total	39.9 (10.06)	39.6 (10.02)
STAXI-2 Trait Anger	27.5 (6.73)	27.0 (6.47)
STAXI-2 State Anger	23.5 (8.98)	23.3 (9.36)
Beck Depression Inventory-II	24.7 (14.58)	26.3 (13.67)
STAI State Anxiety	50.6 (11.69)	50.4 (11.32)
STAI Trait Anxiety	59.0 (11.23)	59.3 (10.51)

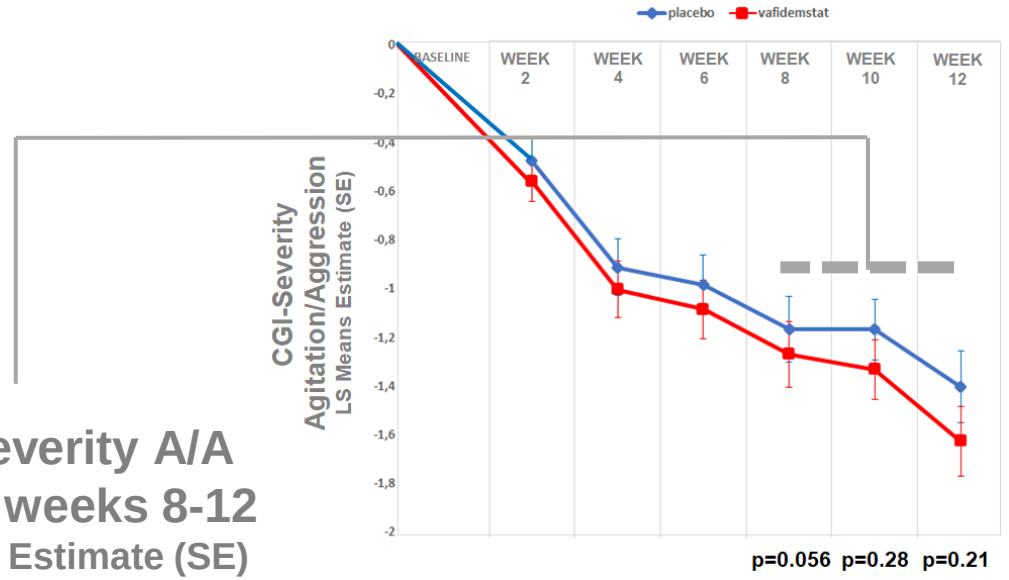
No Statistical Significance in the two Primary Endpoints: BPDCL and CGI-S A/A



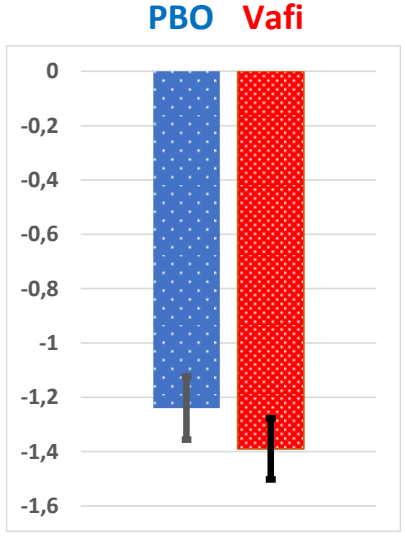
BPDCL-Total Score Across weeks 8-12
LS Means Estimate (SE)



