Pioneering personalized medicine in epigenetics

ORYZON

JUNTA GENERAL DE ACCIONISTAS

MADX: ORY

28 de Junio de 2024

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Epigenetic champion developing new therapies in CNS and Oncology with an advanced pipeline

Growing epigenetic platform with an expanding pipeline to bring treatments to high unmet medical needs in CNS and Oncology

Developing highly potent and selective drugs against LSD1

2 Programs in Phase II with well-defined registrational pathways:

- iadademstat in Oncology
- vafidemstat in CNS

Listed in Europe (Madrid)
MK Cap ~$150M

- €114M raised in equity since listing in 2015
- €28 M raised in equity since 2022

Oryzon investment thesis

A unique dual EPIGENETIC approach

A Phase II molecule in psychiatry (BPD and SCZ)

Area of great interest for Pharma (M&A and licensing)

In conversations with FDA to agree a **Phase III registrational trial** in BPD

Options to expand to precision medicine in rare CNS disorders

A Phase II molecule with promising clinical data in AML and SCLC

Endorsed by the NCI-NIH CRADA Agreement

2 ongoing trials in AML and SCLC that may set up the basis for accelerated approval

Preliminary readouts in 2024-25

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

Two main catalysts in 2024: PORTICO in BPD and FRIDA in AML

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 Final Data ECNP-2024 EoP2 FDA meeting in 2024 ★
Schizophrenia Negative Symptoms & Cognition	**EVOLUTION**						**Recruiting**	Timeline updates in 2024
Kabuki Syndrome	**HOPE**			**Phase Ib/II**			**IND in preparation**	IND in 2024
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	**IIS-X002**			**Phase Ib**			**IND Approved** Sponsor: OSHU	FPI 1H 2024
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 2H 2024
ED-SDLC 1L Combination with ICI	**CRADA-SCLC**				**Phase I/II**		**IND Approved** Sponsor: NCI, Led by MSKCC	FPI Q3 2024
ED-SCLC 1L Combination with ICI	**STELLAR**				**Phase II pivotal**		**IND in preparation** Company sponsored	IND 2025
Other Programs								
ORY-3001 (LSD1i) Sickle Cell Disease							IND enabling tox completed	
ORY-4001 (HDAC6i) CMT, ALS							IND enabling tox ongoing	

Note: Other finalized clinical trials for iadademstat and vafidemstat are not shown. See www.oryzon.com for more details
AML: acute myeloid leukemia; SCLC: small cell lung cancer; NETs: neuroendocrine tumors; ALS: amyotrophic lateral sclerosis; CMT: Charcot-Marie-Tooth disease
FCCC: Fox Chase Cancer Center; MSKCC Memorial Sloan Kettering Cancer Center; OSHU Oregon Health & Science University; IIS: Investigator-initiated study

Important Milestones Ahead

ORYZON can become an FDA-Phase III company in the fall

		2024				2025			
		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Borderline personality disorder Agitation / Aggression & Overall Improvement	PORTICO	TLD	FINAL DATA	EOP2 Meeting FDA		Phase 3 Protocol ready			
AML R/R-Flt3mut+ Combination with gilteritinib	FRIDA		DATA at EHA		DATA at ASH		DATA at EHA	FDA	DATA at ASH
NCI-NIH ED-SCLC 1L Combination with ICI	CRADA-SCLC			FPI			DATA at ESMO		
AML 1L Unfit Patients Combination with azacitidine and venetoclax	IIS-X002			FPI					DATA at ASH

Regulatory Milestone

Clinical Data/ Milestone

ORYZON, the only company developing epigenetic drugs in CNS

VAFIDEMSTAT

A Phase II LSD1 inhibitor for CNS diseases

Two main catalysts in 2024

Program	Study	Preclinical Phase	Phase I		Phase II		Status	Expected Milestone(s)
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Borderline personality disorder Agitation / Aggression & Overall Improvement	**PORTICO**						**Completed** Study has results	Top line data in January 2024 Final Data ECNP-2024 EoP2 FDA meeting in 2024 ★
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Kabuki Syndrome	**HOPE**		**Phase Ib/II**				**IND in preparation**	IND in 2024

- Final Data of PORTICO in BPD
- PORTICO FDA end-of-Phase 2 meeting

Vafidemstat is a small molecule with oral bioavailability and high brain penetration, exhibiting potent and selective inhibition of LSD1

Vafidemstat is safe and well tolerated drug

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

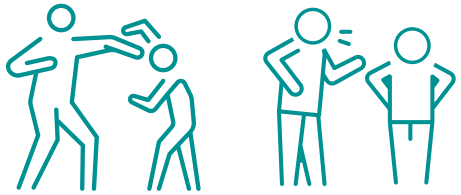
No sexual dysfunction

No extrapyramidal signs

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

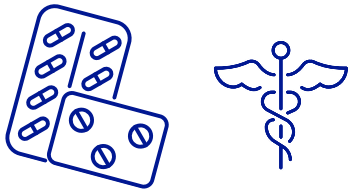
Prevalent & impairing disease

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

Vafi improves these symptoms in:

- BPD patients
- PC models

Oryzon is leading the BPD field ahead of the competition

PORTICO: A Global 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

Endpoints

Primary:

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 (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)
- State-Trait Anger Expression Inventory 2 (STAXI-2)
- State-Trait Anxiety Inventory (STAI)
- Beck Depression Inventory – II (BDI-II)

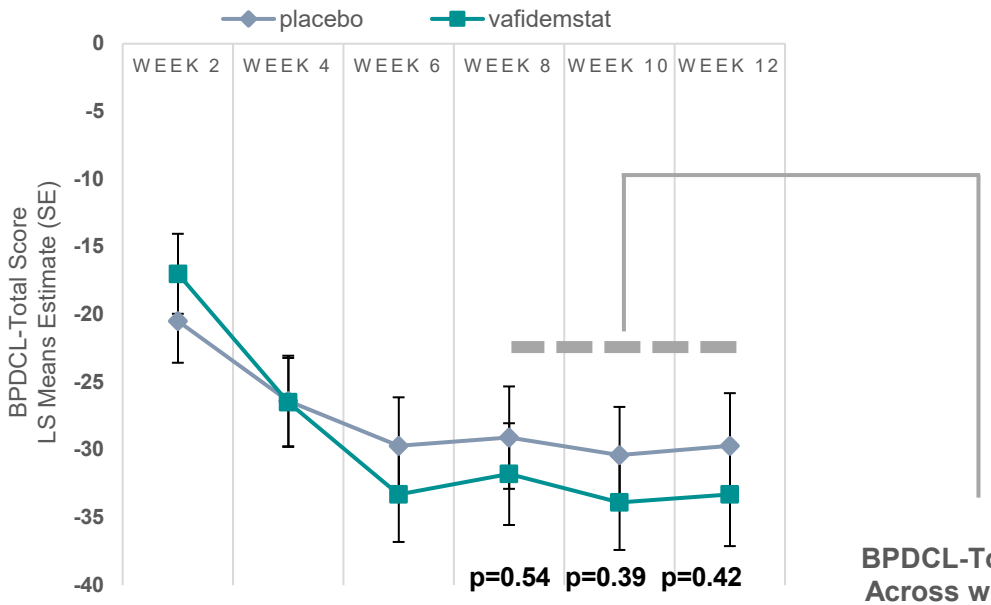
TLD ANALYSIS*

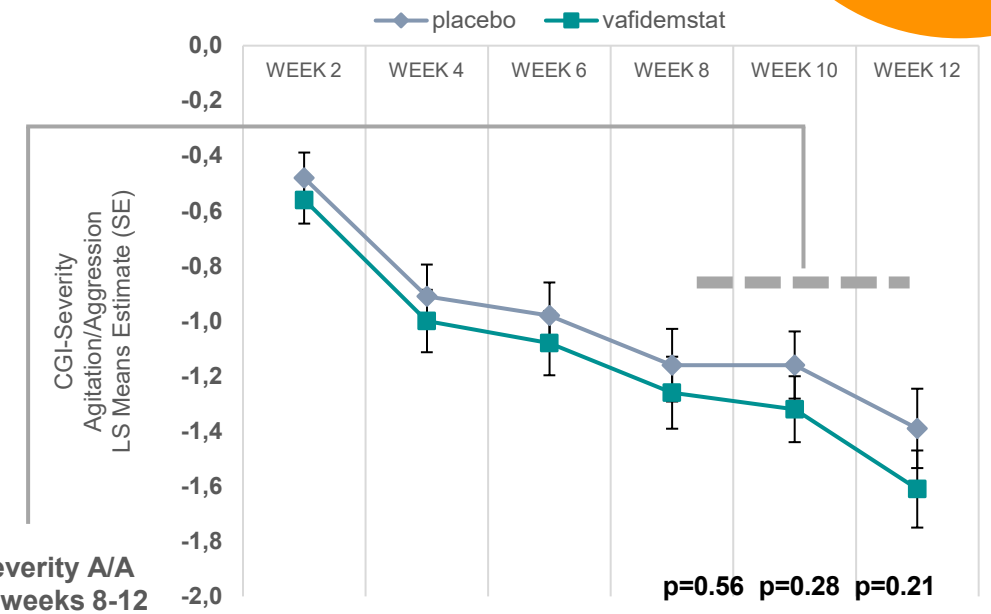
Phase IIb PORTICO study
Efficacy of vafidemstat in Borderline Personality Disorder

