Pioneering personalized medicine in epigenetics

ORYZON

JUNTA GENERAL DE ACCIONISTAS

MADX: ORY

27 de Junio de 2025

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Oryzon, a specialist in epigenetics that develops new targeted therapies in CNS and Oncology

Developing potent and selective **epigenetic drugs** with well-defined registrational pathways:

Vafidemstat, a Phase III-ready asset in Borderline Personality Disorder, and Phase II in Schizophrenia

Iadademstat, a Phase I-II asset in **Oncology**: AML, MDS and SCLC, and in **Hematology**: Essential Thrombocythemia and Sickle Cell Disease

2025: Strong fundamentals driving a positive year

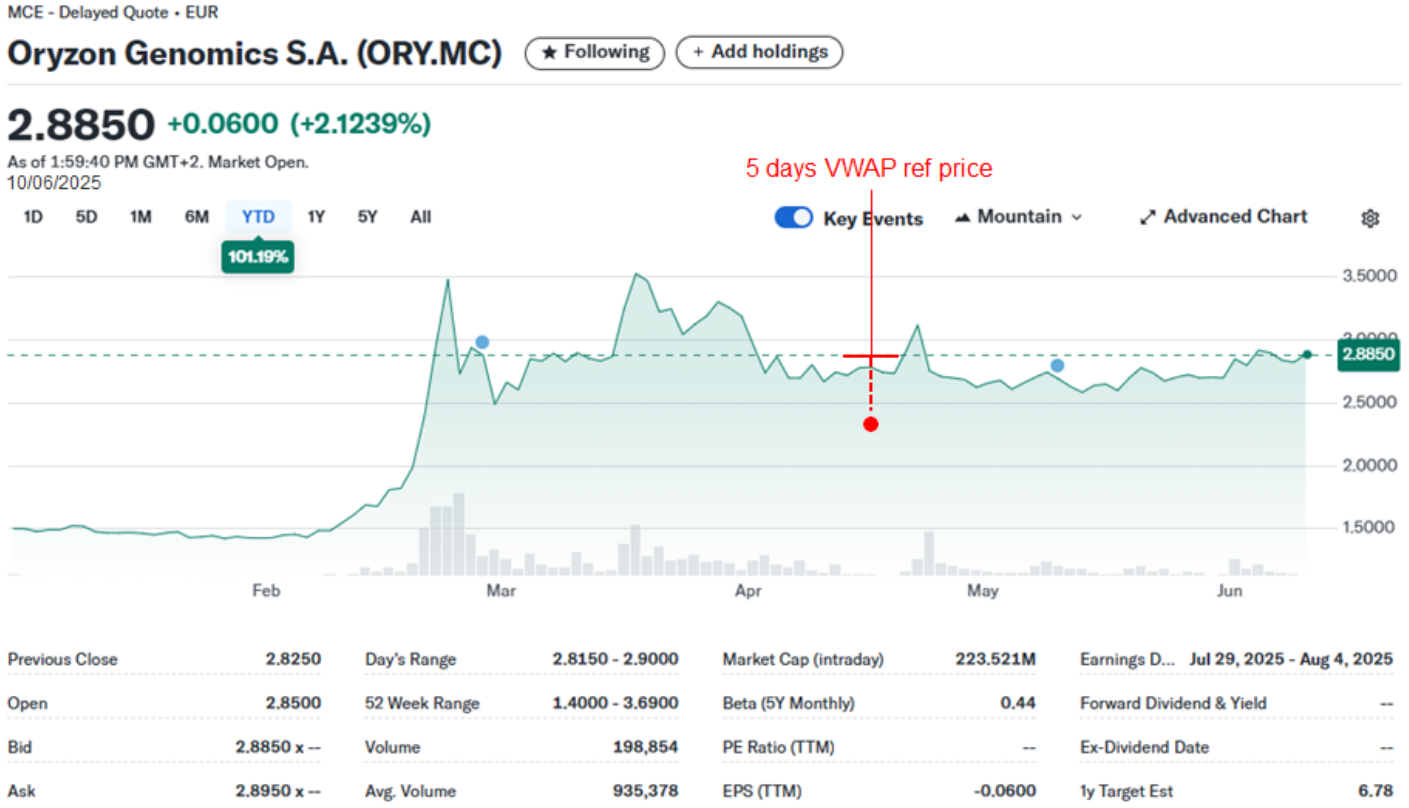
Key Highlights

Robust Stock Performance: Continued positive momentum (~100% YTD increase) reflecting investor confidence in the Company's strategic direction and clinical pipeline.

Successful Recapitalization: Despite adverse macroeconomic conditions, Oryzon has secured approximately €43 million (~$50 million) through a combination of dilutive and non-dilutive financing, strengthening the balance sheet and extending the financial runway.

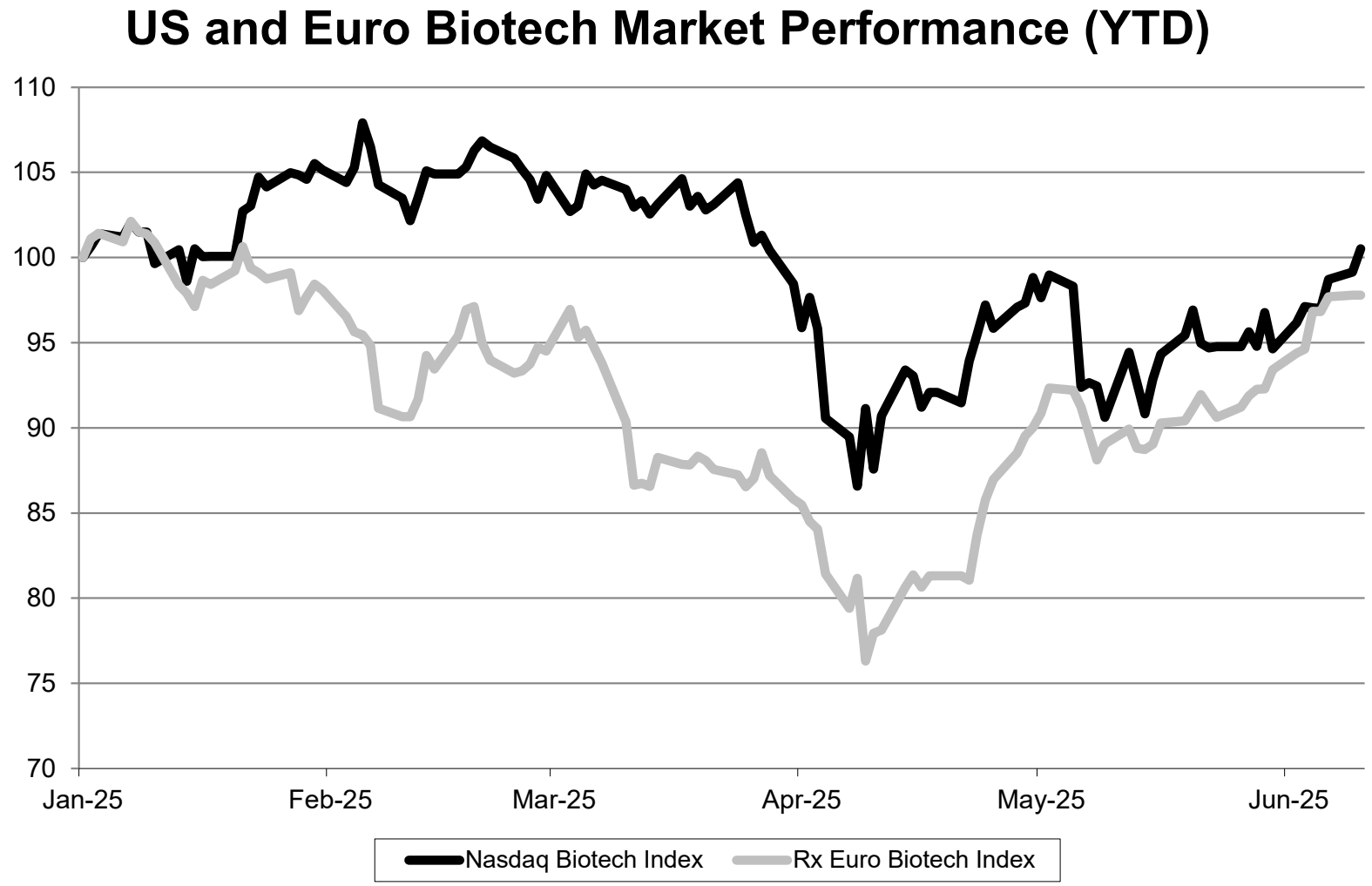
Strong Market Recognition: The Company's recent clinical progresses have been well received by the market, reinforcing its credibility and positioning in the biotech sector.

PIPE April 2025 – Positive Aftermarket Reaction: The round conducted in April 2025 demonstrated solid investor interest, with a favorable performance in the aftermarket, further validating the quality of the investor base and the strength of the underlying equity story.



The transaction was priced at a 15.5 % discount to the 5-day Volume-Weighted Average Price (VWAP), resulting in a final price of €2,35 per share.

2025: ORYZON's YTD performance compares favorably with the industry average



A new BoD with US and EU Industry Independent Directors experienced in M&A

Manuel López-Figueroa, PhD (Independent Lead Director & President of the RemComm Committee)

Dr. López-Figueroa serves as Chief Operating Officer of **IMIDomics** Inc., focusing on treatments for immune-mediated inflammatory diseases. Since 2001, he has served as an Advisor and **Managing Director at Bay City Capital**, one of the world's premier life science investment firms with over $1.6 billion under management and playing a key role in numerous successful investments across its portfolio. Dr. López-Figueroa also acts as **Scientific Liaison for the Pritzker Neuropsychiatric Disorders Research Consortium**, a collaborative group of leaders from top U.S. universities. With over 25 years of experience in neuroscience research, he holds a PhD in Medicine and Surgery, an MS in Molecular and Cell Biology, and has completed post-doctoral work at the University of Michigan and University of Copenhagen, Denmark.

Konstantinos Alataris PhD (Independent)

Serial entrepreneur with +30 yr in the US focused on scaling innovative medical technology companies and orchestrating the successful commercialization of disruptive therapeutics in highly competitive markets. Dr. Alataris brings decades of experience as a founder, CEO, investor, and board member in the medical device industry. Among Other positions he has been CEO and Co-Founder of **Nēsos** President & Chief Executive Officer of **Zosano Pharma** and Founder, President and Chief Executive Officer. Founder of **Nevro Corp (NYSE:NVRO**). Dr. Alataris has also served as **Vice President at Bay City Capital. Dr**. Alataris has also led corporate turnarounds, developing new strategies and rebuilding organizations for success. His deep working expertise spans autoimmune, neurosurgical, neurological, neuropsychiatric, orthopedic, and cardiac disorders, both as an operator and Board member.