p=0.412

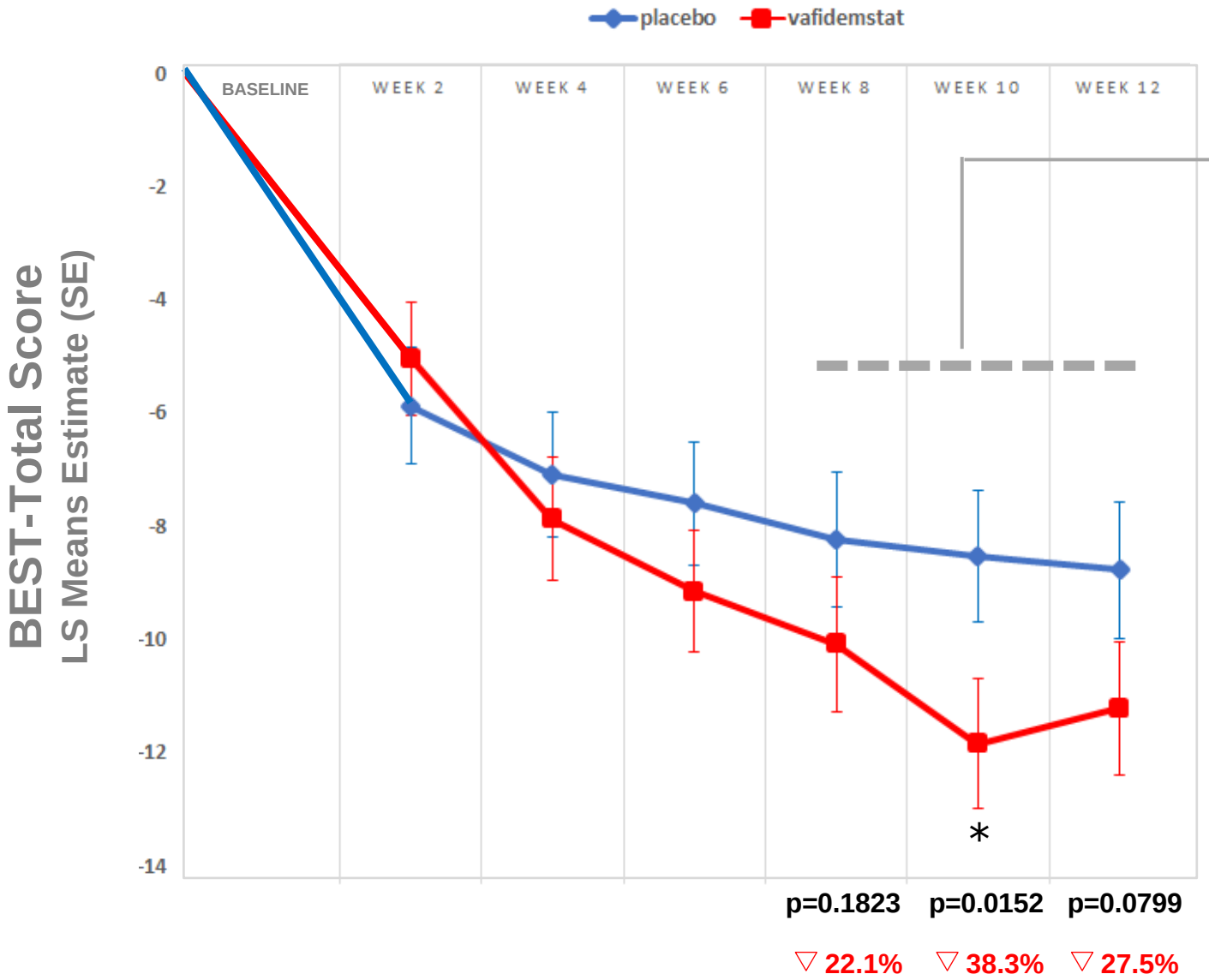


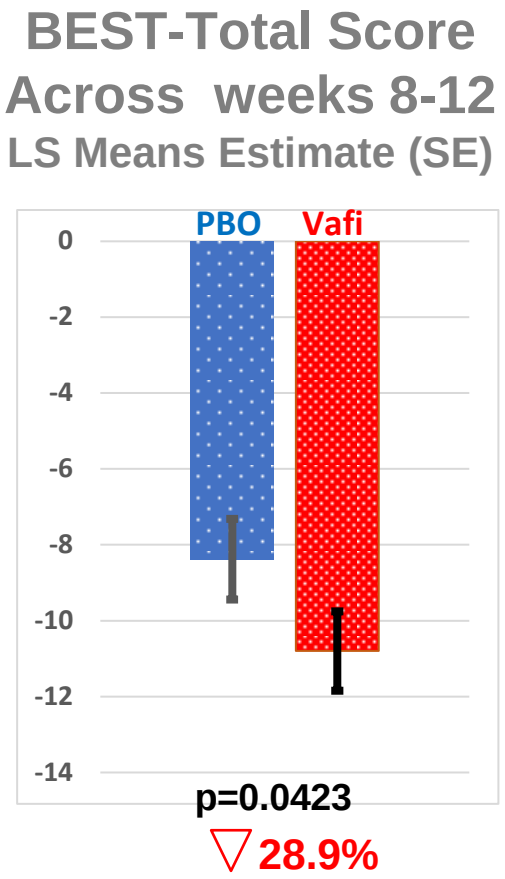
CGI-Severity A/A Across weeks 8-12
LS Means Estimate (SE)