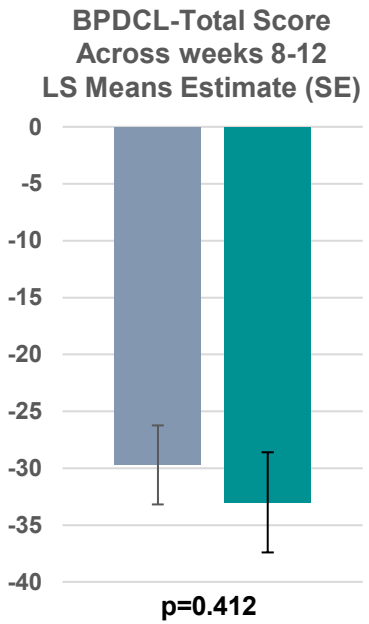
*** FINAL DATA AVAILABLE UNDER CDA**

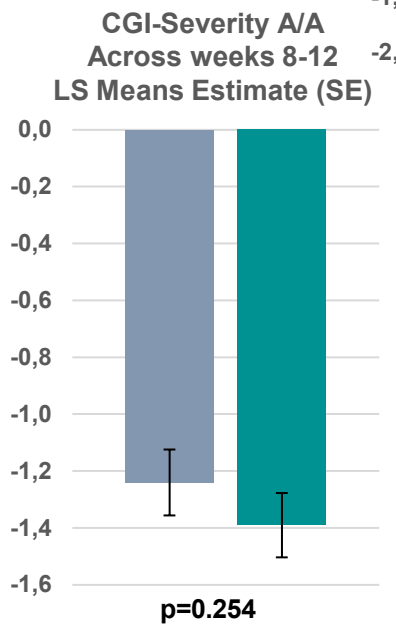
Phase IIb PORTICO study
Efficacy of vafidemstat in Borderline Personality Disorder

No statistical significance in the two primary endpoints: BPDCL and CGI-S A/A

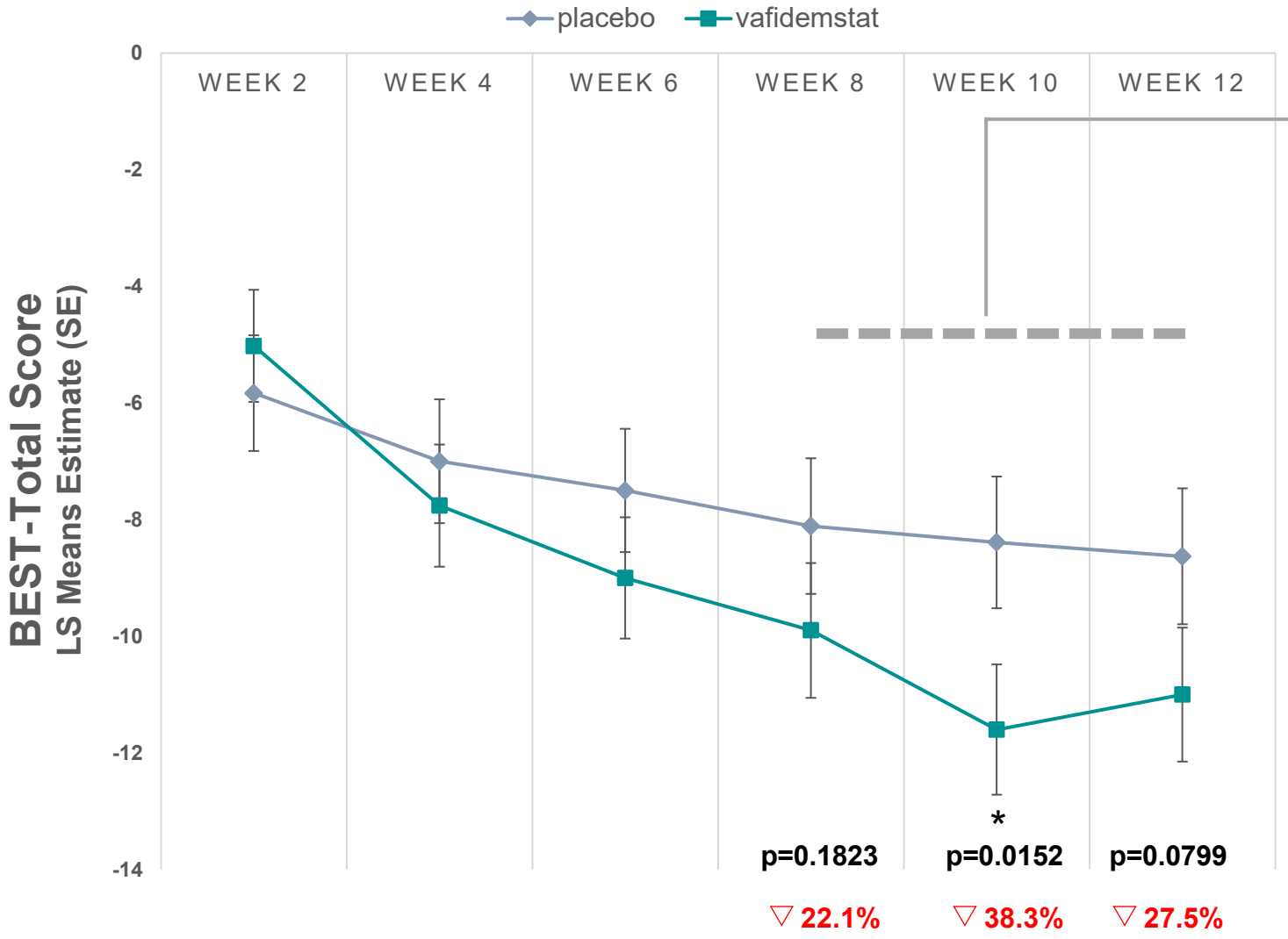


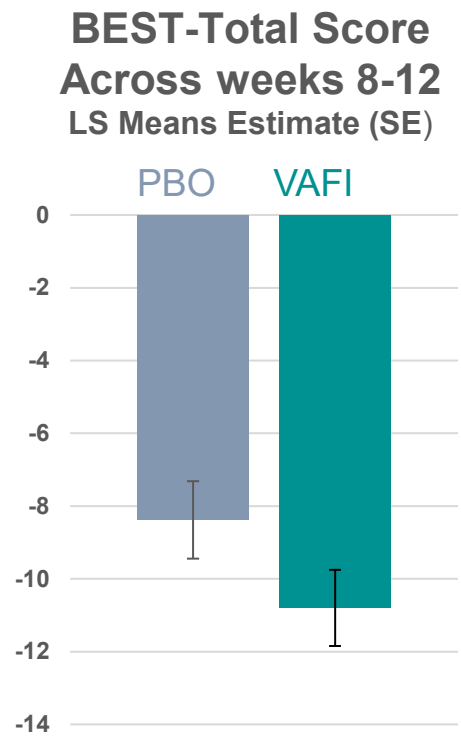






Nominal statistical significance in secondary endpoint: Improvement in BEST across weeks 8-12





p=0.0423

▽ 28.9%

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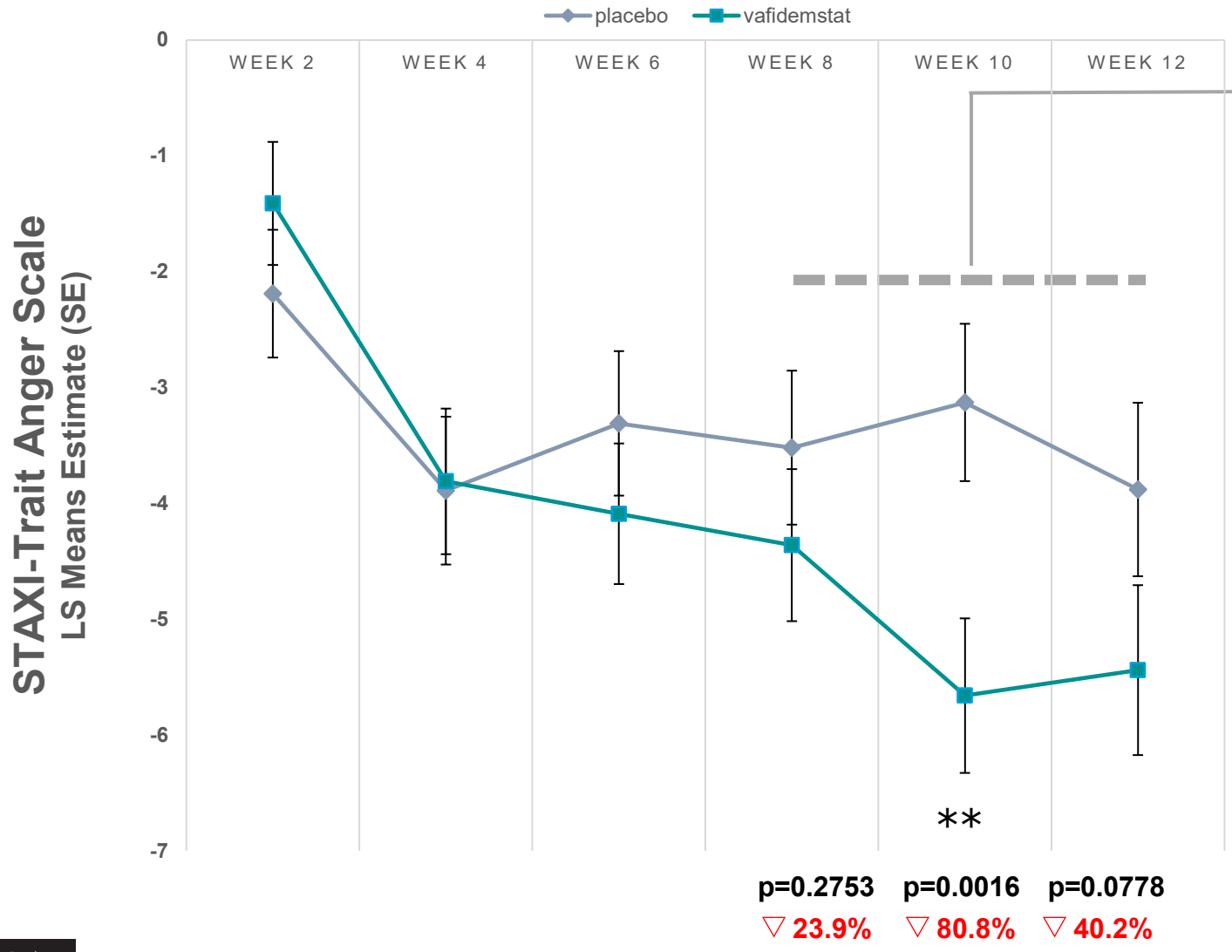
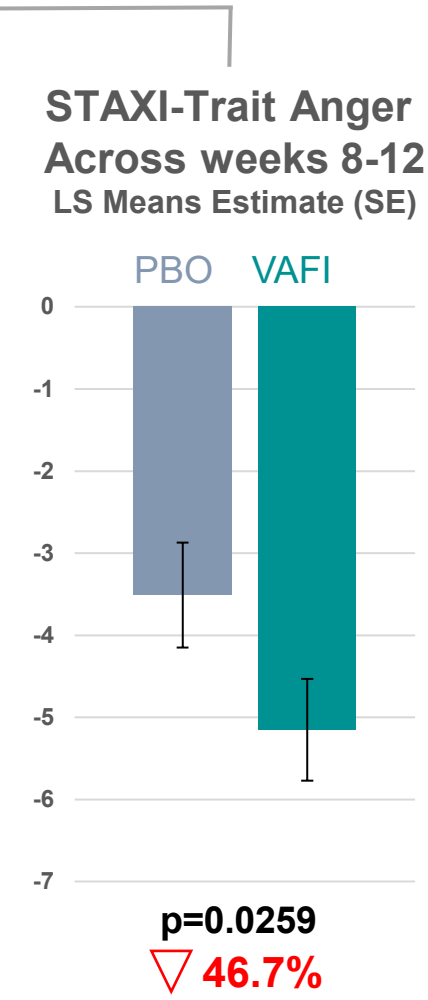
TLD ANALYSIS