Luis Sanchez Quintana (Independent & President of the Audit and Compliance Committee)

Former Partner of PwC. With more than 33 years of professional experience at PwC, including 17 years as a Partner, during which he held the role of **Global Head of the Pharma and Life Sciences Sector**. Audit Partner for Laboratorios Rovi supporting its growth trajectory and eventual IPO. Audit Partner for listed companies in the national pharmaceutical sector as **Pharmamar** and **Faes**, and for Key subsidiaries of multinational groups: **MSD, BMS, AstraZeneca, Roche, Laboratorios Indas, Farmalíder, Teva, GSK, Janssen, Johnson & Johnson, Italfármaco, Unolab**, Grupo Alter, among others. Additionally served in **Tigenix** as responsible partner for **Nasdaq matters** and in **VectiBio** as coordinator and advisor for PwC during its **Nasdaq listing.**

Montse Vendrell PhD (Independent)

She is a partner at **Alta Life Sciences**, a venture capital fund based in Barcelona that invests in life sciences companies. Previously, she served as **CEO of Biocat** (2007-2015), **the Barcelona Science Park** (2014-2015), and the **Barcelona Institute of Science and Technology (BIST)**, She holds **a PhD in Biology from the University of Barcelona** (1991), she completed post-doctoral research at Hoffmann-La Roche (NJ, USA, 1992-1994) and at the Spanish National Research Council (CSIC, 1995-1997). She also holds a Master's in Scientific Communication from UPF-Barcelona School of Management (1997), completed the General Management Program (PDG) at IESE (2007).Currently, she also serves as **Chair of the Executive Committee of the Pasqual Maragall Foundation** for research In Alzheimer's Disease.

Pierre Beaurang PhD (Independent)

Dr. Beaurang holds PhD in Molecular & Cell Biology by the University of California Berkeley. Dr Beaurang has been Chief Executive Officer at Nitrase Therapeutics. He is an expert in oncology and immunology and in Business Development. He has been Chief Business Officer at **Nurix Therapeutics (NASDAQ:NRIX)** and Founding Team member and Executive Director of Businness Development at **Five Prime Therapeutics (NASDAQ: FPRX acquired by Amgen)**

ORYZON

CARLOS BUESA: Chairman of the Board, Founder and CEO

ORYZON, the only company developing epigenetic drugs in CNS

VAFIDEMSTAT

A Phase III-ready LSD1 inhibitor for CNS diseases

LSD1 inhibition, a promising therapeutic option in CNS disorders

ORYZON is the only company to have developed an LSD1 inhibitor for CNS

Currently ready for Phase III clinical development

Vafidemstat's pharmacology supports use in different mental diseases

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

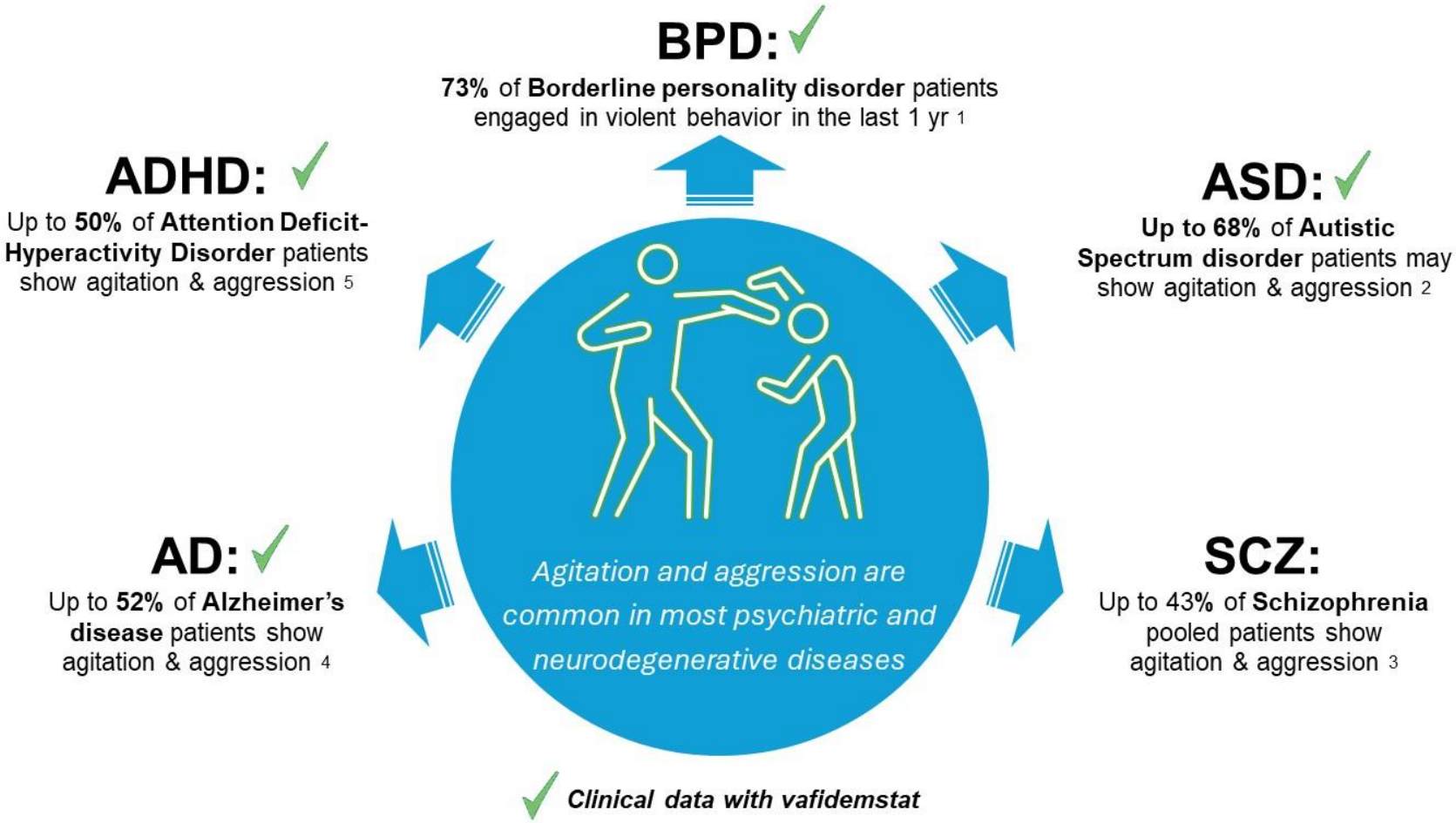
Vafidemstat improves sociability

Vafidemstat reduces aggression

Vafidemstat improves memory

Borderline Personality Disorder, Schizophrenia, Autism, ADHD, others

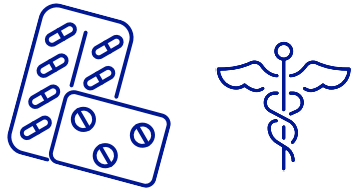
We are specialized in Aggression, a huge medical need in CNS diseases



[1] Source: https://doi.org/10.1521/pedi.2009.23.6.541
[2] Source: https://doi.org/10.1016/j.rasd.2014.05.006
[3] Source: https://dx.doi.org/10.5498/wjp.v12.i1.1; https://doi.org/10.1016/j.ajp.2019.101846
[4] Source: https://pubmed.ncbi.nlm.nih.gov/9178055/
[5] Source: https://doi.org/10.1089/cap.2015.0126

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

(~$3Bn potential peak sales in BPD)



Prevalent & impairing disease

9 million in US & EU

Two main types of symptoms

Psychiatric symptoms
+
Agitation/Aggression
(including self-aggression)

No approved drugs yet

Patients on off-label anti-psychotics

Vafidemstat improves these symptoms in:

- BPD patients
- PC models

Oryzon is leading the BPD field ahead of the competition

Vafidemstat Current Clinical Development

- Exploring large multifactorial indications (Borderline Personality Disorder, Schizophrenia and Autism)
- Exploring also feasibility in some rare genetically-driven neurodevelopmental disorders (Phelan McDermid, Fragile X, Kabuki, etc)

VAFIDEMSTAT	Study	Preclinical	Phase I	Phase II	Phase III	FILED
Vafidemstat (ORY-2001) - the only CNS optimized LSD1 inhibitor in clinical development						
Borderline personality disorder Agitation/Aggression & Overall Improvement	**PORTICO (Phase II)** **PORTICO-2 (Phase III)**				*In prep*	
Schizophrenia Negative Symptoms / Positive Symptoms / CIAS	**EVOLUTION**					
Autistic Spectrum Disorder Aggresion / repetitive behaviour	**HOPE-2** **(Phase II In Study feasibity)**					

- Positive Outcome Minutes from FDA End-of-Phase II meeting received in Sept 2024
- PORTICO-2 Phase III protocol submitted to FDA
- FDA IND approval for Phase III in BPD expected 2H25. FPI expected in 4Q2025
- Country expansion ongoing for the Phase II in Schizophrenia

ORYZON

FDA End-of-Phase II Meeting official minutes: summary

Study design and efficacy endpoints discussion for the registrational Phase III study (PORTICO-2)

FDA's feedback supports the initiation of the Phase III trial

- Agitation-Aggression in BPD acknowledged as a possible therapeutic indication
- FDA agrees that Oryzon may pursue a Phase III study using STAXI-2 Trait anger as a primary efficacy endpoint measure
- Secondary endpoints will include patient-rated and clinician-rated scales to assess agitation/aggression and overall BPD improvement

A new and prestigious US-centric Clinical Advisory Board for CNS

Alan F. Schatzberg one of the most renowned American psychiatrist. Since 1991, he has been the Kenneth T. Norris Jr . Professor of Psychiatry and Behavioral Sciences at Stanford University School of Medicine. He was chair of the department Psychiatry and Behavioral Sciences at Stanford from 1991 to 2010. He is also the co-editor-in-chief of the Journal of Psychiatric Research. Alan Schatzberg, as the APA president in 2009–10, was identified as the principal investigator on a federal study into the drug mifepristone for use as an antidepressant being developed by Corcept Therapeutics, a company Schatzberg had created and in which he had several million dollars' equity.

Eric Hollander, M.D. Professor, Department of Psychiatry and Behavioral Sciences at Albert Einstein College of Medicine in NYC. Director, of the Autism and Obsessive Compulsive Spectrum Program, Department of Psychiatry and Behavioral Sciences. His main areas of research are CBDV in Autism Spectrum Disorder (ASD); Oxytocin in Prader Willi Syndrome (PWS); Vasopressin 1a antagonists in ASD; alpha-1 chemotrypsin in ASD; Intermittent Explosive Disorder; Tourette Syndrome; TMS in OCD and ASD

Dr. Emil F. Coccaro is a psychiatrist in Columbus, Ohio and is affiliated with Ohio State University Wexner Medical Center. He received his medical degree from New York University Grossman School of Medicine and has been in practice for more than 20 years. He is an expert in Aggression and he has contributed with the creation of The Overt Aggression e creation of The Overt Aggression Scale Modified (OAS-M) for clinical trials targeting impulsive aggression and intermittent explosive disorder

Dr. Sarah Fineberg is Assistant Professor of Psychiatry at Yale University investigating the neurobiological mechanisms behind borderline personality disorder (BPD) and related mental health conditions. She is also interested in testing the efficacy of novel and emerging treatments. She has participated in several BPD studies

PORTICO-2 Phase III: a 350-patient study

Aggression: Primary endpoint (STAXI-2 Trait Anger) + key Secondary endpoint (OAS-M)

- Randomized, double blind, placebo-controlled, adaptive trial
- N= 350 (randomized 1:1)

Through discussions with the CAB, we have reached an agreement on the Phase III protocol's endpoints, ensuring they are both highly informative and closely aligned with the FDA's traditional requirements

Endpoints

Primary: efficacy in agitation/aggression by **STAXI-2 Trait Anger**

Key secondary: efficacy in agitation/aggression by a ClinRO FDA-accepted scale (**OAS-M**)