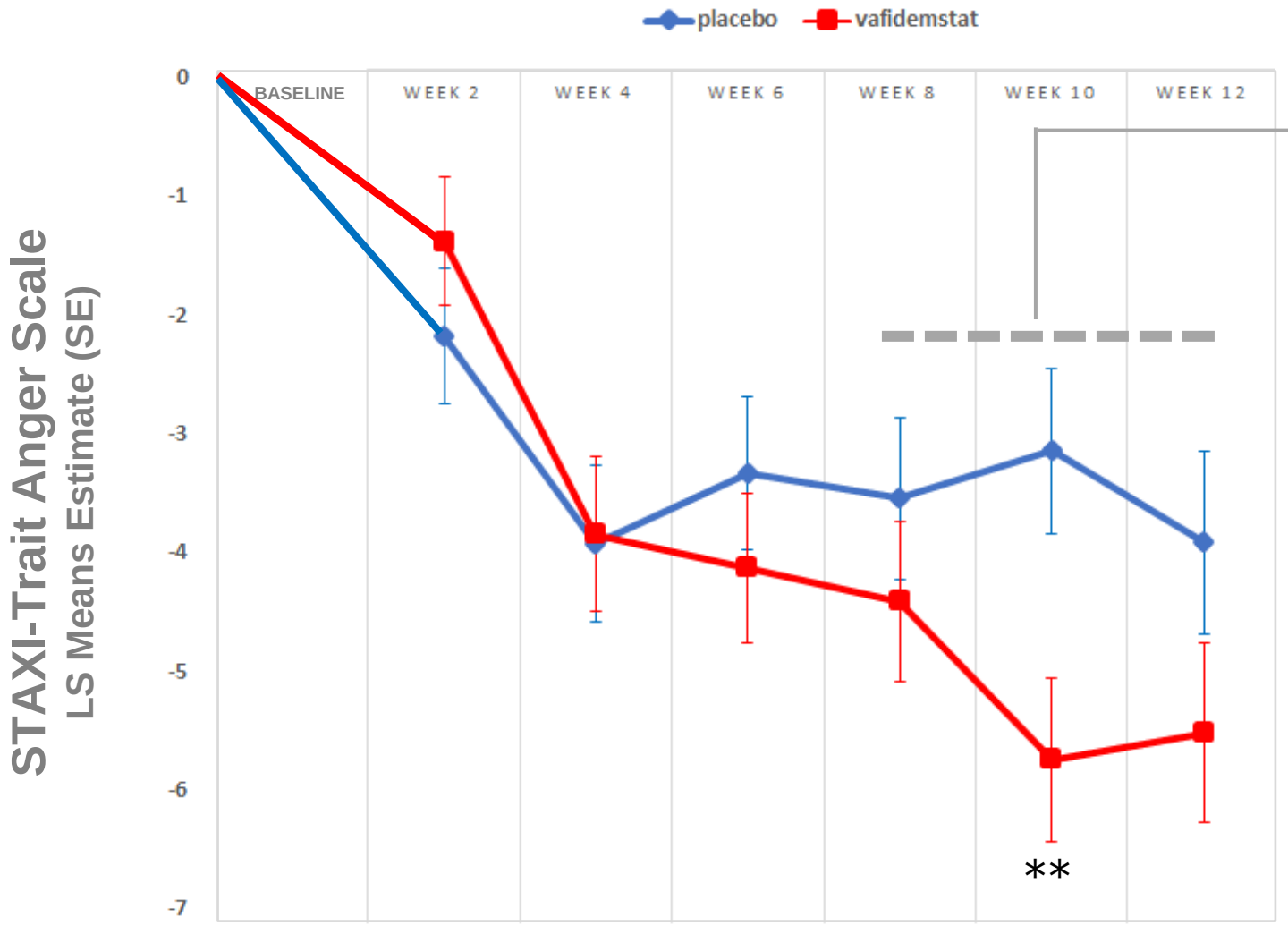
p=0.254

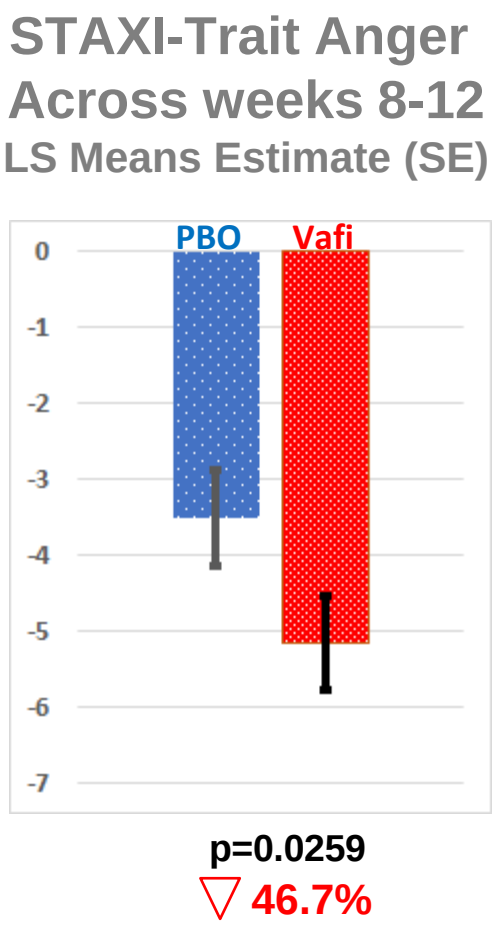
Nominal Statistical Significance in Secondary endpoint: Improvement in BEST across weeks 8-12





Nominal Statistical Significance in Secondary endpoint: Improvement in STAXI Trait Anger across weeks 8-12