Phase IIb PORTICO study
Efficacy of vafidemstat in Borderline Personality Disorder

Nominal statistical significance in secondary endpoint: Improvement in STAXI Trait Anger across weeks 8-12





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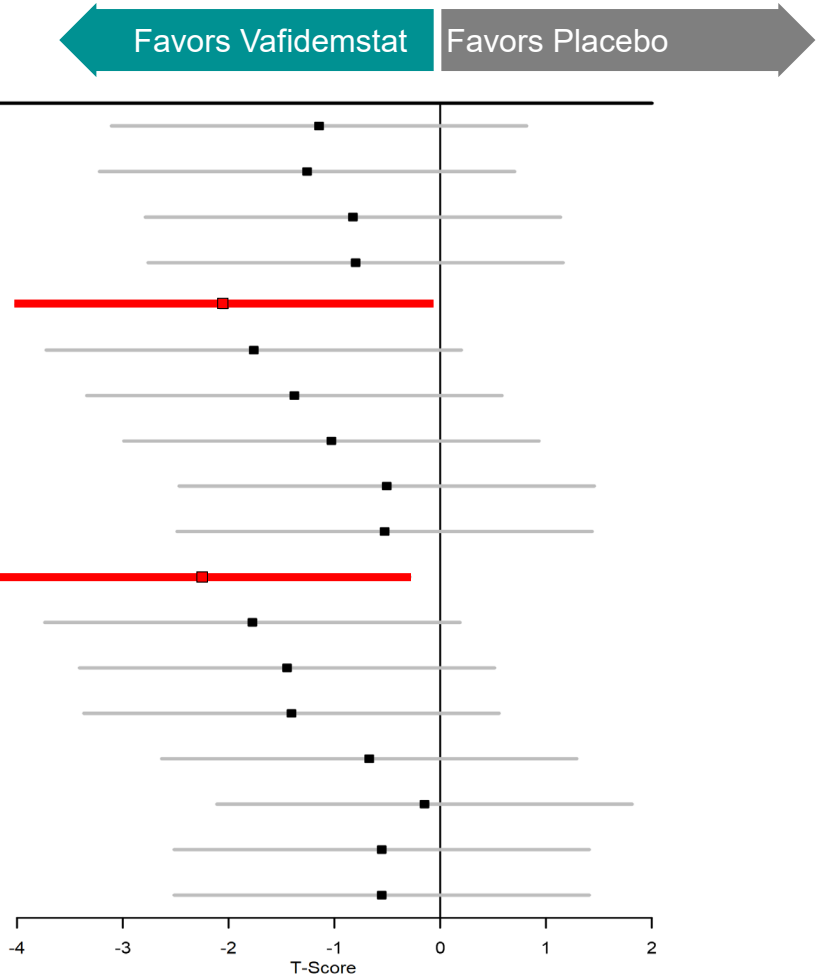
Phase IIb PORTICO study
Efficacy of vafidemstat in Borderline Personality Disorder

PORTICO: All primary and secondary 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

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

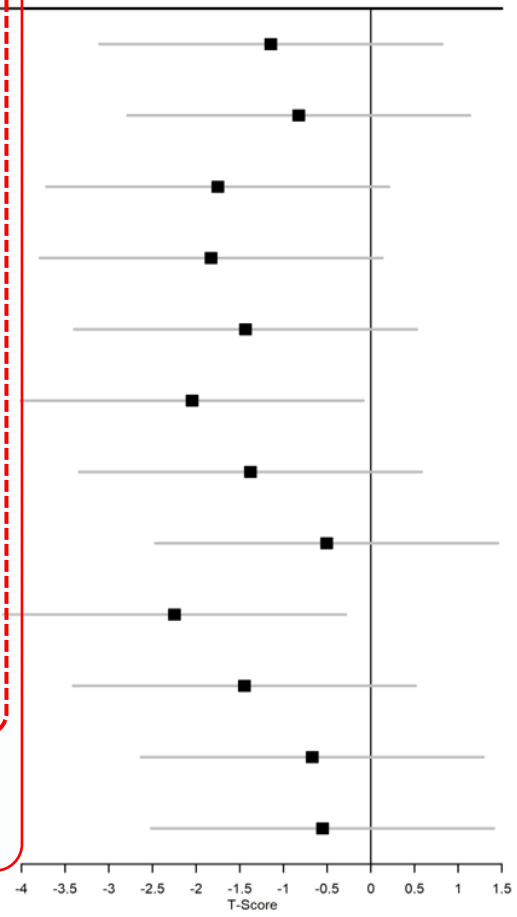
BPD is a multisymptomatic disease with psychiatric, behavioral, and functional outcomes.

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

Topline safety: vafidemstat-treated patients showed a reduced inclination towards self-harm

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 (started before treatment)
  - Subject's dose was not changed, the condition 'Recovered/Resolved' within 7 days, and the subject completed the trial

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* *7 cases of numerical, clinically insignificant, and transient platelet (PLT) reductions & 1 transient and rapidly self-resolved thrombocytopenia (TP) grade 1*

PORTICO: Final Summary of TLD

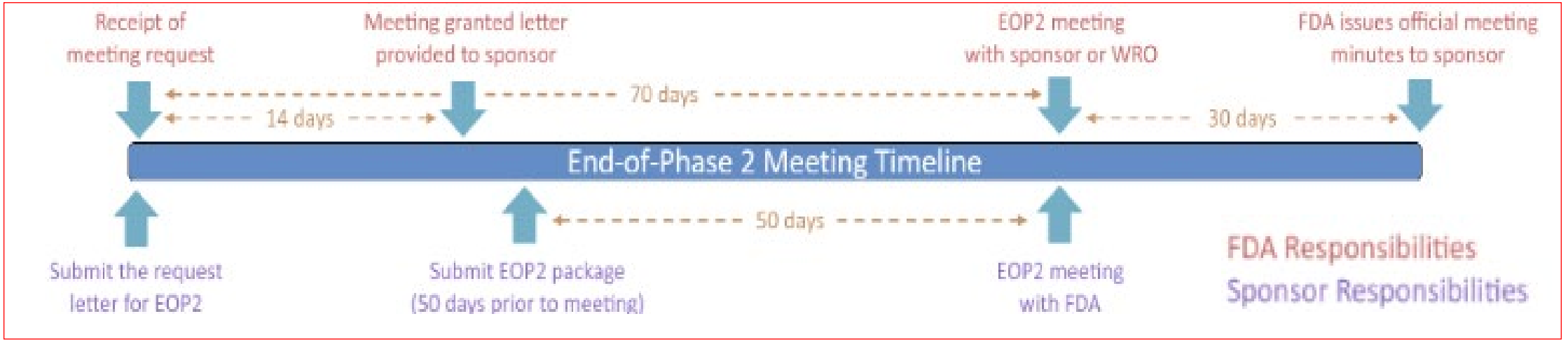
PORTICO's efficacy and safety results support further clinical development and Oryzon intends to request an end-of-Phase 2 meeting with the FDA to discuss plans for a registrational BPD Phase III trial

FDA: Requested an End-of-Phase 2 Meeting

Objective: To obtain agreement on study design, safety, and efficacy endpoints for the upcoming registrational Phase 3 study (PORTICO-2)

EOP2 meeting briefing package:

- Summaries of previous investigations
- Information of Phase 2 trial PORTICO
- Synopsis of protocol of PORTICO-2 Phase 3 study
- Other info



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

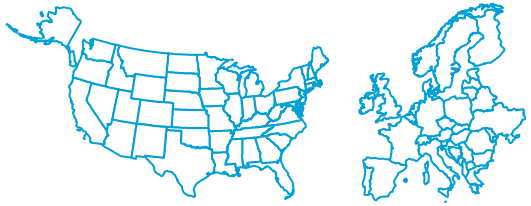
EVOLUTION: an ongoing schizophrenia PoC study with vafidemstat

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

- Expected recruitment: 100 patients*
- 2 arms, vafi as add-on to SoC vs placebo
- 6 months of treatment
- Primary endpoints: Cognition and Negative Symptoms**
- Currently 11 sites active and recruiting
- Spanish government funded
- To be converted into a global trial***

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

* To be reassessed after PORTICO data analysis
** Trial design under optimization after PORTICO learned lessons
*** Pending additional resources

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.