Secondary – efficacy improvements in:
- Overall improvement by BEST
- Overall improvement by CGI (overall disease)
- Depression by BDI-II

Secondary – safety

Exploratory:
- PK
- Target engagement
- Exploratory biomarkers
- Genetic polymorphisms

Phase III protocol submitted to FDA on June 20

After numerous constructive interactions with the agency

FDA's feedback has been key to refine the protocol

- Agitation-Aggression in BPD acknowledged as a possible therapeutic indication
- STAXI-2 Trait anger (Patient Rated Scale) as a primary efficacy endpoint measure is complemented with OAS-M as key secondary endpoint (Clinician Rated Scale)
- Phase III protocol and SAP submitted
- Qualitative research and Psychometric analyses have also been added following FDA recommendations

FDA response expected in September

Vafidemstat demonstrated a relevant clinical benefit in reducing agitation /aggression across ASD, ADHD and BPD patients in PoC Phase IIa study

- ASD: Autistic Spectrum Disorder
- ADHD: Attention deficit & Hyperactivity Disorder
- BPD Borderline Personality Disorder

PCN Psychiatry and Clinical Neurosciences

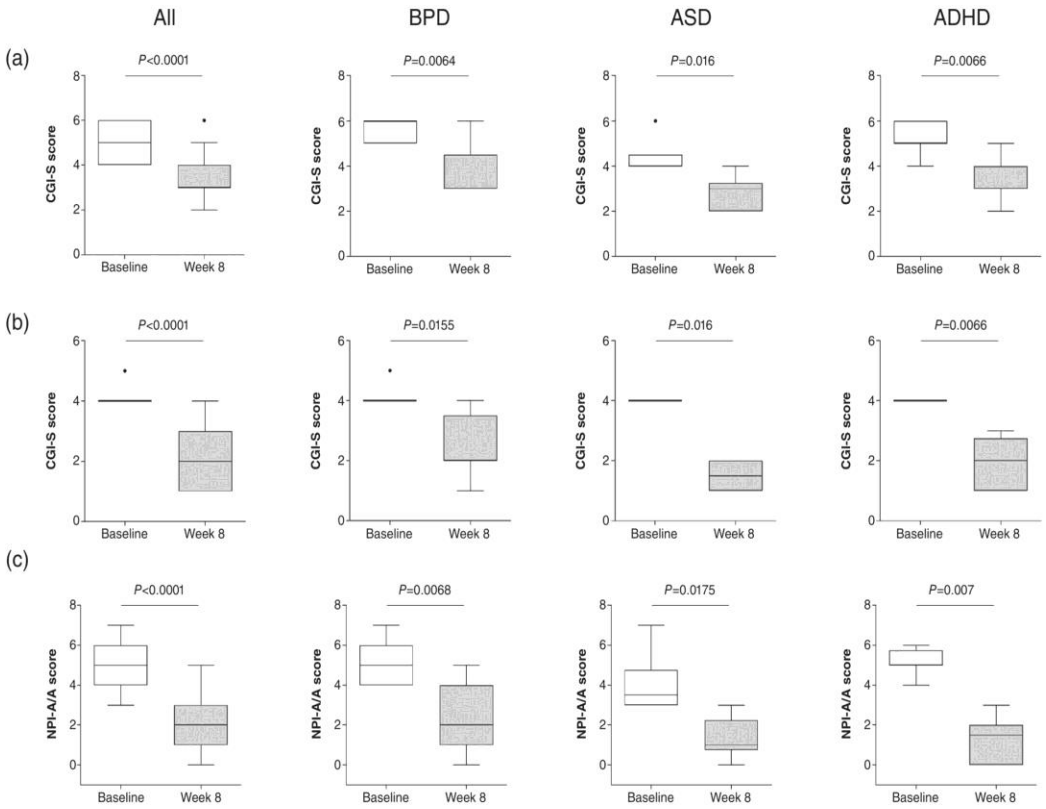
Regular Article | Open Access

REIMAGINE: A central nervous system basket trial showing safety and efficacy of vafidemstat on aggression in different psychiatric disorders

Marc Ferrer MD, PhD, Vanesa Richarte MD, PhD, Laura Gisbert MD, PhD, Jordi Xaus PhD, Sonia Gutierrez BSc, MSc, Maria Isabel Arevalo PhD, Michael Ropacki MA, PhD, Roger Bullock MD, Carlos Buesa PhD, Josep Antoni Ramos-Quiroga MD, PhD

First published: 12 February 2025 | https://doi.org/10.1111/pcn.13800

Clinical Trial Registration: REIMAGINE EudraCT#: 2018-002140-88.



Eight-week vafidemstat treatment led to a **statistically significant reduction in agitation/aggression** compared with baseline across all the assessments (all participants, $p < 0.0001$)

We have performed an observational study in Shank3 patients to inform a possible Phase II study with vafidemstat in this population

Phelan-McDermid Syndrome (PMS) is a rare genetic neurodevelopmental disorder primarily caused by deletions in the SHANK3 gene.

70–90% of PMS patients show ASD-like features:

- Social communication deficits
- Repetitive behaviors
- Sensory sensitivities
- Aggressivity

Unsupervised hierarchical clustering of the first 19 patients identified 3 groups, characterized by a different profile of cognitive and behavioral scores. Validated with additional 11 subjects from a test cohort

frontiers | Frontiers in Psychiatry

TYPE Original Research
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Phenotype and psychometric characterization of Phelan-McDermid syndrome patients: pioneering towards personalized medicine

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Aggression in ASD: clinical studies under evaluation for vafidemstat

To be conducted initially in Spain at reduced cost through the EU-IPCEI grant

- **Fragile X Syndrome (FSX)** is the most common inherited cause of intellectual disability, affects approximately 1 in 4,000 males and 1 in 8,000 females. Nearly all (>90%) male and female individuals were reported to have engaged in some aggression over the previous 12 months. Furthermore, aggressive behaviors in male individuals were severe enough that 30% had caused injuries to caregivers, and 22% had caused injuries to peers or friends.
- **Phelan-McDermid syndrome (PMS)** is a rare genetic condition (prevalence estimate 1/30,000 births) primarily caused by a terminal deletion on the 22q13. Aggressive behavior is seen in approximately 25% of affected individuals

Exploring strategic collaborations with biotech companies to leverage AI platforms for the selection of patients most likely to benefit from vafidemstat

Strengthening vafidemstat's IP protection in BPD & Aggression

Treatment of Aggression (WO2019/025588):

- **Allowed/granted in Australia, Europe, South Korea, Hong Kong, Malaysia, Philippines and Russia**.
- Pending in US and additional countries.

Treatment of BPD/non-aggression symptoms of BPD (WO2020/188090):

- **Allowed/granted in Europe, Japan, Mexico, Russia, and Singapore**.
- Pending in US and additional countries.

Vafidemstat in Schizophrenia

Genetic and physiological connections between LSD1 and schizophrenia pathology

Vafidemstat in Schizophrenia

Genetic link between LSD1 and SCZ

Preclinical data in in- vitro and in animal models supporting LSD1 inhibition as a new MoA in SCZ

No approved drugs yet in negative symptoms or Cognitive Impairment symptoms

Strong market interest & huge M&A activity

Schizophrenia, still an unmet medical need

Vafidemstat may improve different symptoms in schizophrenia patients

A prevalent & impairing disease 20 million 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: + $4.1 Billion

Moderate competition

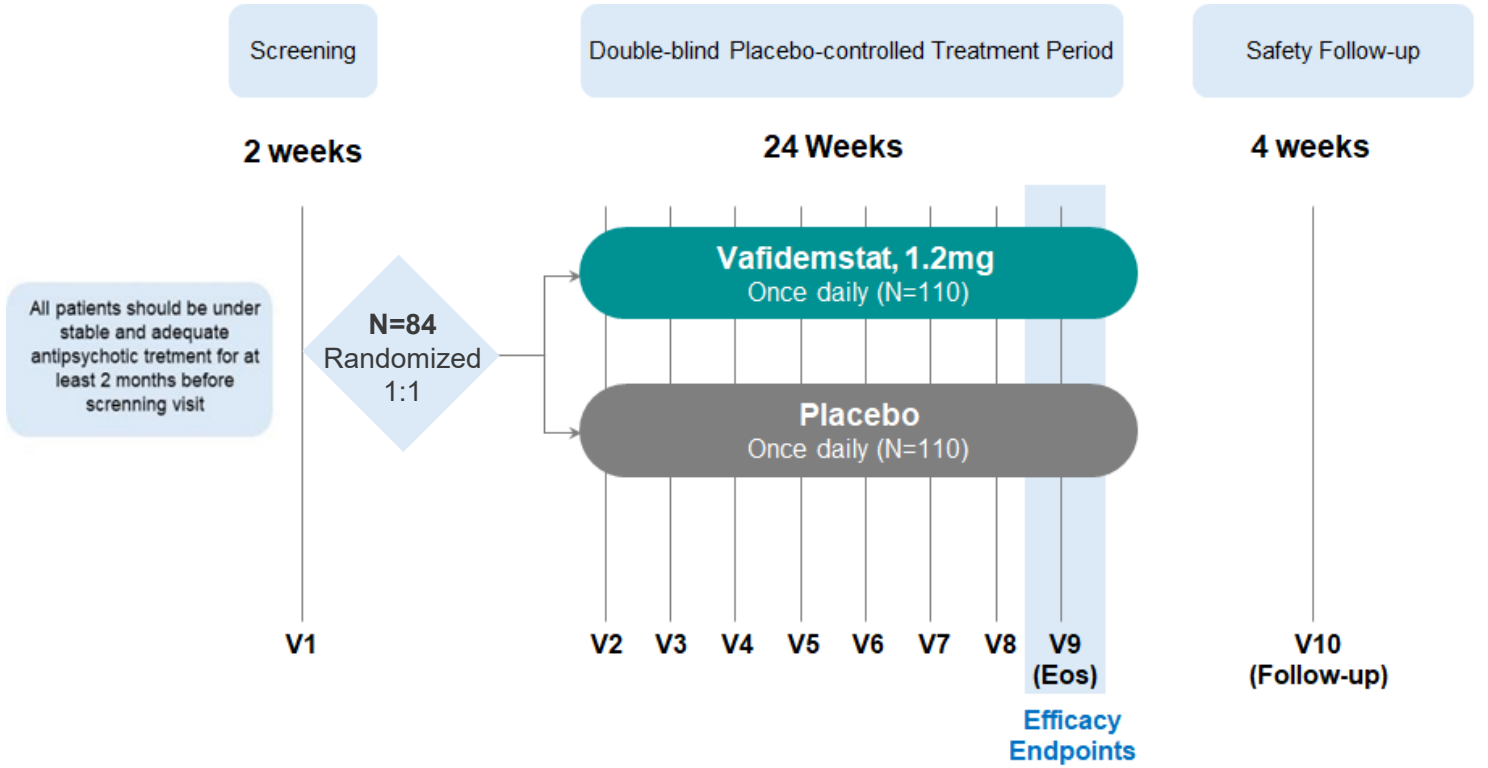
EVOLUTION: International expansion and re-sizing

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

- Our Phase IIb trial (EVOLUTION) was currently recruiting only in Spain due to financial constrains
- International Expansion ongoing in 5 European countries after the recent fundraising
- With the lessons learned from PORTICO, a reassessment of number of patients needed to obtain a clinically meaningful impact has been conducted and the trial is being re-sized to a total number of 84 patients
- Primary endpoint: Negative Symptoms
- Secondary endpoints: Positive and Cognitive Impairment Symptoms
- A high-quality trial designed to meet the standards of registrational studies in the indication: multicenter, double-blind against a control arm, with regulatory-accepted endpoints.