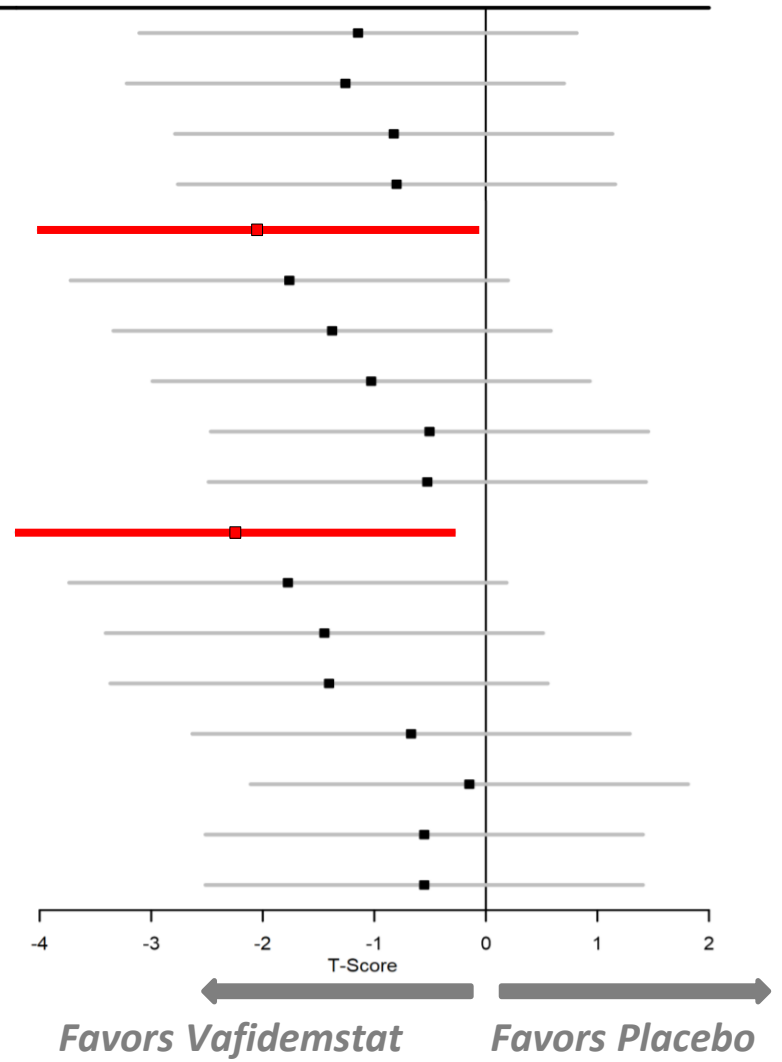




PORTICO: All efficacy endpoints consistently favored vafidemstat over placebo

Full Analysis Set

Parameter	Analysis Type	P-value	Difference	CI	T-Score
CGI02-Severity	Average Mean	0.2541	-0.16	(-0.42,0.11)	-1.14
	Week 12 Mean	0.2103	-0.22	(-0.56,0.12)	-1.26
BPDCL1-Total Score	Average Mean	0.4107	-3.24	(-11.01,4.52)	-0.82
	Week 12 Mean	0.4253	-3.61	(-12.53,5.31)	-0.80
BEST01-Total Score	Average Mean	**0.0423**	-2.43	(-4.77,-0.09)	**-2.05**
	Week 12 Mean	**0.0799**	-2.35	(-4.98,0.28)	**-1.76**
BD201-Total Score	Average Mean	0.1699	-2.11	(-5.14,0.91)	-1.38
	Week 12 Mean	0.3054	-1.71	(-5.00,1.58)	-1.03
STAXI1-State Anger Scale Raw Score	Average Mean	0.6143	-0.49	(-2.38,1.41)	-0.50
	Week 12 Mean	0.6004	-0.57	(-2.69,1.56)	-0.52