Significant improvement in vafidemstat IP protection in BPD

- Formal “Intention-to-grant” communication recently received from the European patent office for Oryzon’s European patent application EP18748921.6 entitled “Methods of treating behavior alterations”. Allowed claims cover the use of vafidemstat in the treatment of aggression and social withdrawal.
- “Intention-to-grant” communication also received for the corresponding patent application in Korea; allowed claims cover the use of vafidemstat in the treatment of aggression and social withdrawal
- A corresponding patent has also been granted in Russia.
- Oryzon has additional patent filings pending in additional countries

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 +$3,5 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

LSD1i in clinical development

- **In AML**
  - Leukemic Stem Cells are forced to differentiate by LSD1i
  - LSD1i synergizes with other agents in AML as azacitidine, gilteritinib, and venetoclax amongst others
  - Clinical evidence of benefits in diverse AML patients
- **In SCLC and other Neuroendocrine tumors**
  - INSM1 / HMG20A and other TFs decoupled
  - ASCL-1 oncogenic program is deactivated by reinducing Notch-1
  - LSD1i induces the tumor cells to produce MHC-1 and PDL-1 receptor and boosts immune system
  - Strong preclinical evidence of benefits
- **In epithelial cancers** → Strong preclinical evidence of benefits
- **In Myelofibrosis** → Preliminary clinical evidence of benefits
- **In Polycythemia Vera** → Preliminary clinical evidence of benefits
- **In Thrombocytemia** → Preliminary clinical evidence of benefits
- **In Sickle Cell Disease** → Strong preclinical evidence of benefits

ladademstat: first and potentially best-in-class LSD1 inhibitor in oncology

- A unique asset to address specific cancers (rare or orphan designations)
- Focusing on clinical execution in hemato-oncology and solid tumors with a registrational plan
- Reinforcing institutional collaborations
- Exploring niche indications in collaborative settings (NIH)
- Setting an optimal long-term corporate strategy

ODD AML ODD SCLC	ODD AML
CRADA Agreement ORYZON-NCI	Excellence Program EU Commission

Multiple Shots on goal in Oncology & leverage on CRADA-NCI agreement

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
AML 1L Unfit Patients Combination with azacitidine and venetoclax	**IIS-X002**			**Phase Ib**			**IND Approved** Sponsor: OSHU	FPI 1H 2024
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 2H 2024
ED-SDLC 1L Combination with ICI	**CRADA-SCLC**				**Phase I / II**		**IND Approved** Sponsor: NCI, Led by MSKCC	FPI 1H 2024 ★
ED-SCLC 1L Combination with ICI	**STELLAR**				**Phase II pivotal**		**IND in preparation** Company sponsored	IND 2025

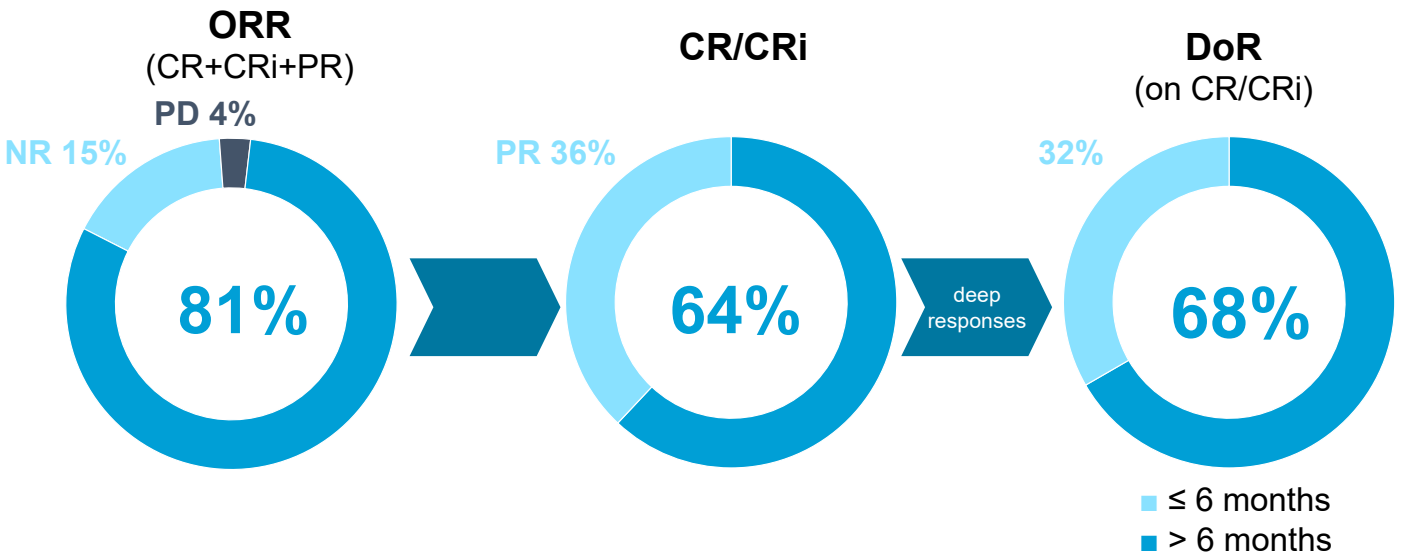
Note: Other finalized clinical trials for iadademstat are not shown. See www.oryzon.com for more details
AML: acute myeloid leukemia; SCLC: small cell lung cancer; NETs: neuroendocrine tumors; ICI: immune checkpoint inhibitors
FCCC: Fox Chase Cancer Center; MSKCC Memorial Sloan Kettering Cancer Center; OSHU Oregon Health & Science University; IIS: Investigator-initiated study

ORYZON

AML Program:
ALICE and FRIDA 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]

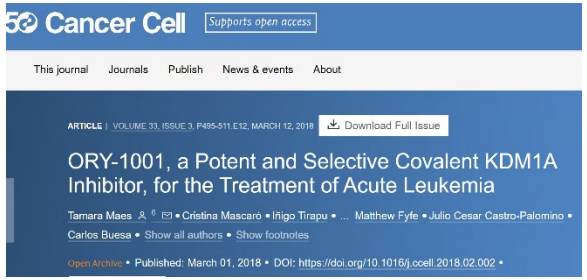
CR/CRi pts		
n=14	**n**	**%**
MRD neg	10 out of 11 evaluable	**91%**
Achieved TI (RBC & Plt)	10	**71%** 10/14

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 results published in Lancet Hematology in May 2024

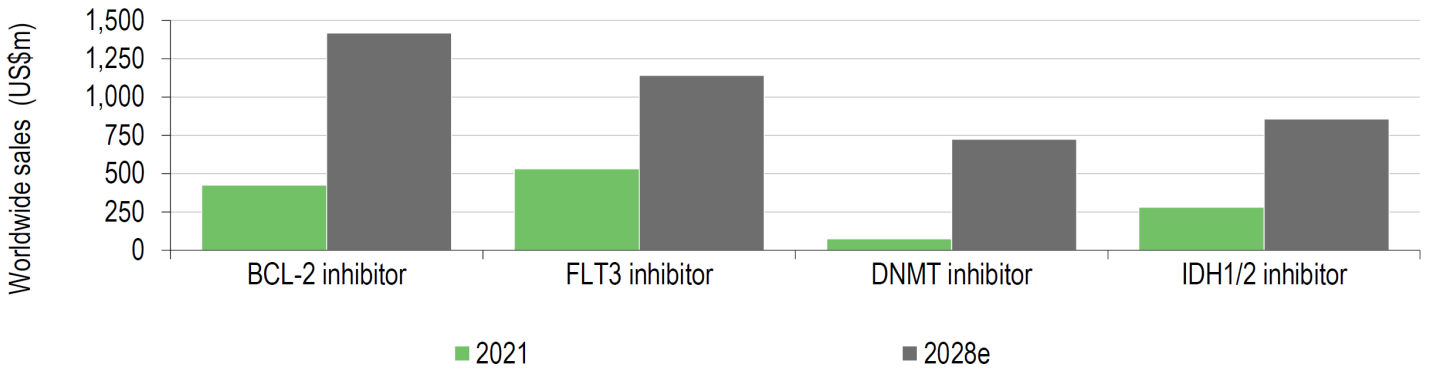
One of the most influential scientific journals in the field of oncology

This notable publication is a continuation of Oryzon's previous pioneering research featured in the **Journal of Clinical Oncology** (First-in-Human study in AML with iadademstat) and **Cancer Cell** (Characterization of iadademstat as a potent and selective LSD1 inhibitor), cementing the company's position at the forefront of epigenetics in oncology and LSD1 innovation



FLT3mut+ R/R AML, the best and shortest market opportunity for iadademstat

- In a competitive market, R/R AML is an underserved population: **Majority of AML patients relapse after 1L treatment and require further treatment**
- FLT3 is the most common mutation in AML (**30-40%**)
- These patients are now treated with **gilteritinib,** yet there is a **high medical need (mEFS 2.8 months & CR+CRi 34%)**
- **Very strong preclinical synergism between gilteritinib and iadademstat**
- **Global FLT3 inhibitors market expected to reach $2.06 Billion by 2032***



R/R-AML Flt3mut+ space is a significant market opportunity

(Source Edison Research 2023 & Evaluate Pharma)

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

Inclusion Criteria

Adult pts with Relapsed/ Refractory FLT3m^{+} AML

- Refractory or relapsed to first- or second-line treatment
- ECOG 0-2
- Normal liver and renal function
- Prior frontline midostaurin or sorafenib or quizartinib or gilteritinib under specific circumstances

Approximately 15 sites

Escalation

Up to ~6 pts/dose level

	Iadademstat PO	Gilteritinib PO
Dose level +1	150 µg, 4 weeks	120 mg
Starting dose	100 µg, 4 weeks	120 mg
Dose level -1	75 µg, 4 weeks	120 mg
Dose level -2	75 µg, 3 out of 4 weeks	120 mg