EVOLUTION: Study in expansion to 5 additional EU countries

Readout: expected in 1H 2027



Endpoints

Primary endpoint:
Improvement in Negative Symptoms

Secondary endpoints – Efficacy

Improvements in:

- Cognitive impairment associated with schizophrenia (CIAS)
- Positive symptoms of schizophrenia
- Positive and Negative Syndrome Scale (PANSS) Total Score
- Functional impairment in adult schizophrenia patients

Secondary endpoints - Safety

- To evaluate vafidemstat safety in adult schizophrenia patients

Strong market interest & huge M&A activity

Multibillion acquisitions in the psychiatric arena with schizophrenia as the hottest spot

THE WALL STREET JOURNAL.

BUSINESS | ENERGY & OIL

AbbVie to Buy Cerevel Therapeutics for $8.7 Billion

Deal is AbbVie's second major acquisition in the last two weeks

By Ben Glickman Follow
Dec. 6, 2023 4:46 pm ET

Share Resize Listen (1 min)

AbbVie said the deal complements its existing neuroscience portfolio currently on the market.
PHOTO: BRIAN SNYDER/REUTERS

AbbVie ABBV 1.35% ▲ will acquire neuroscience-drug maker Cerevel Therapeutics CERE -0.13% ▼ Holdings for $45 a share, giving the company an equity value of about $8.7 billion.

Vafidemstat Commercial Assessment (I)

Significant Commercial Potential

Vafidemstat could achieve NRA sales of +$6Bn at peak in 2036

- BPD multi-symptom treatment represents the most substantial peak revenue opportunity of +$3 Bn
- Schizophrenia negative symptoms treatment also represents a large opportunity, where global net revenues could reach +$2.5Bn at peak

Vafidemstat Commercial Assessment (II)

Global CNS Market Dynamics

Vafidemstat commercial expectations in the two large indications (BPD and SCZ) are in line with the current dynamics of the psychiatric markets and with the commercial success achieved by other assets

- The market size of Schizophrenia positive symptoms treatment represents +$10 Bn of sales in 2023. This dynamic provides valuable guidance on the market size for the treatment of negative symptoms and cognitive impairment-associated symptoms in this disease
- The global anxiety disorders and depression treatment market size was $8.5 Bn in 2019 and is expected to reach $13 Bn by 2027
- The global ADHD treatment market size was ~$30 Bn in 2021 and is expected to reach $45 Bn by 2027

- **Invega +$4.11Bn sales in 2023**

- **Abilify+ Rexulti +$1.4Bn sales in 2022**

- **Vyvanse $3.8Bn sales in 2022**

IADADEMSTAT

A Phase II LSD1 inhibitor for oncological diseases

ONCOLOGY-HEMATOLOGY PROGRAM (iadademstat)

Relying on our CRADA agreement with the NCI-NIH

program ready to be licensed

iadademstat is the most potent LSD1 inhibitor in clinical development

AML 1L

- Encouraging data in Unfit population in combo with azacitidine
- Special efficacy in unfit populations poorly responding to Ven-Aza
- Preliminary encouraging data in triple combo Ven-Aza-Iada

AML R/R Flt3+

- Phase Ib ongoing US only
- Encouraging data in combination with gilteritinib
- In a dose extension

SCLC 1L-ED

- Phase Ib-II randomized trial sponsored by NCI under our CRADA. US only
- FPI April 2025. Recruiting
- 40 pt to be recruited
- Led by MSKCC.
- +30 sites in the US

SCD / Beta-Thal

- Commercially-validated MoA (HbF ind) & best modality (oral)
- Superior to current SoC and other dvpment-stage agents
- PoM & superiority demonstrated in the most relevant and predictive animal model

Iadademstat: multiple Shots on goal in Oncology & leverage on CRADA-NCI agreement

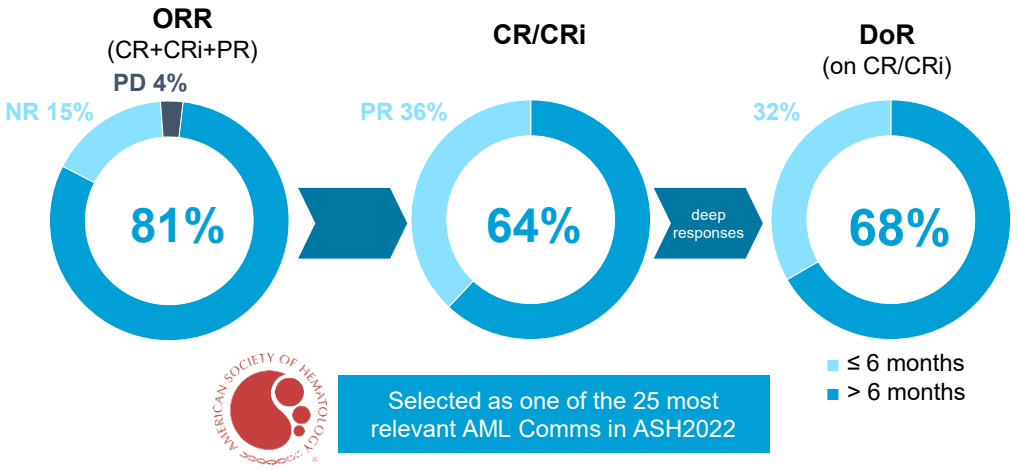
The oncology program represents a significant upside and requires only a modest investment, as most studies are funded through the CRADA agreement with the NCI-NIH

Program	Study	Preclinical Phase	Phase I		Phase II		Status	Expected Milestone(s)	
			Phase Ia	Phase Ib	Phase IIa	Phase IIb			
Oncology: Iadademstat (ORY-1001) – Selective LSD1 inhibitor									
AML 1L Unfit Patients Combination with azacitidine	ALICE						**Completed** Study has results	Final positive results published May 2024 (Lancet Haematology)	
AML 1L Unfit Patients Combination with azacitidine and venetoclax	ALICE-2 (IIS-X002)			Phase Ib			**Recruiting** Sponsor: OHSU	2nd cohort enrolled	
AML 1L Unfit Patients Combination with azacitidine and venetoclax	ALICE-3 (CRADA-AML)			Phase Ib			**Recruiting** Sponsor: NCI Led by UPMC	1st patient dosed	
AML R/R-Flt3mut+ Combination with gilteritinib	FRIDA			Phase Ib			**Recruiting**	Initial data presented at EHA-2024 Next data update ASH-2025	★
MDS Combination with azacitidine	IIS-X005			Phase I			**Recruiting** Sponsor: MCW	1st patient dosed	
Neuroendocrine High Grade R/R Combination with paclitaxel	C-X001 NET Basket						Collab Study with FCCC	Study Closed	
ED-SCLC 1L Combination with ICI	STELLAR-0 (CRADA-SCLC)				Phase I / II		**Recruiting** Sponsor: NCI, Led by MSKCC	1st patient dosed	★

CRADA: Cooperative Research and Development Agreement; FCCC: Fox Chase Cancer Center; ICI: immune checkpoint inhibitor; IIS: investigator-initiated study; MSKCC: Memorial Sloan Kettering Cancer Center; NCI: National Cancer Institute; NETs: neuroendocrine tumors; OHSU: Oregon Health & Science University; SCLC: small cell lung cancer; UPMC: University of Pittsburgh Medical Center.
Note: Study names indicated for IIS or CRADA trials correspond to Oryzon's internal names for these trials

Iadademstat Combination with Azacitidine is a Safe and Effective Treatment in First Line Acute Myeloid Leukemia. Final Results of the ALICE Trial

Rapid, deep, and durable responses



Selected as one of the 25 most relevant AML Comms in ASH2022

Summary of Responses		
n = 27	**n**	**%**
CR	9	**33%**
CRi	5	**19%**
PR	8	**30%**
NR	4	**15%**
PD	1	**4%**
CR/CRi	14	**52%**
ORR (CR/CRi/PR)	22	**81%**
TTR	n=22 Median [95% CI]	**2.1 mos** [1.1,2.6]
DoR	n=22 Median [95% CI]	**8.8 mos** [1.8,17.4]

CR/CRi pts		
n=14	**n**	**%**
MRD neg	10 out of 11 evaluable	**91%**
Achieved TI (RBC & Plt)	10	**71%** 10/14

CR: Complete Remission; CRi: Complete Remission with incomplete hematologic recovery; PR: Partial Response; NR: No response; PD: Progressive Disease; ORR: Overall Response Rate; MRD: Measurable Residual Disease; TTR: Time To Response; DoR: Duration of Response; TI: Transfusion Independence; RBC: Red blood cells; Plt: Platelets

ALICE-2 (IIS) a triple combo Ven-Aza-lada in first line unfit AML patients

- NCT06357182
- PI: Dr. Curtis Lachowiez, OHSU Knight Cancer Institute
- Sponsor OHSU
- N = 24

Status:

- FPI: August 2024
- Expected completion: May 2026
- **First Cohort accrued: 3 pts**
  - **No DLTs reported**
  - **No safety concerns**
  - **The 3 patients are in CR/CRi/CRh**
- Second cohort enrolled

ORYZON

FRIDA: a Phase Ib trial in R/R AML as a foundation for a potential accelerated development.

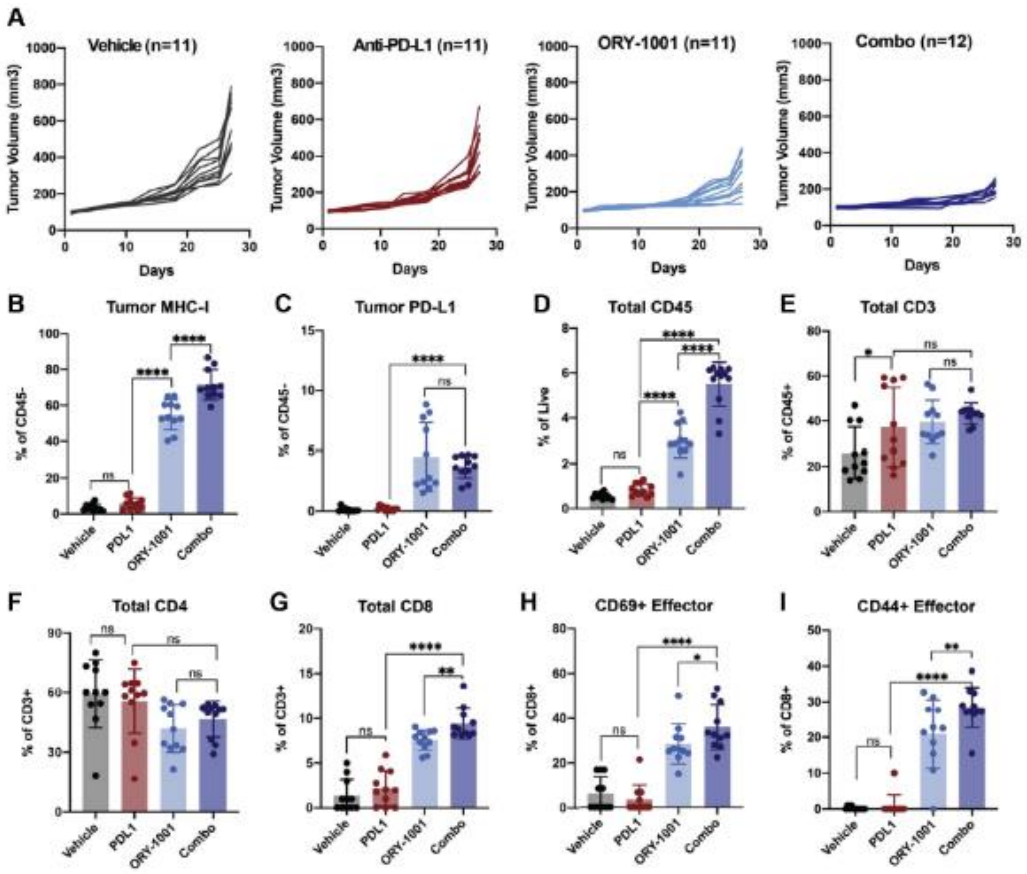
Initial observations at EHA-2024: Fast time to responses & Encouraging antileukemic activity

