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An Epigenetic champion determined to bring new therapies to the patients

Jun 2022-Jun 2023



2021-2023 continued to be a challenging period for the global economy



A clinical strategy focused on registration in CNS and Oncology



A US oriented strategy with a first-in-class US team



Clinical advances with trial completions and interim analysis in our Phase IIb in BPD



Adapting to a persistent adverse market condition



Securing additional Funds to guarantee operations

2022-23 Company Milestones & Principal investment thesis

- Two uncorrelated advanced clinical assets with Multiple Shots on goal
- Potentially transforming catalysts in 2024
- Focus is now on executing and setting an optimal longrun corporate strategy reinforcing the BD angle
- Additional assets in earlier stages to increase the optionality for the company
- The company continues its preps to get listed in NASDAQ



^{*} Collaborative study with Fox Chase Cancer Center

Note: Finalized clinical trials for iadademstat and vafidemstat are not shown. See $\underline{www.oryzon.com}$ for more details

AML: acute myeloid leukemia; SCLC: small cell lung cancer; NETs: neuroendocrine tumors; ALS: amyotrophic lateral sclerosis





Vafidemstat: the only LSD1 inhibitor to treat CNS indications, including large multifactorial ones such as borderline personality disorder (BPD) and schizophrenia (SCZ)

Mechanism of Action

- A potent (nM) oral inhibitor of LSD1 with high BBB penetration
- LSD1i induces the neuronal plasticity & downregulates neuroinflammation
- LSD1i modulates the response to environmental stress and improves aggressivity and sociability
- Modulates the glutamatergic signal

Key Clinical Data

- Safety and effectiveness demonstrated as a single agent. Good Pharmacology: ORAL; no DDIs
- Various trials (+400 people treated):
 - Reduction of inflammatory markers
 - Reduction in aggression (REIMAGINE basket trial; 30 patients with BPD, ADHD, and ASD pts)
 - Improvements in overall patient functioning, particularly in BPD patients

Safe & well tolerated



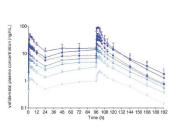
No differences between placebo and vafidemstat-treated patients

Excellent Brain Penetration



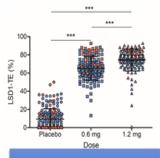
An optimal CSF: plasma ratio of 0.9

Oral, once a day



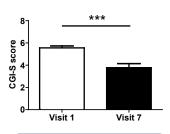
PK data supports once-daily dosing in both adult and elder subjects

RP2D established



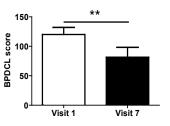
PK and Drug Occupancy Established in large human trials at 2 doses

Reduces Aggression



Reduces Aggression in BPD, ADHD and ASD patients after 2 months of treatment

Improves BPD disease



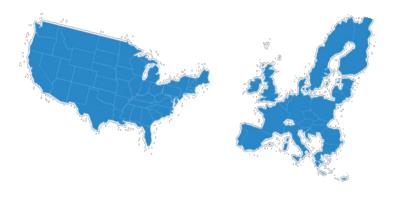
Reduces overall severity in BPD patients after 2 months of treatment



Borderline personality disorder: an unmet medical need & a huge 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 antipsychotics





Vafi improves these symptoms in:

- **BPD patients**
- o in PC models

Highest Revenue Drug Category: Anti-psychotics followed by antidepressants

Aggregated sells: ~ 1 Billion

O Phase III trials
2 Phase II trials



Expected peak sales for vafi

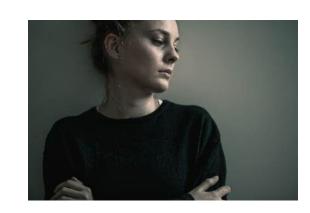
US\$ ~3 billion



Ongoing Study: a Phase IIb in Borderline Personality Disorder

PORTICO:

An adaptative randomized double blind Phase IIb trial with vafidemstat in Borderline Personality Disorder patients



- PORTICO (NCT04932291): will enroll 188 patients
- Double blind, placebo-controlled, with two primary independent endpoints:
 - Overall clinical BPD improvement
 - Improvement in aggression
- Actively enrolling in EU and US
 - Several safety analyses by the independent DMC showed safety & tolerability
 - A prespecified interim analysis (w 90 patients) successfully passed in 1Q23 (To assess futility & signal size)

Final read out 4Q23-1Q24

EVOLUTION:

An adaptative, randomized double-blind 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
- EVOLUTION: Double-blind, placebo-controlled adaptive trial design (n=100)
- Vafidemstat as an add-on to SoC. 6 months of treatment
- Primary endpoints: efficacy to address SCZ
 Negative and cognitive symptoms
- Actively recruiting patients in the EU

A Prevalent & impairing disease 20 millio ww.