3+3 design

Pharmacologically active dose/s

Expansion

Up to ~ 14 pts/dose cohort

Dose C1:
Iadademstat + Gilteritinib

Dose C2:
Iadademstat + Gilteritinib

Bayesian Monitoring

MASSACHUSETTS GENERAL HOSPITAL

***PI*: Dr. Amir Fathi**, *Leukemia Lead & Program Director, Center for Leukemia at Massachusetts General Hospital and Dana Farber Cancer Center (Harvard Medical School)*

Final Analysis (Selected endpoints)

Primary	Secondary	Exploratory
• Safety • RP2D	• Efficacy: CR/CRh, OS, EFS,ORR, DoR • Transfusion rates	• MRD • Gene mutation status • Biomarkers

ORYZON

EHA-2024: FRIDA – Encouraging efficacy

Fast time to responses

- 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% patients achieved complete remission (CR), complete remission with partial hematological recovery (CRh) or complete remission with incomplete blood count recovery (CRi) in DL-1 cohort
- 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.
- Third Cohort ongoing: Next FRIDA release expected at ASH-2024

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%

Neuroendocrine Program

ladademstat: potentially first and best-in-class LSD1 inhibitor in SCLC and other Neuroendocrine tumors

Mechanism of Action

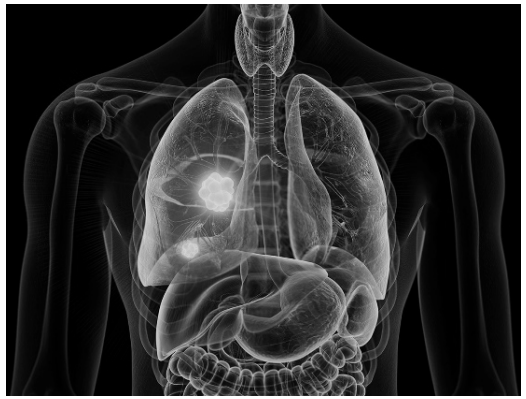
LSD1 is required for survival & proliferation of **neuroendocrine/SCLC tumor cells**

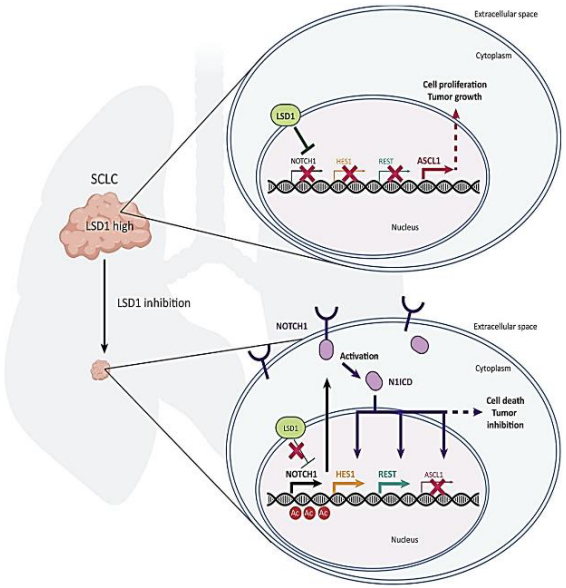
ladademstat **induces Notch**, a well characterized tumor suppressor in SCLC **and represses ASCL1**

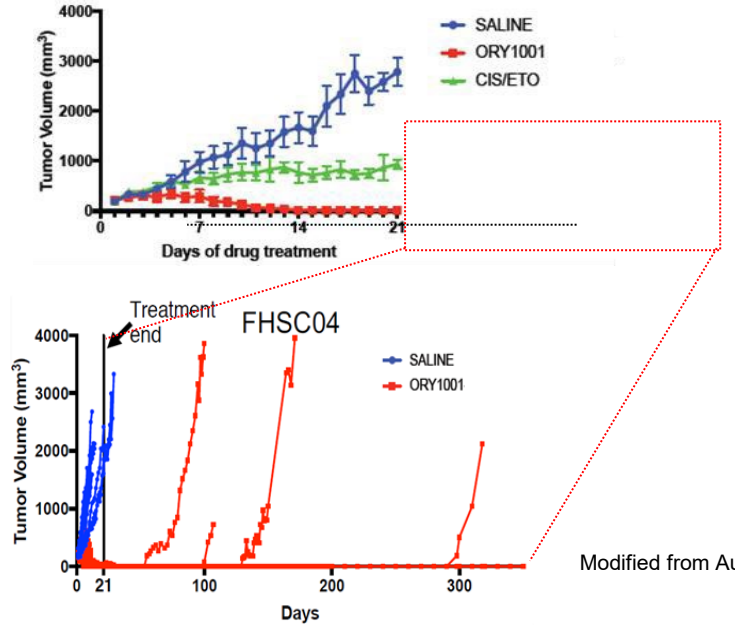
ladademstat blocks LSD1's actions and promotes neuroendocrine/SCLC tumor differentiation and death

ladademstat synergizes with ICIs and boosts the host immune system by increasing T cell infiltration and preventing T-cell exhaustion

SCLC is very aggressive and represents ~ 15% of all lung cancers







Modified from Augert et al., 2019. Sci Signal

From Trends in Molecular Medicine 25(4)
DOI:10.1016/j.molmed.2019.02.009

NEXT-CTEP-NCI Program – CRADA: new 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. Noura Choudhury

Memorial Sloan Kettering Cancer Center

ORYZON to provide drug
IND approved
Expected start 2Q24

- MSKCC
- JHU Sidney Kimmel Comprehensive Cancer Center at the John Hopkins
- Dana Farber at Harvard Cancer Center
- Ohio State Univ Cancer Center
- MD Anderson
- City of Hope Cancer Center
- UPMC Hilman Cancer Center (University of Pittsburgh)
- Univ. Health Network Princess Margaret Cancer Center Toronto
- Yale University
- National Cancer Institute

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

ORYZON

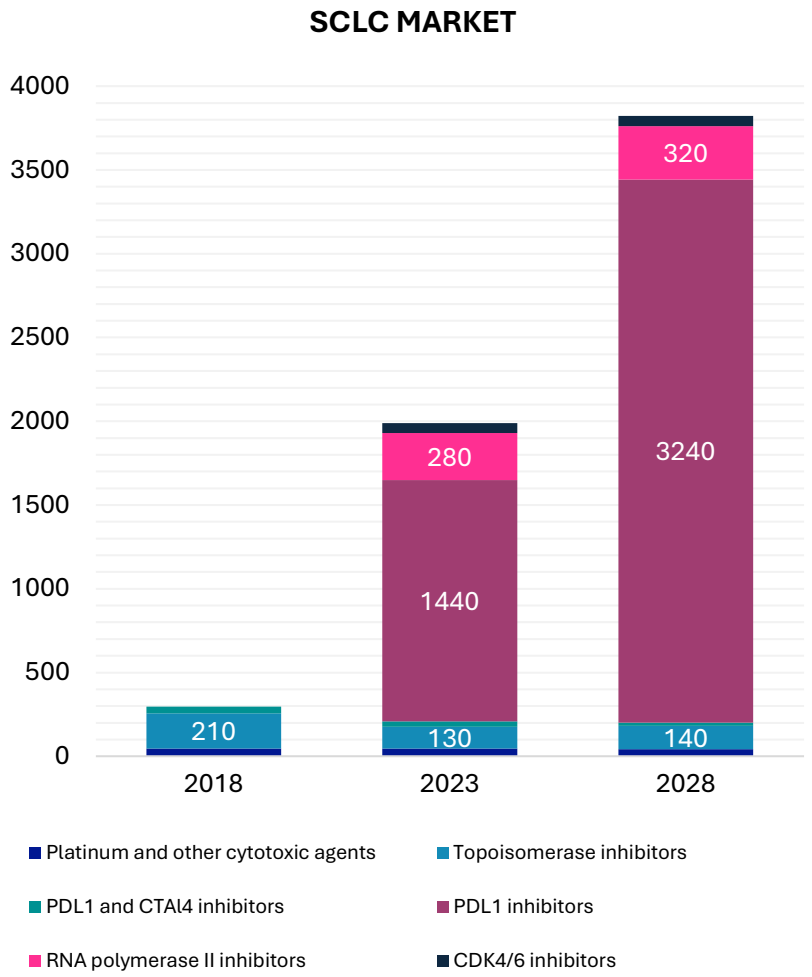
ED-SCLC, an interesting market opportunity

Best route to Market: Combo with IO, 1L ED-SCLC in maintenance

Tolerability profile of both drugs suggesting high compatibility

The **global market for small-cell lung cancer drugs** expected to reach **+$3.4 billion by 2027,** expanding at a CAGR of 19.4% over the forecast period, driven by the approval and uptake of premium-priced targeted therapies

Iadademstat peak sales are estimated to be +$1.5 billion in 1L maintenance therapy



Oryzon Financials

A LIQUID COMPANY (BME & EQUIDUCT TRADING)

NASDAQ PREPS

Legal Preps for the disclosures needed to list the company in Nasdaq **Done**

Auditing Preps (DELOITTE) to reconciliate the Spanish GAAPs with the US-GAAPs (PCOBs) **Done**

GSM has authorized the Board to issue ADS (American Depositary Shares) securities to list in Nasdaq

GSM to authorize a capital increase of up to €100M

TREASURY

CASH RUNWAY to 2025

Cash at Dec 31 2023, €12.26 M

Cash at end of May 2024, €10.5 M

~3M to be received from Other Grants and Sources

Multiyear Grant from IPCEI EU Next Generation program

IPCEI Med4Cure Project granted by EU

ORYZON selected as Associated Partner in the first Important Project of Common European Interest (IPCEI) in the health sector (Med4Cure project)