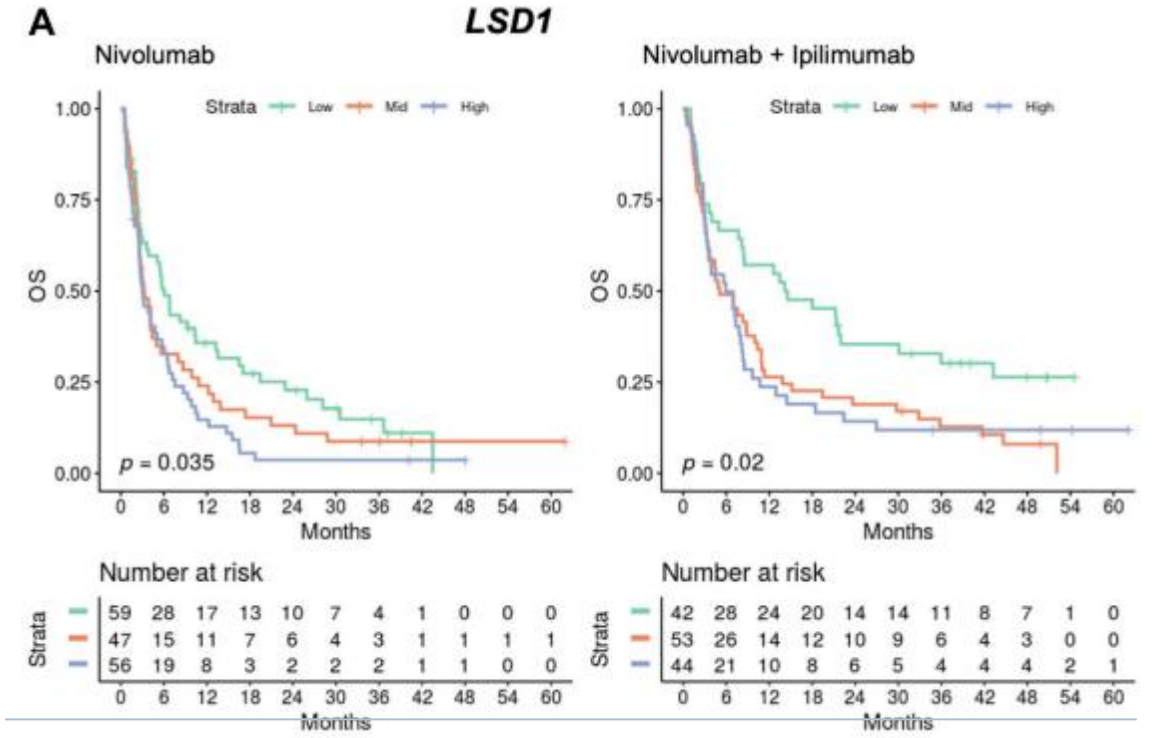
- Actively recruiting
- Encouraging antileukemic activity observed, with 9 out of 13 patients (ORR 69%) **achieving bone marrow (BM) blast clearance in the first cycle.**
- TTR faster than Giltertinib. Most responses are already seen by the end of the first cycle, with a **median time to CR/CRh/CRi of 35 days**
- 43% achieved complete remission (CR), complete remission with partial hematological recovery (CRh) or complete remission with incomplete blood count recovery (CRi) in DL-1
- All but 2 patients were refractory to prior standard regimens including venetoclax,7+3 and midostaurin.
- Two patients (one in the starting cohort and one in DL-1 cohort) have undergone hematopoietic stem cell transplantation.
- Results warrant study continuation for this challenging patient population to treat in the current environment (RWD of gilteritinib alone shows CR of 20%)
- Recommended DL-1 for expansion up to 12 subjects (total) at this DL-1.

Best responses	Starting dose (n=6)	DL-1 (n=7)
CR	-	1 (1 HSCT)
CRh	-	1
CRi	2	1
MLFS	3 (1 HSCT)	1
NR	1	3
ORR	5 out of 6 83%	4 out of 7 57%
% CR/CRh/CRi	33%	43%

Iadademstat and anti-PD-L1 combination inhibits SCLC progression

- Iadademstat renders the SCLC cells visible to the immune system
- Iadademstat synergizes with ICIs and boosts the host immune system by increasing T cell infiltration and preventing T-cell exhaustion





Analysis of epigenetic determinants of antigen presentation identified LSD1 gene expression as a correlate of worse survival outcomes for patients treated with either nivolumab or the combination of nivolumab and ipilimumab

Memorial Sloan Kettering Cancer Center

Memorial Sloan Kettering Cancer Center

ORYZON

Nguyen et al., 2022 and Rudin et al., 2023

NEXT-CTEP-NCI Program (CRADA): ongoing SCLC trial in combination with ICI

Testing the Combination of an Anti-cancer Drug, Iadademstat, With Other Anti-cancer Drugs (Atezolizumab or Durvalumab) at Improving Outcomes for Small Cell Lung Cancer

ClinicalTrials.gov ID: NCT06287775

Sponsor: National Cancer Institute (NCI)

Led by Dr. Charles Rudin

Memorial Sloan Kettering Cancer Center

ORYZON to provide drug
IND approved
Actively recruiting (+30 hospitals across the US)

- MSKCC
- JHU Sidney Kimmel Comprehensive Cancer Center at the John Hopkins
- Ohio State Univ Cancer Center
- City of Hope Cancer Center
- University of Pittsburgh Cancer Institute
- Yale University
- National Cancer Institute
- And many others

Enrollment (Estimated)
45-50 pts

Primary Objective

To compare the **progression-free survival (PFS)** between the combination of iadademstat plus immune checkpoint inhibitor (ICI) versus ICI maintenance alone.

Secondary Objectives

- To compare objective response rate **(ORR)** and overall survival **(OS)** between treatment arms.
- To evaluate the safety of combination iadademstat plus ICI.

NIH NATIONAL CANCER INSTITUTE
DCTD Division of Cancer Treatment & Diagnosis

IADADEMSTAT

A Phase II LSD1 inhibitor for non-malignant hematological diseases

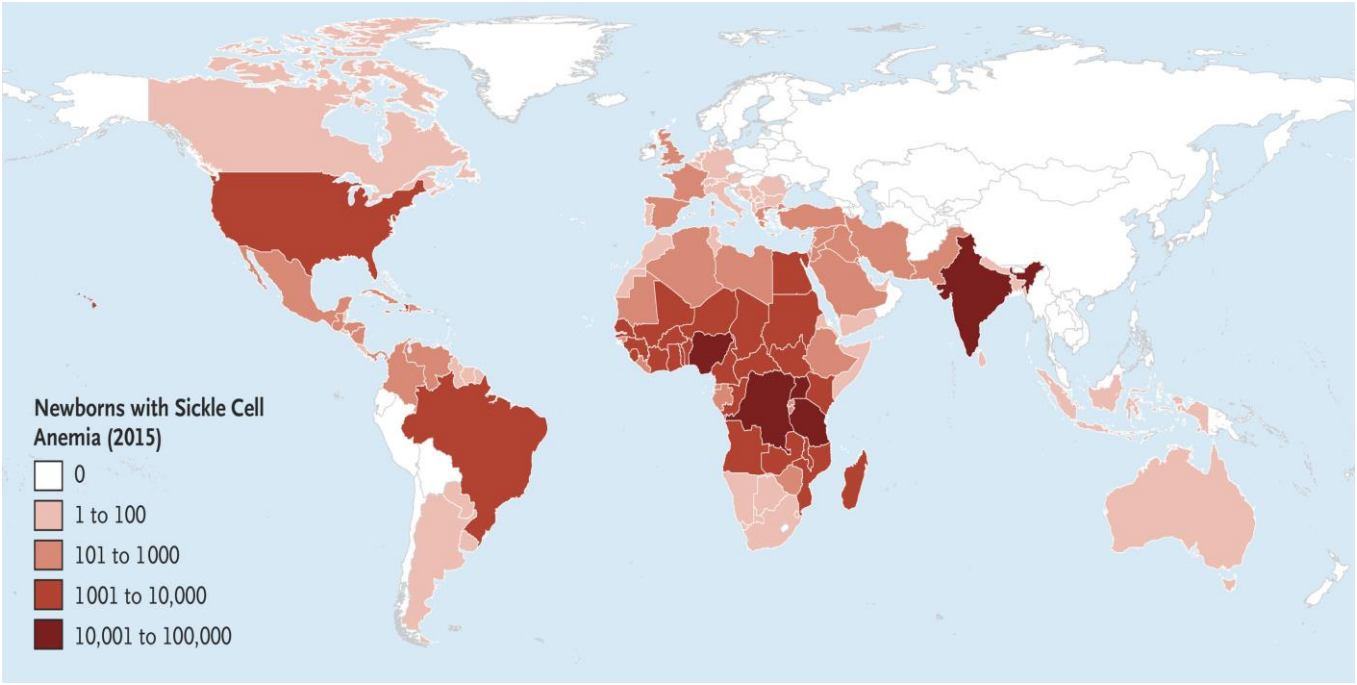
New non-malignant hematology program: Sickle Cell Disease (SCD)

Caused by a genetic mutation in the beta globin gene causing abnormal sickle-shaped red Blood cells (RBC) rigid and sticky that block blood flow and oxygen delivery to all parts of the body. Producing painful VOCs (vaso-occlusive events), which can also cause Acute Chest Syndrome and stroke, organ damage, kidney failure and early mortality

Most common inherited blood disorder in the US (US Prevalence 80,000-100,000)

Approved Treatments
Curative: HSCT (and potentially gene therapies)
Supportive: Blood transfusions, hydroxyurea (HbF inducer), crizanlizumab (P-selectin inhibitor), L-glutamine (antioxidant)