STAXI1-Trait Anger Scale Raw Score	Average Mean	**0.0259**	-1.64	(-3.09,-0.20)	**-2.25**
	Week 12 Mean	**0.0778**	-1.56	(-3.30,0.18)	**-1.77**
STAXI1-AX Index Raw Score	Average Mean	0.1495	-2.22	(-5.25,0.81)	-1.45
	Week 12 Mean	0.1616	-2.41	(-5.78,0.97)	-1.41
STAI01-S-Anxiety Raw Score	Average Mean	0.5035	-0.96	(-3.77,1.86)	-0.67
	Week 12 Mean	0.8825	-0.25	(-3.65,3.14)	-0.15
STAI02-T-Anxiety Raw Score	Average Mean	0.5813	-0.67	(-3.05,1.72)	-0.55
	Week 12 Mean	0.5813	-0.67	(-3.05,1.72)	-0.55



**P-values are uncorrected for multiplicity*

ORYZON

Global statistical test (GST) consistent with a global treatment effect favoring vafidemstat

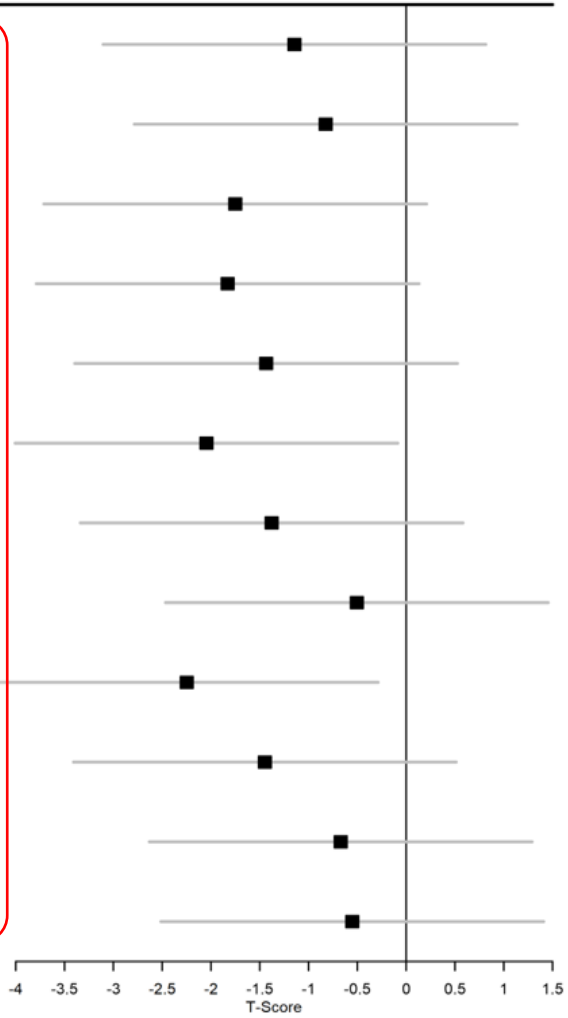
BPD is a multisymptomatic disease with psychiatric, behavioral, and functional outcomes.