~5 million in US & EU



Market Value in 2021

US\$ ~8 billion



Three main types of symptoms

Positive or Negative

Cognitive Impairment



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

Single Best seller: + \$ 3.5 Billion



No approved drugs yet for Negative symptoms (60%) Cognitive Impairment (70%)





Moderate competition





Vafidemstat Commercial Assessment (I)

Significant Commercial Potential

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

 BPD multi-symptom treatment represents also a substantial peak revenue opportunity of +\$3Bn

 Schizophrenia negative symptoms treatment represents also 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 +\$7.8 Bn of sales in 2019, estimated to be US\$ 9.8 Bn by 2030. 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



Abilify+ Rexulti +\$1.4Bn sales in 2022



Vyvanse \$2.76Bn sales in 2021







LSD1 inhibition is a validated epigenetic approach for targeted therapies in Oncology

- In ONCOLOGY, LSD1i MoA has been exquisitely well-defined
- Class Validation: competitor LSD1i acquisition for \$1.35B by MERCK, and ongoing BMS's LSD1i Phase II program
- Oryzon's iadademstat is 20-200 fold more potent than Merck's LSD1i bomedemstat
- CRADA agreement signed with NCI-NIH provides an independent high-quality scientific endorsement

Merck to acquire Imago for \$1.35 billion

Merck has signed agreement to acquire Imago for \$1.35 billion to further investigate potential of bomedemstat for myeloproliferative neoplasms and other bone marrow diseases.





CRADA Agreement ORYZON-NCI

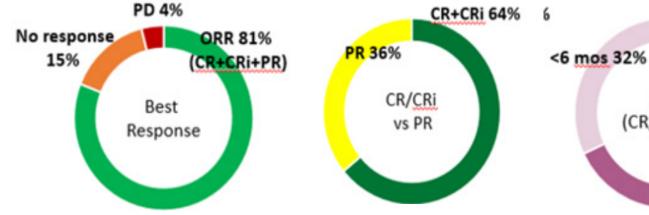


ladademstat: final results of ALICE trial presented at ASH-2022

Key Clinical
Data in ALICE
as PoC

- Multicenter, single arm, open label PhIIa trial in **elderly unfit AML patients** (n=36)
- ladademstat + azacitidine
- Final data presented at ASH-2022. Selected for Oral presentation.
- Shortlisted in the 25 most relevant AML comms to be considered for 2023 HIGHLIGHTS OF ASH
- Combination is safe and effective
- Responses are rapid, deep, and durable
- RP2D established
- Responses seen in patients with a diverse array of AML mutations





≥6 mos 68%

DoR

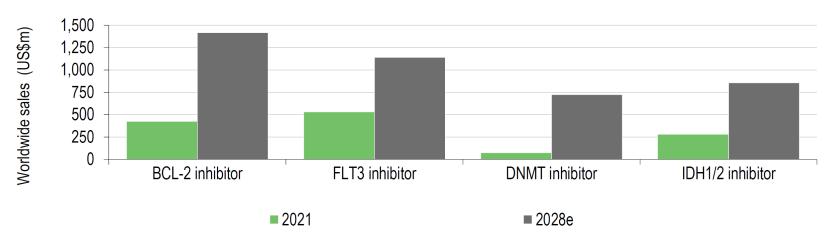
(CR/CRi pts)

FLT3mut+ R/R AML, an interesting market opportunity

Combo w gilteritinib, best route to market

- In a competitive market, R/R AML is an underserved population: The 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%)
- Global FLT3 inhibitors market is expected to reach \$2.06 Billion by 2032*

*https://www.bloomberg.com/press-releases/2022-08-30/bis-research-study-projects-the-global-flt3inhibitors-market-to-reach-2-06-billion-by-2032



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

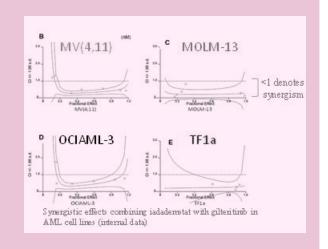
(Source Edison Research 2023 & Evaluate Pharma)



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

FRIDA: A Phase Ib in FLT3 mut+ R/R AML patients combining iadademstat and gilteritinib (Xospata®)

- ladademstat and gilteritinib show a strong synergism, providing a strong preclinical rationale for enhanced clinical benefit
 - Primary objectives: evaluate safety/tolerability, and determine the RP2D of the combination
 - Secondary objective: evaluate the efficacy of the combination (CR rate, DoR, MRD)
 - Up to 50 patients
 - Study conducted in the US. Recruiting
 - Agreement with FDA to discuss next steps for pivotal trial development after this Phase Ib