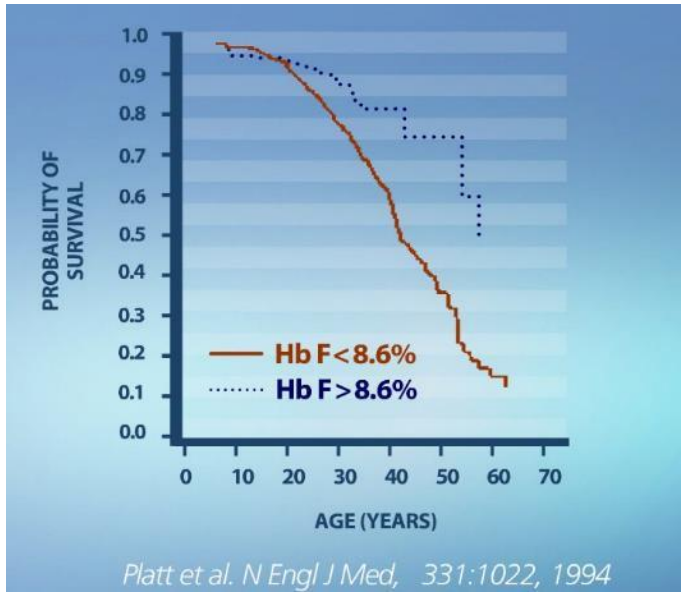
Market Opportunity
The US market is valued at $4.8B by 2030



Fetal (Y) globin inhibits polymerization of HbS (SCD mutated Hb) addressing the specific pathophysiology of the disease

Any increment of fetal Hb (HbF) reduces severity of SCD; HbF > 8.6% or absolute 0.5 g HbF/dl normalizes survival

Natural History



NIH Landmark study In SCD (1978-1998)
~4000 subjects

HbF > 8.6% improves survival to normal range for race

Increases in HbF to a level of ≥ 8.6% or absolute HbF to ≥ 0.5 gm/dl correlate with survival and may serve as surrogate endpoints for potential accelerated approval

Hydroxyurea

Current Standard of Care

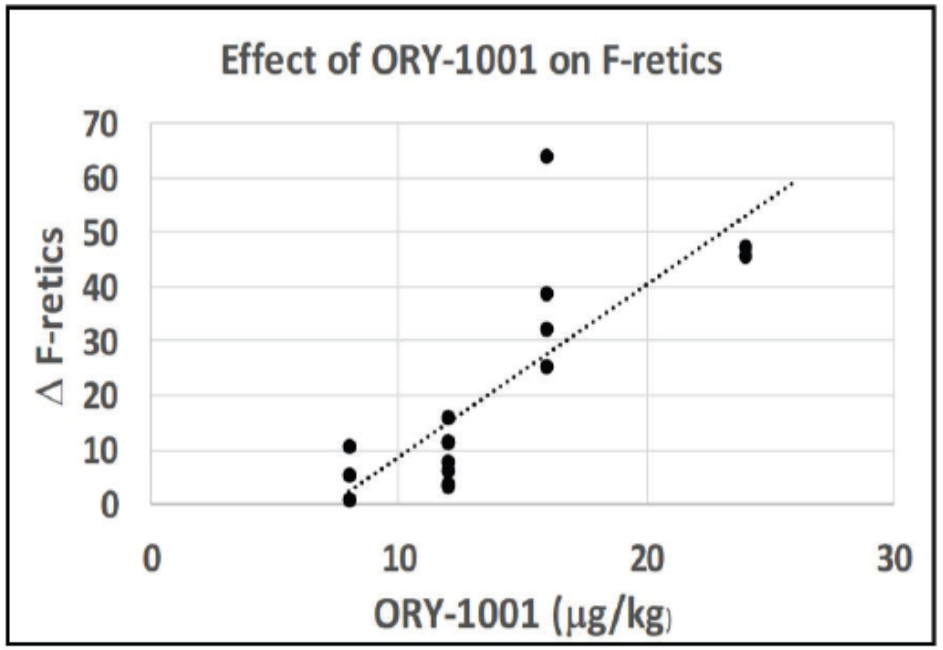
- \+ Potential to ameliorate disease pathology
- − Non-responders
- − Waning efficacy
- − Safety and tolerability issues

ORYZON

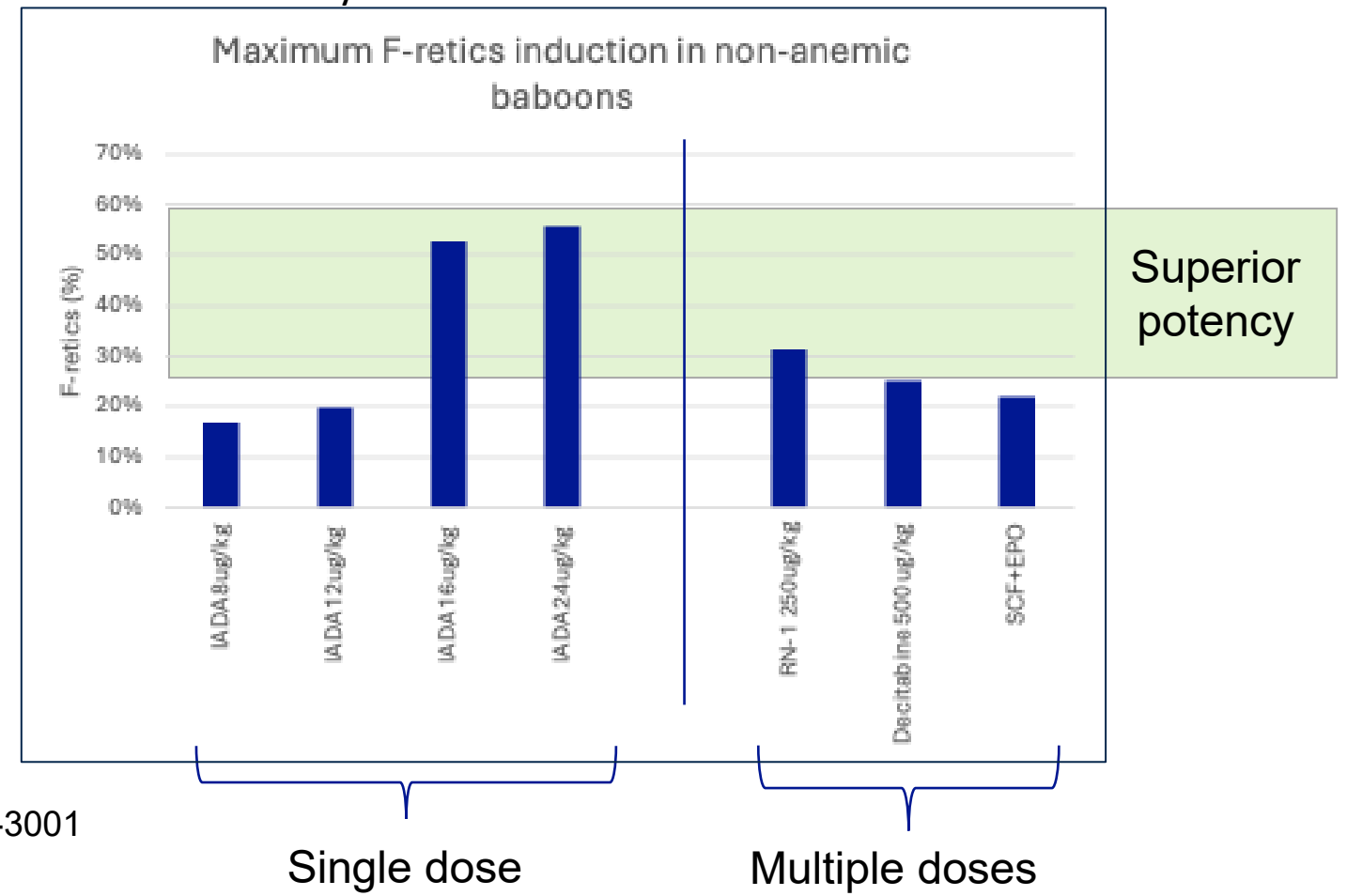
Proof-of-mechanism with iadademstat in non-anemic baboon model

IADADEMSTAT effective and superior at inducing F-retics (young red cells expressing HbF)

- Single dose was effective in increasing F-retics within 8 days in most relevant animal model without any associated neutropenia, thrombocytopenia or consistent effects on reticulocyte counts



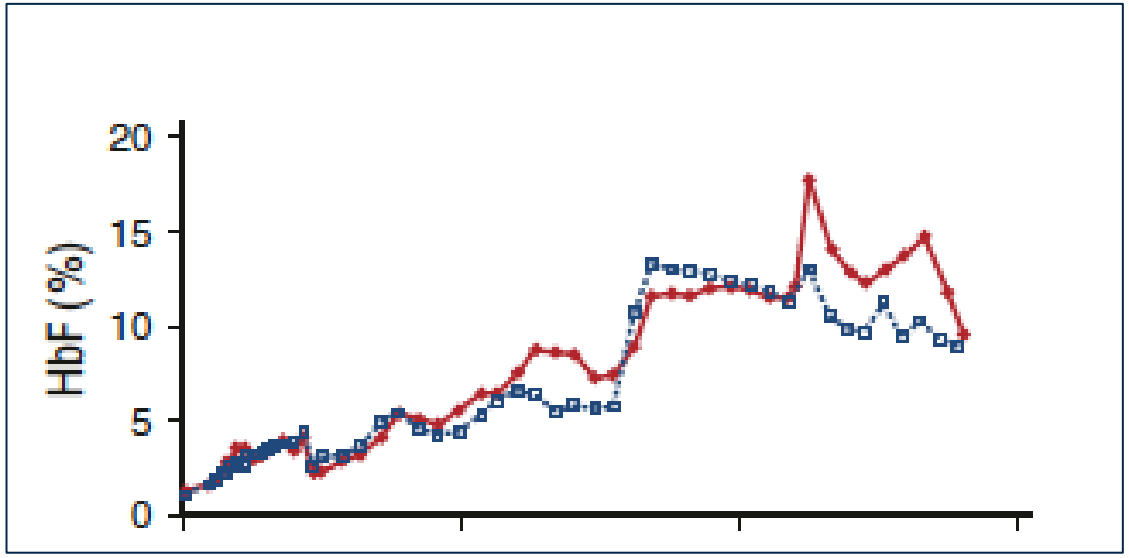
Ibanez V. et al., Blood (142) Supp 1,2023.