- A non-creditable, non-refundable EU Grant
- Oryzon individual budget will cover activities since January 2023

European Commission | EN English | Search | Search

Home > Press corner > €1 billion of State aid

Available languages: English

PRESS RELEASE | 28 May 2024 | Brussels | 6 min read

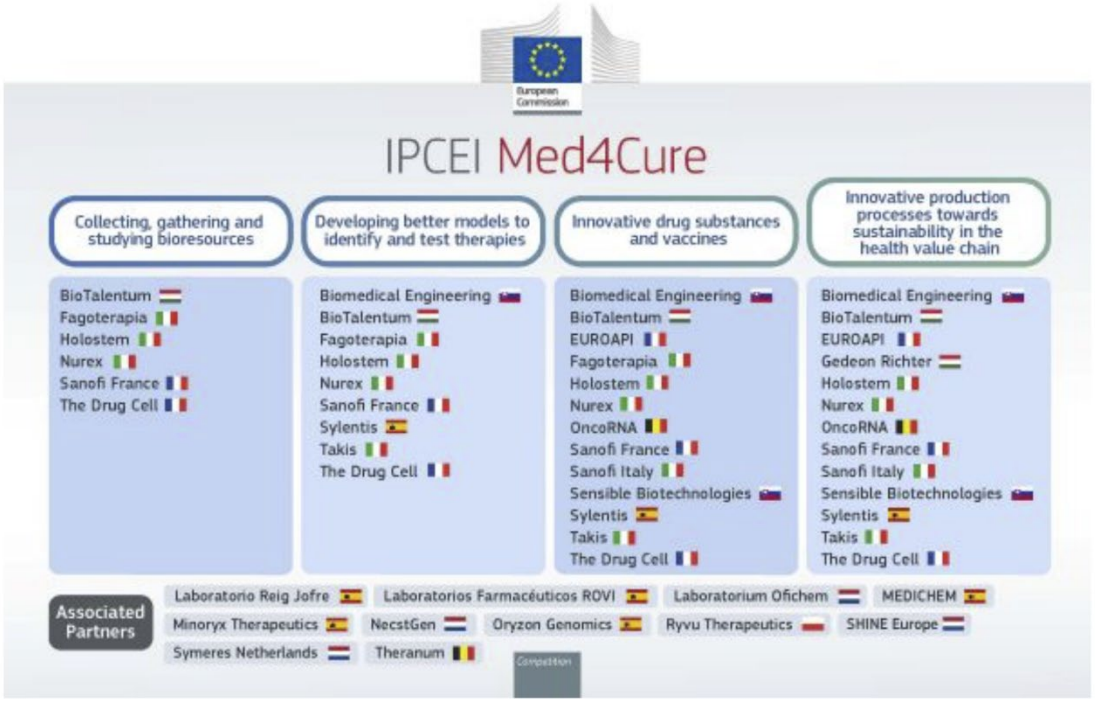
Commission approves up to €1 billion of State aid by six Member States for the first Important Project of Common European Interest in the health sector

Page contents

The European Commission has approved, under EU State aid rules, the first Important Project of Common European Interest ('IPCEI') to support research, innovation and the first industrial deployment of healthcare products, as well as innovative production processes of pharmaceuticals. This IPCEI will notably contribute to the European Health Union's objectives by delivering innovations addressing diseases for which there are no satisfactory means of prevention or treatment and by increasing the EU's preparedness for emerging health threats.

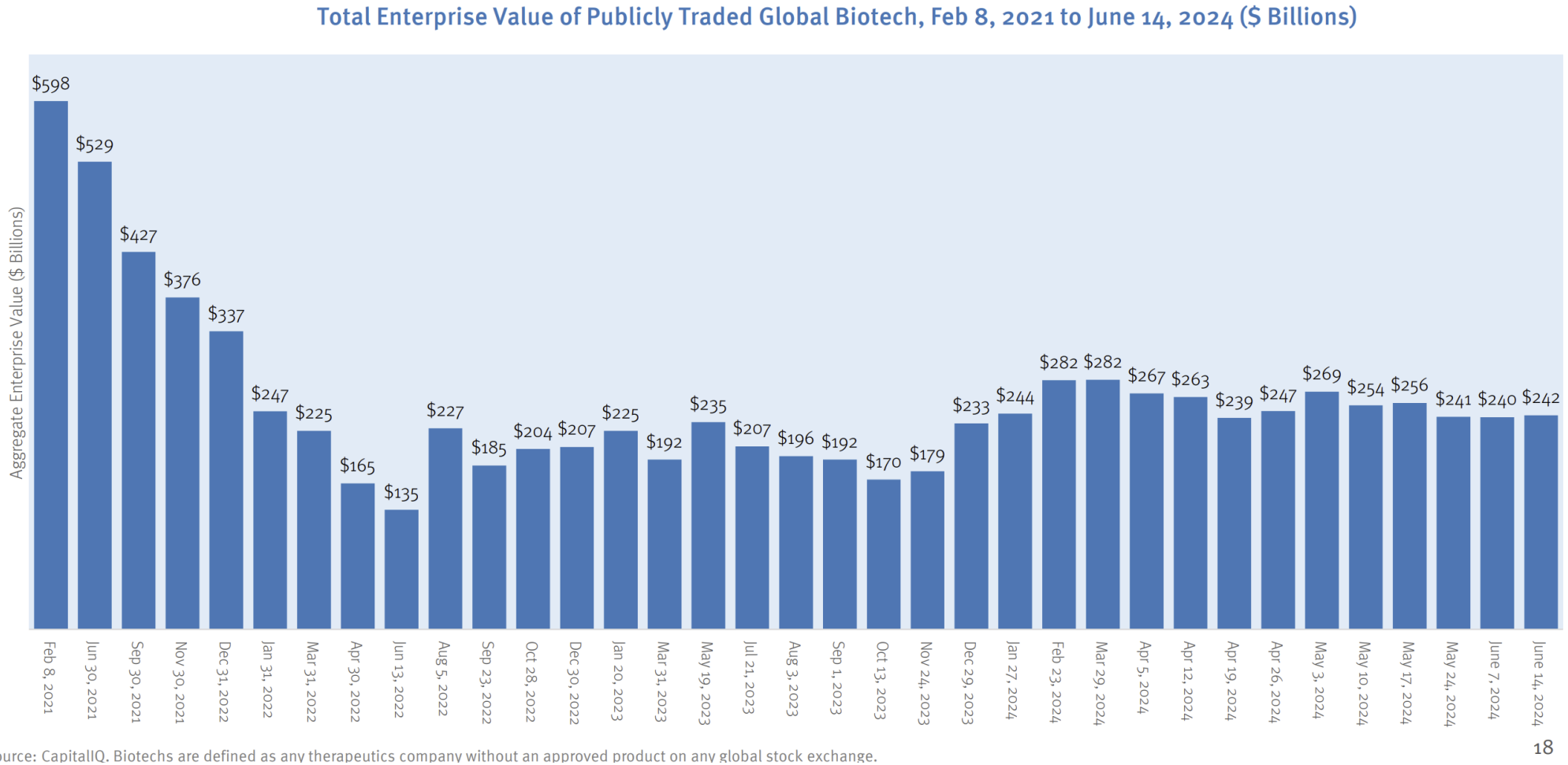
The project, called **'IPCEI Med4Cure'**, was jointly notified by six Member States: Belgium, France, Hungary, Italy, Slovakia and Spain.

The Member States will provide up to €1 billion in public funding, which is expected to unlock additional €5.9 billion in private investments. As part of this IPCEI, 13 companies with activities in one or more Member States, including nine small and medium-sized enterprises ('SMEs'), will undertake 14 highly innovative projects.



The Biotech Sector still facing fundamental challenges

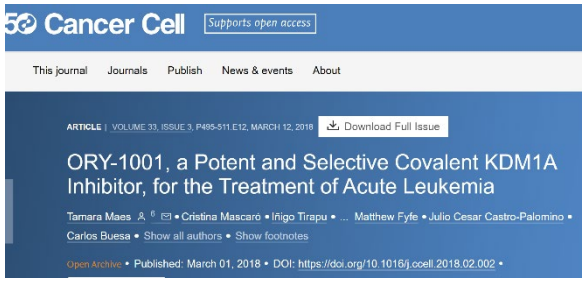
The biotech sector, which experienced significant value corrections starting in 2021, appears to have stabilized. Favorable macroeconomic trends and advancements in biotechnology may support a robust recovery by 2025.



Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

18

In a challenging Market Oryzon is endorsed by its results , its IP and its science