GST is designed to address whether a treatment is efficacious across different aspects of a condition. GST efficiently summarizes a treatment's merit when the medical question is complex.

When a treatment improves all target outcomes, the GST often has a higher power than tests of single outcomes or other multiple-test procedures. As such, GST incorporates the impact of consistent directional change across multiple key target outcomes, even when individual outcomes may not show statistically significant improvement on their own.

Full Analysis Set

Parameter	P-value	Difference	CI	T-Score	GST P-value
CGI02-Severity	0.2541	-0.16	(-0.42,0.11)	-1.14	
BPDCL1-Total Score	0.4107	-3.24	(-11.01,4.52)	-0.82	0.2476
BEST01-A_Thoughts and Feelings Score	0.0817	-1.31	(-2.79,0.17)	-1.75	0.1419
BEST01-B_Behaviors Negative Score	0.0692	-0.56	(-1.17,0.04)	-1.83	0.0920
BEST01-C_Behaviors Positive Score*	0.1531	-0.47	(0.17,-1.11)	-1.43	0.0694
BEST01-Total Score	0.0423	-2.43	(-4.77,-0.09)	-2.05	
BD201-Total Score	0.1699	-2.11	(-5.14,0.91)	-1.38	0.0689
STAXI1-State Anger Scale Raw Score	0.6143	-0.49	(-2.38,1.41)	-0.50	0.0845
STAXI1-Trait Anger Scale Raw Score	0.0259	-1.64	(-3.09,-0.20)	-2.25	0.0573
STAXI1-AX Index Raw Score	0.1495	-2.22	(-5.25,0.81)	-1.45	0.0564
STAI01-S-Anxiety Raw Score	0.5035	-0.96	(-3.77,1.86)	-0.67	0.0664
STAI02-T-Anxiety Raw Score	0.5813	-0.67	(-3.05,1.72)	-0.55	0.0819



GST p-value shows a strong trend. Particularly when considering specifically global improvement in the disease and in agitation/aggression

ORYZON

Topline Safety: vafidemstat was safe and well tolerated

- Treatment Emergent Adverse Events (TEAEs) were slightly lower for those receiving vafidemstat
- Treatment-Related TEAEs were similar between groups
- TEAEs leading to Study Discontinuation, Study Drug Withdrawal or Study Drug Interruption were low overall, 5 on vafidemstat and 3 on placebo
- TEAEs by Severity were consistent between groups, with slightly more Mild and Moderate TEAEs for those receiving placebo
- Severe TEAEs were low, 5 on vafidemstat and 4 on placebo
- The majority of TEAEs Recovered/Resolved by the end of the trial
- There were no deaths in PORTICO, and the only TEAE with sequelae was on placebo

	Placebo (N=104) n (%), e	Vafidemstat (N=106) n (%), e
Treatment Emergent AEs (TEAEs)	68 (65.4%), 214	61 (57.5%), 192
Treatment-Related TEAEs	33 (31.7%), 68	36 (34.0%), 91
TEAEs Leading to Study Discontinuation	1 (1.0%), 1	5 (4.7%), 8
TEAEs Leading to Study Drug Withdrawal	1 (1.0%), 1	5 (4.7%), 8
TEAEs Leading to Study Drug Interruption	3 (2.9%), 4	5 (4.7%), 7
TEAEs by Severity	68 (65.4%), 214	61 (57.5%), 192
Mild	60 (57.7%), 157	51 (48.1%), 128
Moderate	35 (33.7%), 52	29 (27.4%), 57
Severe	4 (3.8%), 5	5 (4.7%), 7
TEAEs by Outcome	68 (65.4%), 214	61 (57.5%), 192
Recovered/Resolved	66 (63.5%), 174	56 (52.8%), 165
Not Recovered/Not Resolved	17 (16.3%), 29	14 (13.2%), 18
Recovering/Resolving	9 (8.7%), 10	8 (7.5%), 9
Recovered/Resolved With Sequelae	1 (1.0%), 1	0 (0.0%), 0
Death	0 (0.0%), 0	0 (0.0%), 0
Unknown	0 (0.0%), 0	0 (0.0%), 0