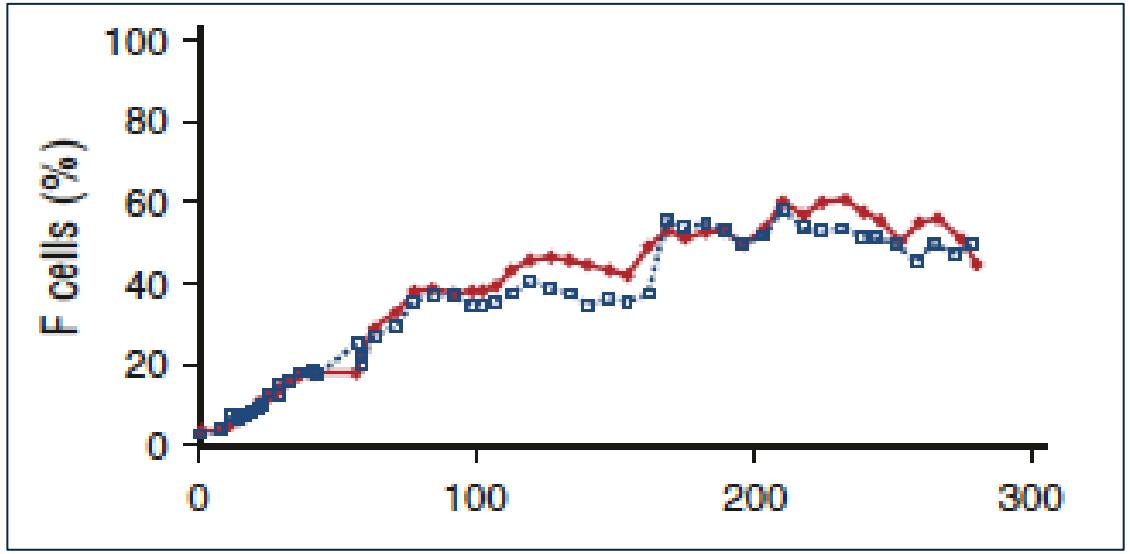


Similar F-retics induction observed after treatment with ORY-3001

Sustained efficacy observed after 9-month treatment in baboons

ORYZON LSD1 inhibitor (w. lower potency than iadademstat) demonstrated prolonged HbF induction





Ibanez et al., Blood 2017, 129:260-263

- Subcutaneous administration at 250 µg/kg per day (5 d/wk) for 264 and 278 days in 2 female baboons

- No effects observed on neutrophils, platelets, monocytes, mean corpuscular volume
- Minor reductions in total hemoglobin, red blood cell number and hematocrit observed
- No other physical or behavioral observations

New Phase Ib clinical trial with iadademstat in SCD

CTA (EU IND equivalent) for this new trial submitted to the EMA (AEMPS)
Expected CTA approval September

- Phase Ib study of iadademstat for the treatment of Sickle Cell Disease
- RESTORE (***RE***gulation of ***S***ickling ***T***hr***O***ugh **R**eprogramming **E**pigenetics)
- N = ~40
- PRIMARY OBJECTIVES:
  1. To evaluate the safety and tolerability of iadademstat in adult patients with SCD
  2. To determine iadademstat's Recommended Phase 2 dose (RP2D) for the treatment of adult SCD patients
- SECONDARY OBJECTIVES:
  1. To evaluate the activity of iadademstat in inducing fetal hemoglobin (HbF) for the treatment of SCD patients
  2. Others

ORYZON

CTA: Clinical Trial Application (EU equivalent to IND)

Iadademstat: opportunity in non-malignant hematology

Clinical-stage, best-in-class LSD1 inhibitor for Sickle Cell Disease (SCD) and Beta Thalassemia patients
PoC in preparation in Essential Thrombocythemia (ET)

SCD

- Commercially-validated MoA (HbF induction) and preferred modality (oral)
- Superior to current standard of care and other development-stage agents
- Proof-of-mechanism and superiority demonstrated in most relevant and predictive animal model
- Safety and PK thoroughly established (>150 treated oncology patients to-date)
- CTA submitted. Phase Ib in SCD to start in 2H25
- Possible Accelerated approval development

ET

- Clinically-validated MoA (Platelet reduction) and preferred modality (oral)
- Superior to current standard of care and fast follower to other development-stage agents (Bome)
- Safety and PK thoroughly established (>150 treated oncology patients to-date)
- Phase Ib in ET in preparation (CTA submission 2H25)

Seeking development and commercialization partner for iadademstat in SCD & ET

ORYZON

CTA: Clinical Trial Application (EU equivalent to IND)

Oryzon Financials

A LIQUID COMPANY (BME & EQUIDUCT TRADING)

TREASURY

CASH RUNWAY to 2027

- €43.5M (~$50M) secured through dilutive (PIPE-2025) and non-dilutive (EU-IPCEI Grant) financing
- €4M already received from commercial loans
- ~€4-5M from other grants and sources

NASDAQ PREPS

Legal Preps for the disclosures needed to list the company and **Auditing Preps** to reconciliate the Spanish GAAPs with the US-GAAPs (PCOBs) could be updated quickly

We are attentive to US markets evolution

Important news flow and milestones ahead

ORYZON can become a FDA-Phase III company in the fall with a significant pipeline in Aggression and in psychiatric disorders

Conversations to partner with Pharma continue

- FDA final approval of Phase III BPD protocol in 2H2025
- Expansion and acceleration of Phase II in SCZ. Readout expected in 2027
- PoC execution and readout of Aggression in ASD
- PoC execution and readout in SCD
- PoC execution and readout in ET
- Readouts in 1L-ED SCLC and HemoOnc (AML and MDS)

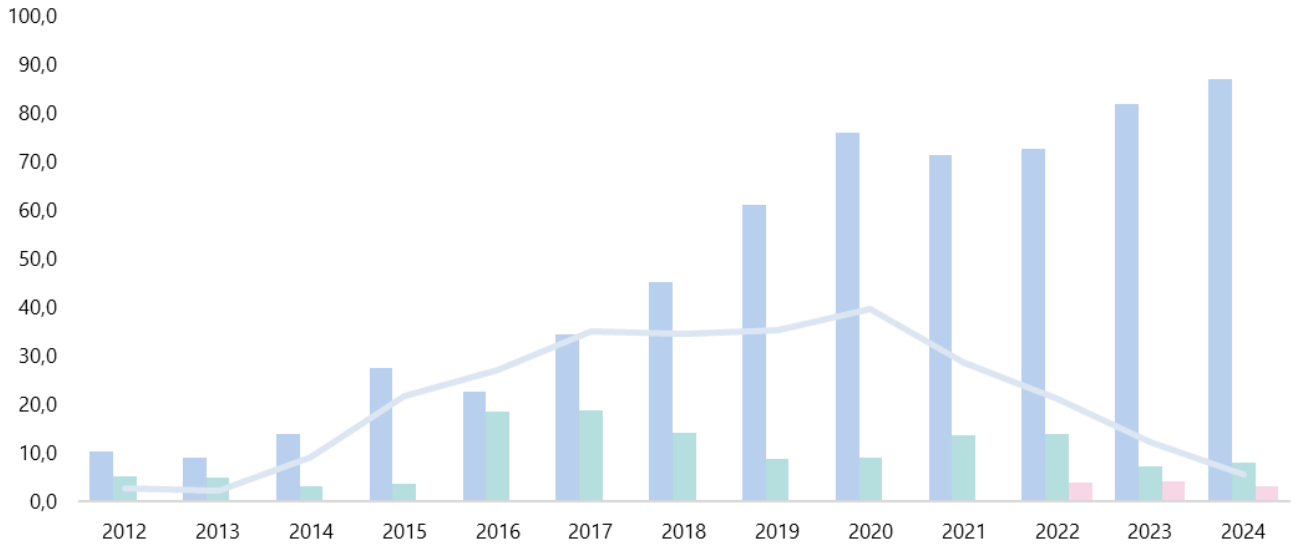
INFORME SOBRE LA MARCHA

GENERAL DE LA COMPAÑÍA

HITOS FINANCIEROS

Estados Financieros – 31 de diciembre de 2024 - Evolución de la solvencia Financiera

Patrimonio neto:	**€87.0m**	**Patrimonio neto:**	**80%**
Tesorería	**€5.6m**	**Recursos permanentes:**	**89%**
Endeudamiento financiero:	**€16.3m**	**Exigible a corto plazo:**	**11%**



€m	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	4Q 2024
Patrimonio Neto	10,3	9,0	13,9	27,6	22,7	34,4	45,1	61,1	75,9	71,3	72,6	81,8	87,0
Tesorería	2,8	2,2	9,3	21,7	27,3	35,2	34,5	35,3	39,6	28,7	21,3	12,3	5,6
Deuda Bancaria	5,3	4,9	3,1	3,6	18,5	18,9	14,1	8,9	9,1	13,8	14,0	7,2	7,9
Bonos convertibles	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	3,9	4,1	3,2
Arrendamiento financiero	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,1	0,1	0,1
Deuda Pública	3,0	4,8	5,0	4,6	4,0	3,9	3,4	3,8	3,0	2,7	2,0	3,8	2,6
Deuda CDTI	1,0	1,0	1,0	0,8	0,7	0,6	0,7	0,6	1,5	1,2	2,2	2,0	1,8
Project Funding	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	1,1	1,0	0,5

FINANCIACIÓN BANCARIA:

- 49.2% de participación en la deuda financiera
- €8.0m de financiación viva
- Sín garantías ni avales

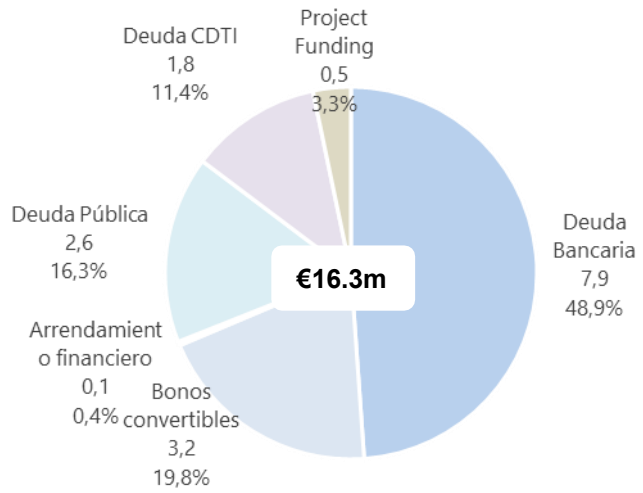
FINANCIACIÓN PÚBLICA y OTROS

- 31,2% de partipación en la deuda pública
- €5,1m de financiación viva

FINANCIACIÓN BONOS CONVERTIBLES EN CAPITAL

- 19.6% Bonos convertibles en capital
- €3.2m de financiación viva

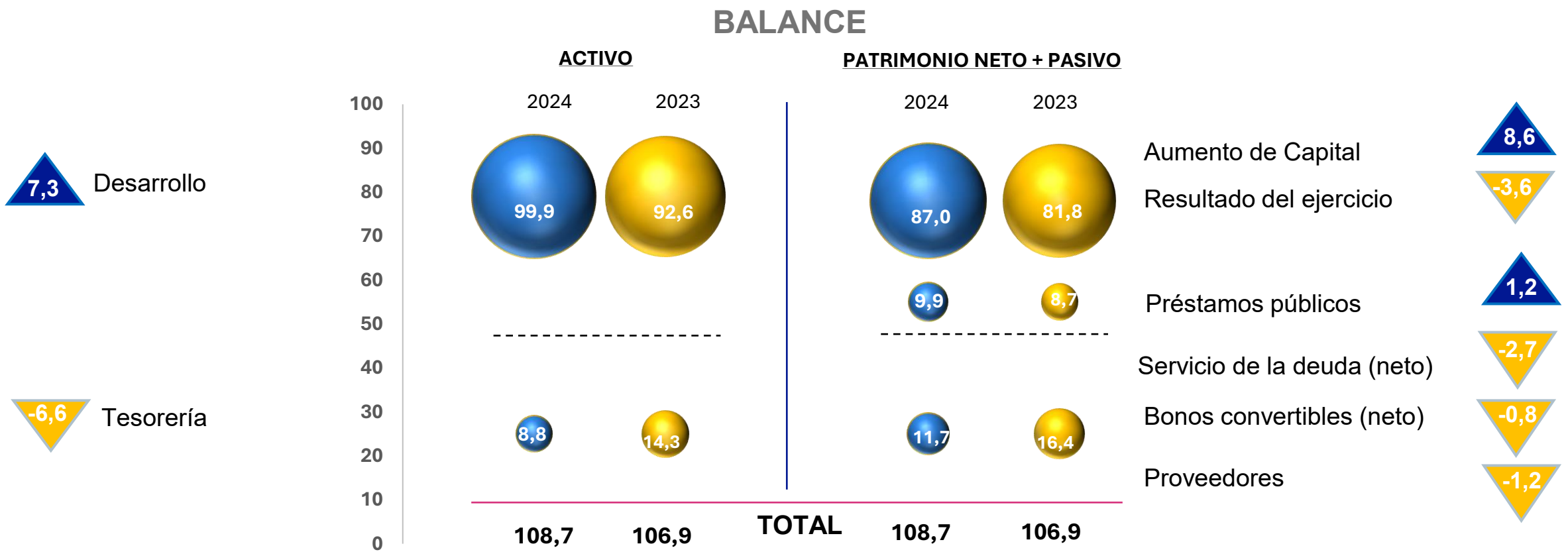
Deuda financiera a 31 de Diciembre 2024



ORYZON

Nota: *Información expresada en Millones de Euros.*

Balance – Evolución 2024 -2023



ORYZON

Nota: *Información expresada en Millones de Euros.*

Cuenta de resultados 2024 - 2023

	FY24	FY23	Var FY24 - FY23
Ingresos por Subvenciones	60	153	(94)
Ingresos por capitalización	7.359	14.192	(6.833)
Ingresos	**7.418**	**14.345**	**(6.927)**
R&D	(5.202)	(11.941)	6.738
Personal	(3.447)	(3.390)	(57)
Gastos Generales	(3.195)	(3.412)	217
Amortización	(148)	(153)	5
Financieros	(998)	(1.555)	557
Impuesto Sociedades	1.906	2.751	(845)
Gastos	**(11.084)**	**(17.698)**	**6.615**
Resultado neto	**(3.665)**	**(3.353)**	**(312)**