ORYZON

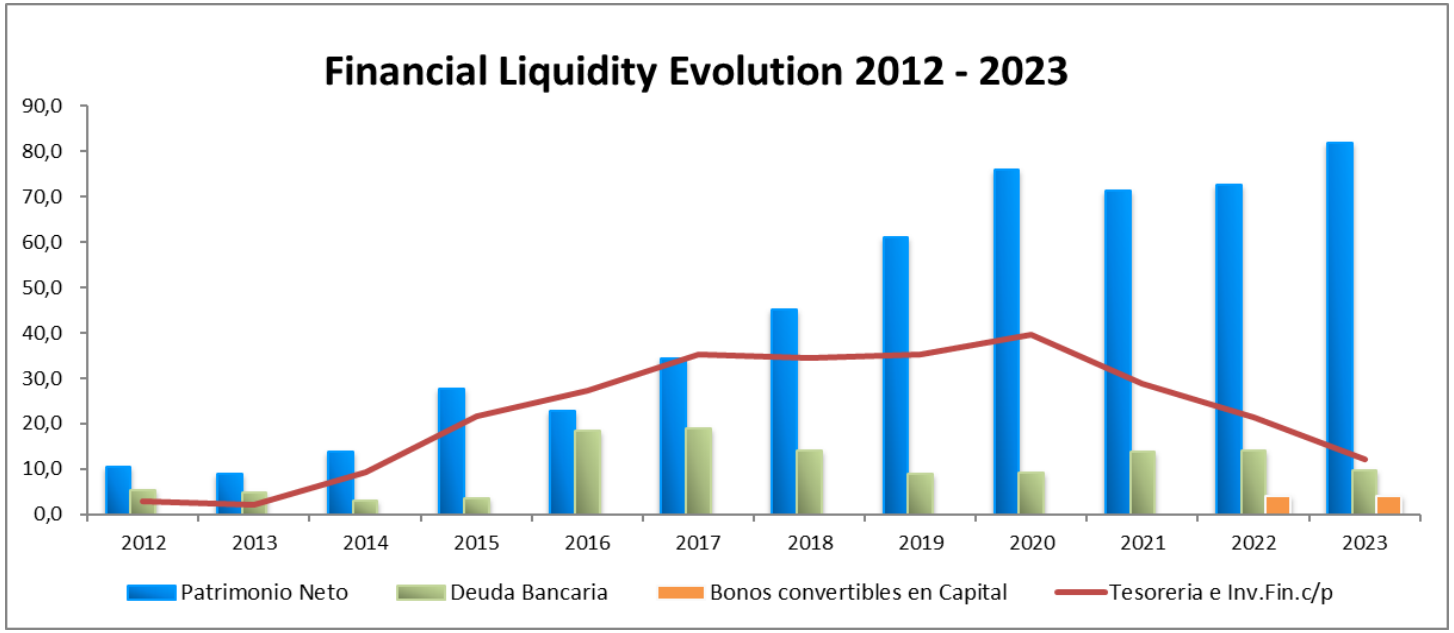
INFORME SOBRE LA MARCHA GENERAL DE LA COMPAÑÍA

HITOS FINANCIEROS (CCAA)

Balance - Evolución de la solvencia financiera

Patrimonio Neto →	81,8 M€
Tesorería e inv. financieras c/p →	12,3 M€
Endeudamiento financiero →	18,5 M€

Patrimonio Neto	→ 77%
Recursos permanentes	→ 85%
Exigible a corto plazo	→ 15%



Millions / €	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
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
Tesoreria e Inv.Fin.c/p	2,8	2,2	9,3	21,7	27,3	35,2	34,5	35,3	39,6	28,7	21,3	12,3
Deuda Bancaria	5,3	4,9	3,1	3,6	18,5	18,9	14,1	8,9	9,1	13,8	14,0	9,6
Bonos convertibles en Capital	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	3,9	4,1
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
Deuda Pública	3,0	4,8	5,0	4,6	4,0	3,9	3,4	3,8	3,0	2,7	2,0	1,7
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
Deuda Kabuki & 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

FINANCIACION BANCARIA:

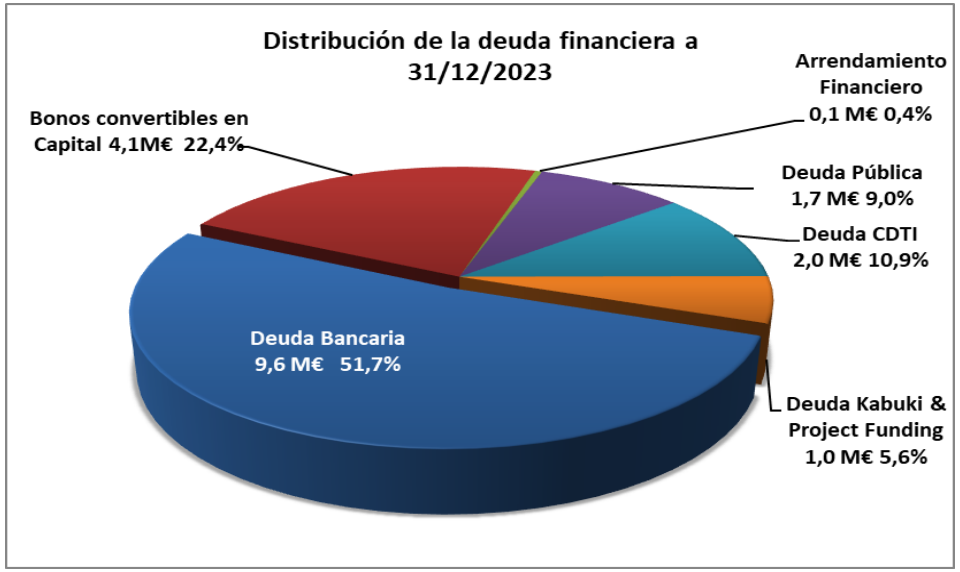
- 51,7% de participación en la deuda financiera
- 9,6M€ de financiación viva
- Sin garantías ni avales

FINANCIACION PUBLICA y OTROS

- 25,9% de participación en la deuda financiera
- 4,8M€ de financiación viva

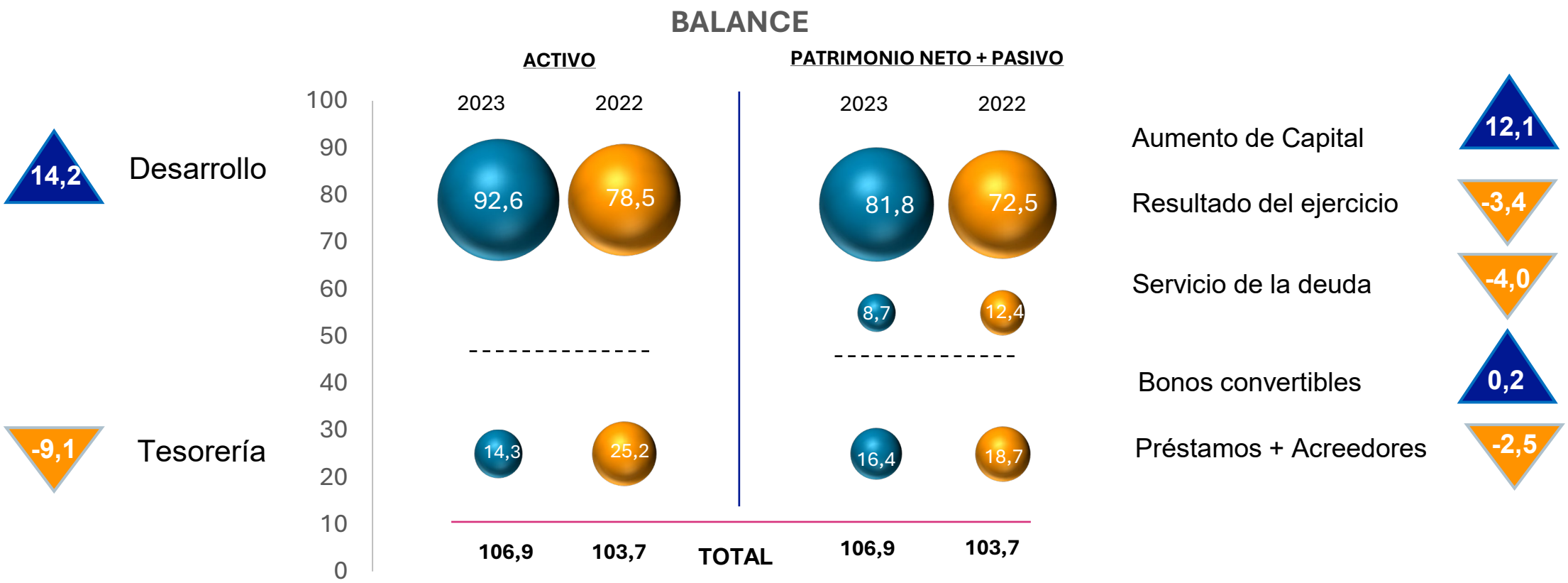
FINANCIACION BONOS CONVERTIBLES EN CAPITAL

- 22,4% Bonos convertibles en capital
- 4,1M€ de financiación viva



Nota: Importes en millones de euros

Balance - Evolución 2023 - 2022



Nota: Importes en millones de euros

Cuenta de Pérdidas y Ganancias – Evolución 2023 - 2022

INGRESOS	Ejercicio 2023	Ejercicio 2022	Variación
Ingresos por Subvenciones	153	255	-102
Ingresos por capitalización	14.192	15.698	-1.507
GASTOS			
I&D	-11.941	-13.574	1.634
Personal	-3.390	-3.163	-227
Gastos Generales	-3.411	-4.540	1.129
Amortización	-153	-167	14
Financieros	-1.555	-1.067	-488
Impuesto Sociedades	2.751	2.325	426
RESULTADO NETO	**-3.353**	**-4.231**	**878**

Inversión I+D 15M (14,2M capitalizado + 0,8M No capitalizado)

5,5 ORY 1001- Iadademstat (FRIDA 3,6)
8,6 ORY 2001- Vafidemstat (PORTICO 7,0)
0,1 ORY 3001

0,8 ORY 4001 y Otras actividades en fases tempranas (no capitalizado)

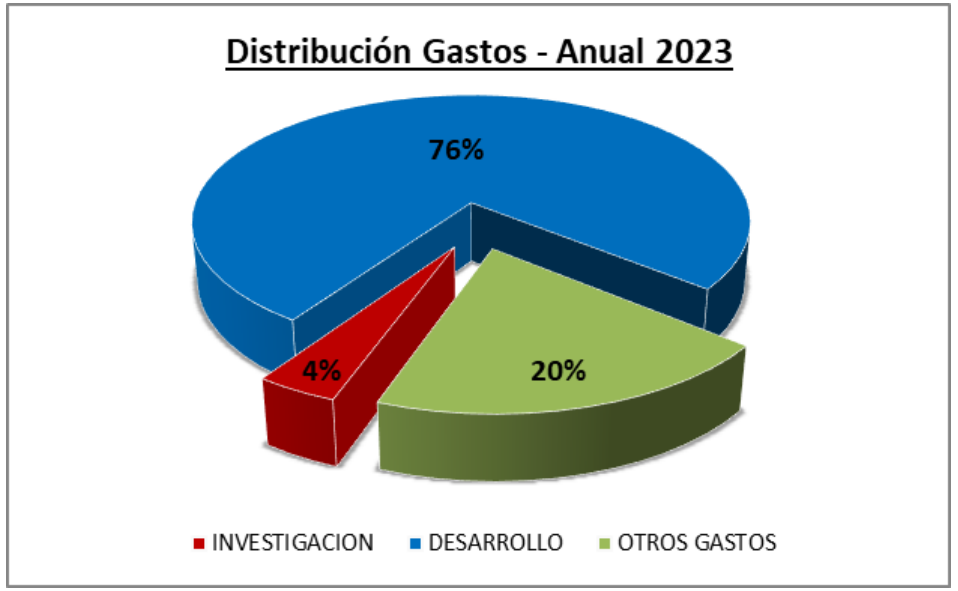
Menor coste de estructura

Intereses implícitos Bono Convertible (sin salida de caja)