PORTICO: Topline Safety – Treatment Emergent & Serious AEs

Treatment-Emergent Adverse Events by Preferred Term Occurring in ≥ 5% of Subjects

	Placebo (N=104) n (%), e	Vafidemstat (N=106) n (%), e
TEAEs by Preferred Term	**68 (65.4%), 214**	**61 (57.5%), 192**
Headache	17 (16.3%), 18	13 (12.3%), 16
Nasopharyngitis	18 (17.3%), 22	9 (8.5%), 11
Tension headache	6 (5.8%), 17	5 (4.7%), 11
Platelet count decreased	1 (1.0%), 1	8 (7.5%), 8
Nausea	2 (1.9%), 2	6 (5.7%), 6
Intentional self-injury	6 (5.8%), 10	1 (0.9%), 2

Serious Adverse Events

- There was 1 serious AE, a kidney infection, in a vafidemstat treated subject
  - Case was independently judged by the PI as 'Unlikely Related' to treatment.
  - Subject's dose was not changed, the condition 'Recovered/Resolved' within 7 days, and the subject completed the trial.

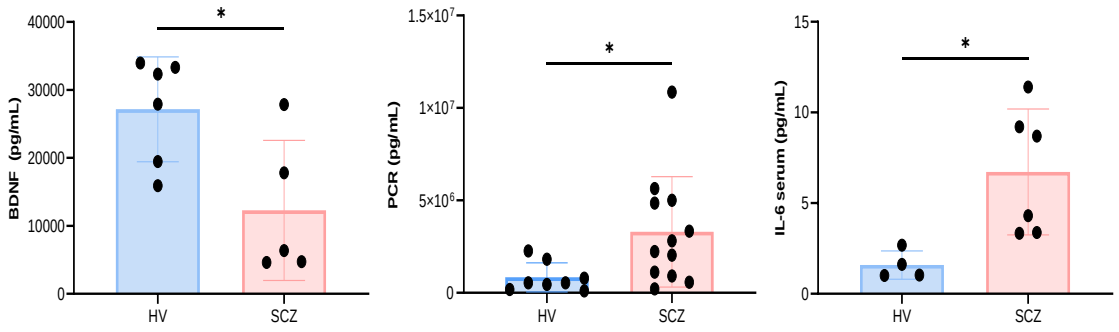
ORYZON

PORTICO will explore biomarker correlatives (as will also do EVOLUTION trial in SCZ)

Increasing evidence suggests that inflammatory responses have an important role in the pathophysiology of neurological disorders

- **In Schizophrenia,** changes have been identified in cytokine levels, correlating with behavioral symptoms severity and their potential clinical implication
- **In Borderline personality disorder**, patients have a lower level of BDNF and a higher level of tumor necrosis factor (TNF)-α and interleukin (IL)-6 in peripheral blood
- **PORTICO measured several blood biomarkers (analyses ongoing)**
- **Correlations with the different endpoints expected in 1Q 2024**

Basal levels in Schizophrenia patients (Evolution) and Healthy volunteers



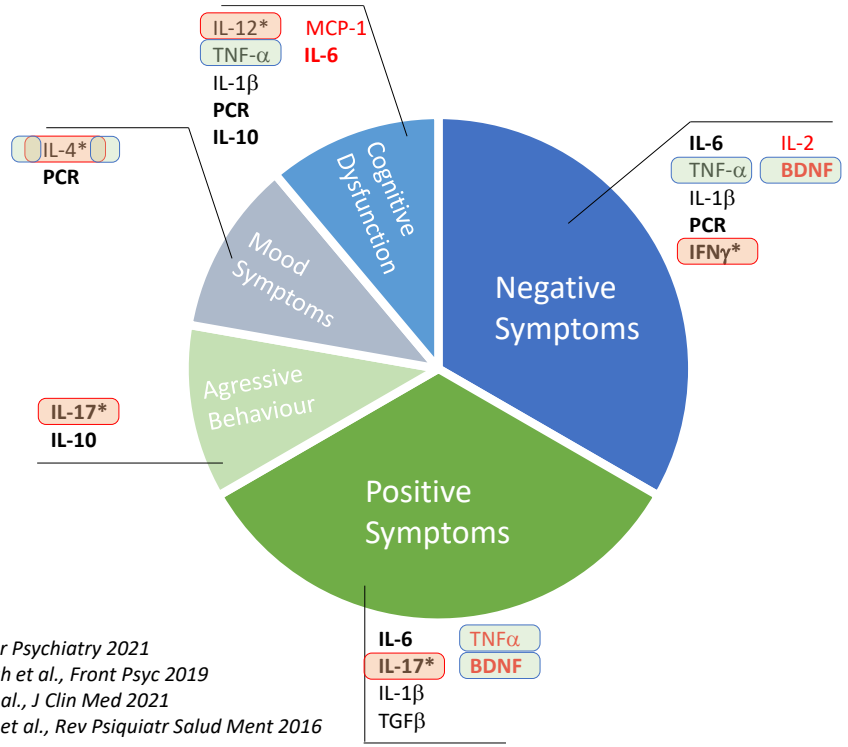
Cytokine alterations in Schizophrenia domains