ORY 2001- Vafidemstat (- 5,7m PORTICO)
ORY 1001- ladademstat (- 1m FRIDA)

Reducción gastos generales

Reducción intereses bono convertible

Reducción monetización IS

Intereses:
€0,4m cash outflow
€0,6m no cash outflow

Intereses
€0,4m cash outflow
€1,2m no cash outflow

ORYZON

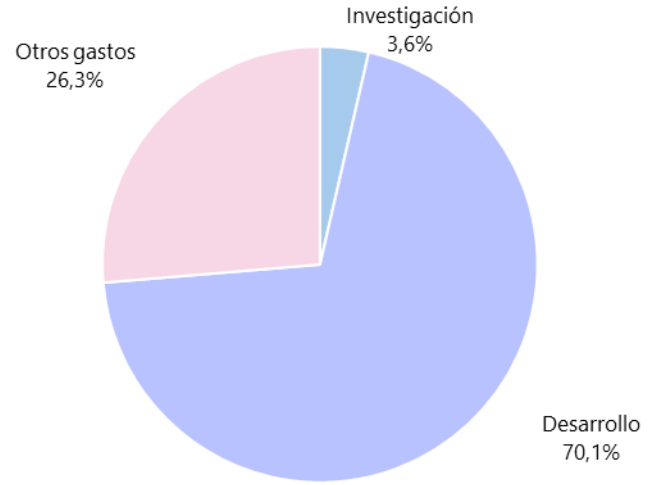
Nota: *Información expresada en Miles de Euros.*

Desarrollo vs Investigación / Otros Gastos

FY24

€k	FY24
Investigación	715
Desarrollo	7.642
Gastos R&D	**8.357**
Otros gastos	4.928
Total Gastos operativos[(1)]	**13.285**

FY23



€k	FY23
Investigación	737
Desarrollo	14.313
Gastos R&D	**15.050**
Otros gastos	5.378
Total Gastos operativos[(1)]	**20.428**

Nota: Excluidos los ingresos financieros; los resultados por la variación del valor razonable en instrumentos financieros; y los ingresos del Impuesto sobre Beneficios / Incluidas las diferencias de cambio por su importe neto.

Nota: *Información expresada en Miles de Euros.*

Estado de Cambios en el Patrimonio Neto

PATRIMONIO NETO A 31.12.2023	**81.775**
Resultado del ejercicio	-3.665
Ampliaciones de Capital	8.412
Subvenciones (Neto de efecto fiscal)	505
Otras variaciones del patrimonio neto	17
PATRIMONIO NETO A 31.12.2024	**87.042**

ORYZON

Nota: *Información expresada en Miles de Euros.*

Estado flujos de efectivo – 31 de Diciembre de 2024

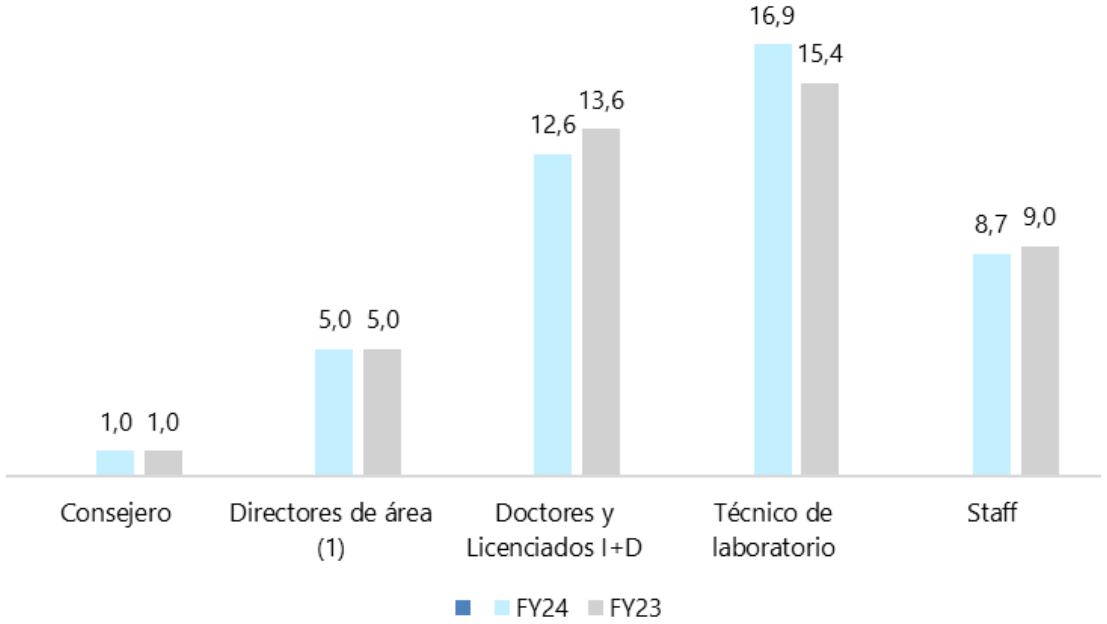
	TOTAL	ACTIVIDADES DE EXPLOTACION Y TIPOS DE CAMBIO	ACTIVIDADES DE INVERSIÓN	ACTIVIDADES DE FINANCIACIÓN
TESORERIA A 31.12.2023	**12.257**			
Cash In				
Subvenciones	1.579			1.579
Bonos Convertibles	7.000			7.000
Préstamos	6.529			6.529
Cash Back	-	-		
Cash Out				
Préstamos	(8.155)			(8.155)
CAPEX	(7.811)		(7.811)	
Costes Financieros netos	(293)	(293)		
Gastos Ordinarios	(5.488)	(5.488)		
TESORERIA A 31.12.2024	**5.619**	**(5.781)**	**(7.811)**	**6.953**

ORYZON

Nota: *Información expresada en Miles de Euros.*

Otra información - personal medio

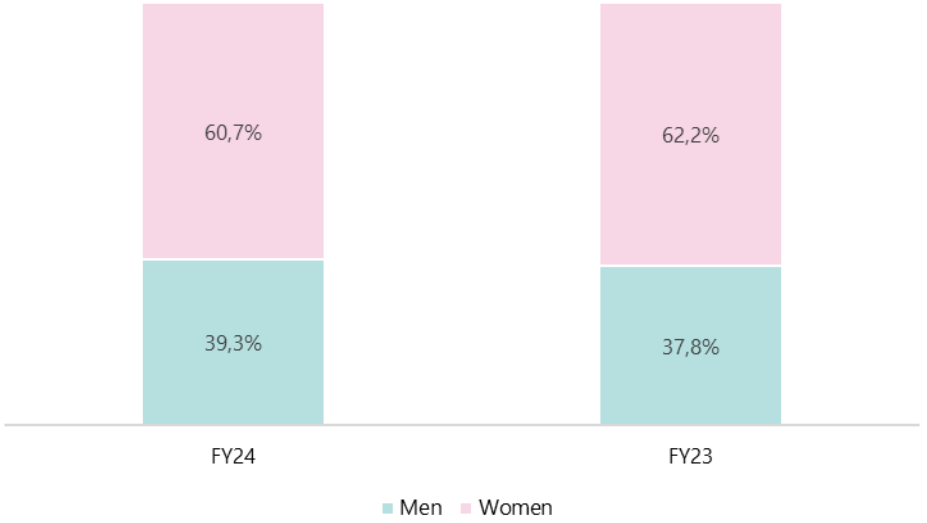
Distribución por categorías



FTE medios	FY24	FY23
Consejero	1,0	1,0
Directores de Area [1]	5,0	5,0
Doctores y Licenciados I+D	12,6	13,6
Técnico de laboratorio	16,9	15,4
Staff	8,7	9,0
Total	**44,2**	**44,0**

[1] No incluye Managers de Área con contratos comerciales

Distribución por género



FTE medios	FY24	FY23
Intensidad personal	33	33
Investigador	75%	75%

Informe de auditoría de las cuentas anuales del ejercicio 2024

Informe de Auditoría de Cuentas Anuales emitido por un Auditor Independiente

A los accionistas de Oryzon Genomics, S.A.

INFORME SOBRE LAS CUENTAS ANUALES

Opinión

Hemos auditado las cuentas anuales de Oryzon Genomics, S.A. (la Sociedad), que comprenden el balance a 31 de diciembre de 2024, la cuenta de pérdidas y ganancias, el estado de cambios en el patrimonio neto, el estado de flujos de efectivo y la memoria correspondientes al ejercicio terminado en dicha fecha.

En nuestra opinión, las cuentas anuales adjuntas expresan, en todos los aspectos significativos, la imagen fiel del patrimonio y de la situación financiera de la Sociedad a 31 de diciembre de 2024, así como de sus resultados y flujos de efectivo correspondientes al ejercicio terminado en dicha fecha, de conformidad con el marco normativo de información financiera que resulta de aplicación (que se identifica en la nota 2.a de la memoria) y, en particular, con los principios y criterios contables contenidos en el mismo.

Fundamento de la opinión

Hemos llevado a cabo nuestra auditoría de conformidad con la normativa reguladora de la actividad de auditoría de cuentas vigente en España. Nuestras responsabilidades de acuerdo con dichas normas se describen más adelante en la sección *Responsabilidades del auditor en relación con la auditoría de las cuentas anuales* de nuestro informe.

Somos independientes de la Sociedad de conformidad con los requerimientos de ética, incluidos los de independencia, que son aplicables a nuestra auditoría de las cuentas anuales en España según lo exigido por la normativa reguladora de la actividad de auditoría de cuentas. En este sentido, no hemos prestado servicios distintos a los de la auditoría de cuentas ni han concurrido situaciones o circunstancias que, de acuerdo con lo establecido en la citada normativa reguladora, hayan afectado a la necesaria independencia de modo que se haya visto comprometida.

Consideramos que la evidencia de auditoría que hemos obtenido proporciona una base suficiente y adecuada para nuestra opinión.

Thank you!

Pioneering personalized medicine in epigenetics