Mayor Cash Back IS (2023 vs 2022)

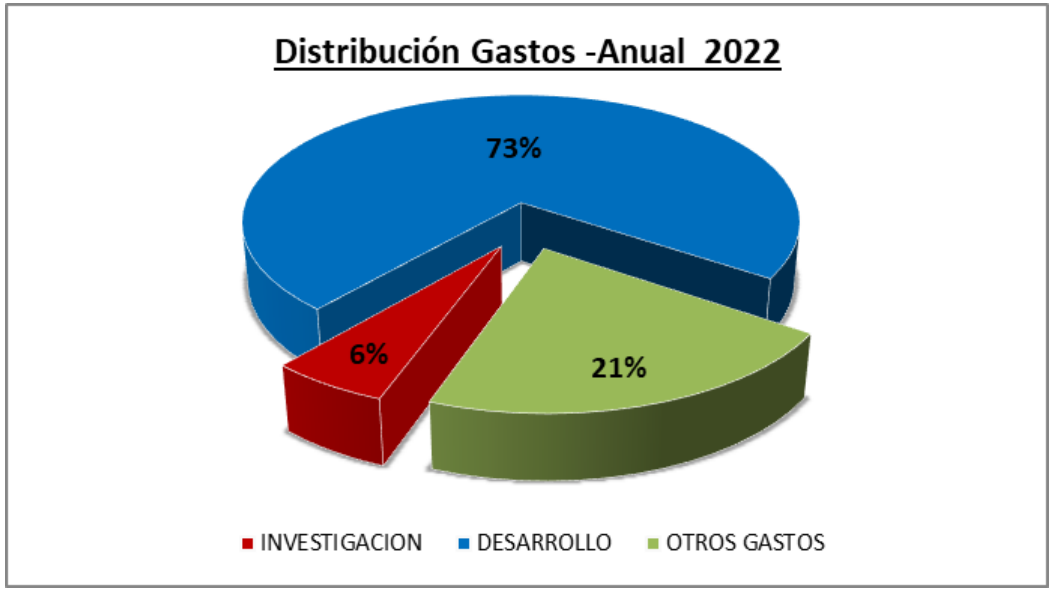
Nota: Importes en miles de euros

Cuenta de Pérdidas y Ganancias (Gastos Explotación – Investigación / Desarrollo / Otros gastos)



ACTUAL ANUAL 2023	
GASTOS EN INVESTIGACIÓN	737
GASTOS EN DESARROLLO	14.313
TOTAL GASTO I+D	15.050
OTROS GASTOS	3.845
TOTAL GASTOS EXPLOTACION 2023 (*)	18.895

(*) Excluidos Gastos financieros e Impuesto sobre beneficios



ACTUAL ANUAL 2022	
GASTOS EN INVESTIGACIÓN	1.225
GASTOS EN DESARROLLO	15.698
TOTAL GASTO I+D	16.923
OTROS GASTOS	4.522
TOTAL GASTOS EXPLOTACION 2022 (*)	21.445

(*) Excluidos Gastos Financieros e Impuesto sobre beneficios

Nota: Importes en miles de euros

Estado de Cambios en el Patrimonio Neto

PATRIMONIO NETO A 31.12.2022	**72.572**
Resultado del ejercicio	-3.354
Ampliaciones de Capital	12.052
Subvenciones (Neto de efecto fiscal)	514
Otras variaciones del patrimonio neto	-10
PATRIMONIO NETO A 31.12.2023	**81.774**

ORYZON

Nota: Importes en miles de euros

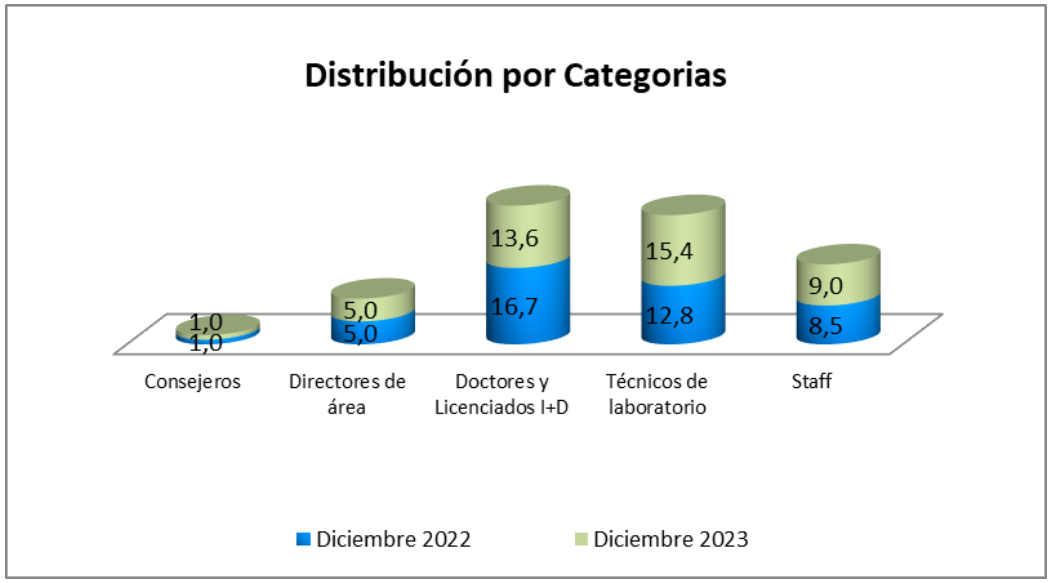
Estado de Flujos de Efectivo

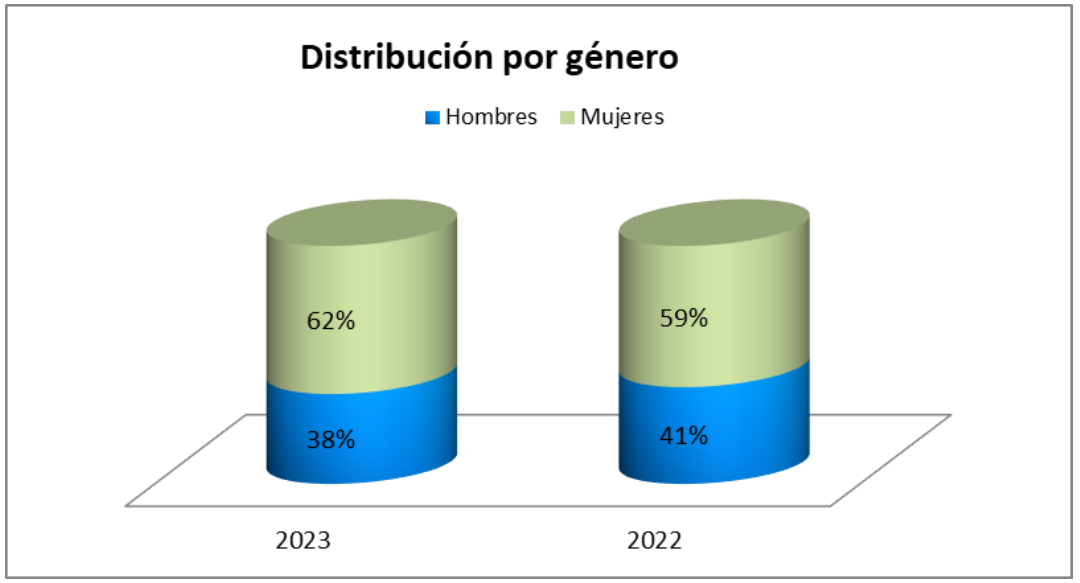
	TOTAL	ACTIVIDADES DE EXPLOTACION Y TIPOS DE CAMBIO	ACTIVIDADES DE INVERSIÓN	ACTIVIDADES DE FINANCIACIÓN
TESORERIA A 31.12.2022	**21.317**			
Cash In				
Subvenciones	76			76
Bonos Convertibles	11.007			11.007
Préstamos	1.742			1.742
Cash Back	4.667	4.667		
Cash Out				
Préstamos	-6.803			-6.803
CAPEX	-14.504		-14.504	
Costes Financieros netos	-370	-370		
Gastos Ordinarios	-4.874	-4.874		
TESORERIA A 31.12.2023	**12.257**	**-578**	**-14.504**	**6.021**

ORYZON

Nota: Importes en miles de euros

Otra información – Memoria - Personal Medio





	Diciembre 2023	Diciembre 2022
Consejeros	1,0	1,0
Directores de área	5,0	5,0
Doctores y Licenciados I+D	13,6	16,7
Técnicos de laboratorio	15,4	12,8
Staff	9,0	8,5
TOTAL	**44,0**	**43,9**

(*) NO Incluye Director de Area con contrato Mercantil.

	2023	2022
INTENSIDAD PERSONAL	**33**	**33**
INVESTIGADOR	**75%**	**75%**

Informe de auditoría de las cuentas anuales del ejercicio 2023

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 de situación a 31 de diciembre de 2023, 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 2023, 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.

Pioneering personalized medicine in epigenetics