(Positive correlation in black, negative in red)

*Cytokines planned to be initially measured in PORTICO & EVOLUTION are **in bold***

** Significant effect demonstrated by vafidemstat treatment in Clinical trials*

** Significant effect demonstrated by vafidemstat treatment in Preclinical models*



Cakici et al., Eur Psychiatry 2021
Momtazmanesh et al., Front Psyc 2019
Dawidowski et al., J Clin Med 2021
Garcia-Alvarez et al., Rev Psiquiatr Salud Ment 2016

DNA sequencing of the participants in the PORTICO study planned

ORYZON

PORTICO: Final Summary as of January 7th, 2023

- Primary endpoints not met.
- Two important pre-specified secondary endpoints reached statistical significance:
  - **Overall improvement in BPD disease severity,** measured by BEST across weeks 8-12 (p=0.042). Clinically meaningful reduction compared to placebo
  - **Improvement in Agitation/Aggression** measured by STAXI-2 across weeks 8-12 (p=0.026). Clinically meaningful reduction compared to placebo
- Reduction in overall BPD disease severity and agitation/aggression consistent with Phase IIa REIMAGINE trial results, albeit measured by different scales (BEST versus BPDCL; STAXI-2 versus CGI-S A/A).
- Results across ALL primary and secondary efficacy endpoints favored vafidemstat over placebo.
- Global Statistical Test (GST-p values) consistent with a global treatment effect favoring vafidemstat.
- Vafidemstat was safe and well tolerated.
- No deaths/suicides, and suicidal ideation was low (one case each in the PBO and vafi treated groups; 0.9% overall).
- This is the first time, to the best of our knowledge, that a large, randomized Phase II BPD trial had two statistically significant secondary endpoints reflecting improvements in agitation/aggression as well as in overall BPD disease severity.

PORTICO's efficacy and safety results pave the way to define further clinical development and Oryzon intends to request an end-of-Phase II meeting with the FDA to discuss plans for a registrational BPD Phase III trial.

An ongoing PoC in SCHIZOPHRENIA with vafidemstat

EVOLUTION: *An adaptative randomized double blind, placebo-controlled Phase IIb trial with vafidemstat in schizophrenia patients*

- **Strong rationale:** LSD1i restores phenotypes in various SCZ mice models
- **High Unmet Need:** No drugs approved yet for cognitive impairment or negative symptoms of SCZ
- Vafidemstat as add-on to SoC
- N=100
- **Cognition.** Treatment span to assess changes in CIAS: 6 months of treatment
- **Primary endpoints:** efficacy to address SCZ **Negative and cognitive symptoms**
- Actively recruiting patients in EU

A Prevalent & impairing disease
20 millio ww.

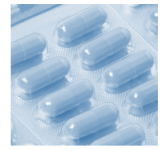
~5 million in US & EU

Three main types of symptoms

Positive or Negative
+
Cognitive Impairment

No approved drugs yet for

Negative symptoms (60%)
Cognitive Impairment (70%)



Vafi improves these symptoms in PC models

Market Value in 2021

US$ ~8 billion

Highest Revenue Drug Category: long-acting injectable (LAI) antipsychotics

Single Best seller:
+ $ 3.5 Billion

Moderate competition

Vafidemstat achieved nominal statistical significance in an exploratory endpoint of cognition using Brief Assessment of Cognition in Schizophrenia (BACS) (p=0.05) in the PORTICO study

Pioneering personalized medicine in epigenetics