Study presented at







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

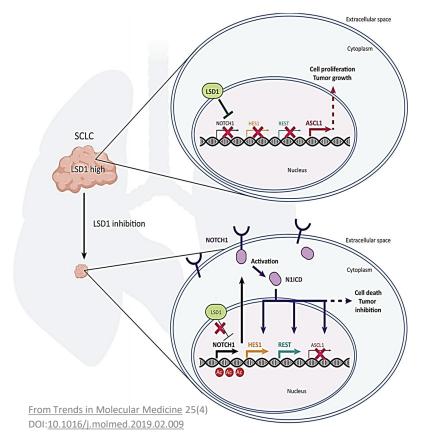
ladademstat: potentially first and best-in-class LSD1 inhibitor in SCLC and other Neuroendocrine tumors

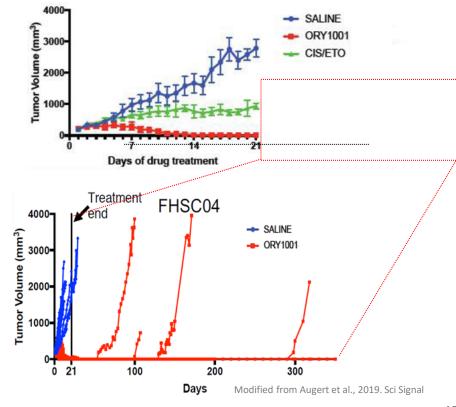
Mechanism of Action

- LSD1 is required for the 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







Neuroendocrine Tumors: a Collaborative PoC basket trial in NETs with iadademstat



NET:

A Phase II study of iadademstat in combination with paclitaxel in platinum-R/R SCLC and extrapulmonary high grade neuroendocrine carcinomas

- High unmet medical need: NETs have dismal outcomes ranging from ORR 5% (extrapulmonary) to ~20-30% in second-line SCLC; with mPFS 3 to 4 months, respectively
- Strong rationale for combination: preclinical data showing synergy between iadademstat and paclitaxel
- Sponsor: Fox Chase Cancer Center
- IND approved
- FPI Jan23, recruiting

PI: Dr. Namrata Vijayvergia
Assistant Chief, Gastrointestinal Medical Oncology
Associate Professor, Department of
Hematology/Oncology
Medical Director, Medical Oncology



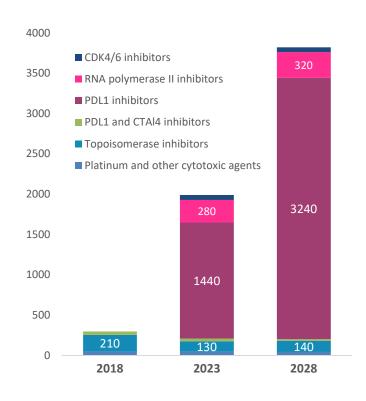


ED-SCLC, an interesting market opportunity

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 is 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
- ladademstat peak sales are estimated to be +\$1.5
 billion in 1L maintenance therapy

SCLC market





STELLAR: A randomized controlled Phase Ib/II study of iadademstat plus a checkpoint inhibitor in 1L patients with metastatic SCLC

- **High unmet medical need** + relatively low bar for improving efficacy due to the modest efficacy improvements (**2 months OS increment with the recent approval of ICI in combo with chemotherapy**) shown in the IMPower-133, CASPIAN, and Keynote-604 trials in 1L SCLC
 - Phase Ib objectives: evaluate safety/tolerability, and determine the RP2D and MTD of iadademstat in combination with ICI
 - Phase II objective: evaluate the efficacy of the combination of iadademstat and ICI vs ICI alone in maintenance after SoC chemotherapy measured as PFS
 - IND 2023



PI: Dr. Hossein Borghaei, Chief, Division of Thoracic Medical Oncology Professor, Department of Hematology/Oncology Co-Director, Immune Monitoring Facility at FCCC



STELLAR could potentially support an accelerated approval if a significant clinical benefit in the population is demonstrated over the efficacy of SoC treatment

ORYZON Research and Clinical Development leverages on collaborations with prestigious international institutions



































A Management Team with Proven Drug Development and Operational Capabilities































BROWN UNIVERSITY















































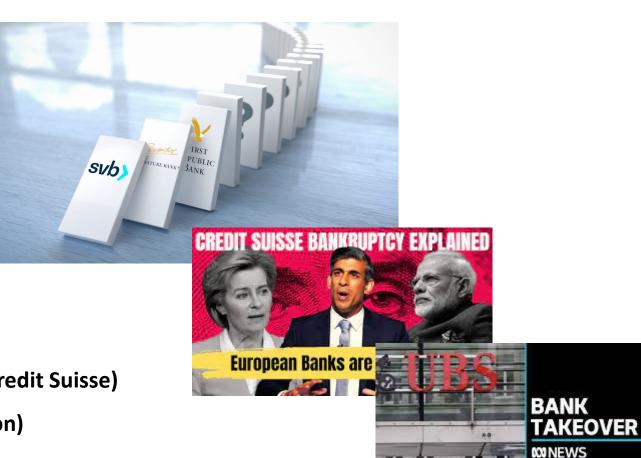






Unprecedented systemic crisis

- Energy Prices
- Inflation rates
- Slower growth
- ECB/FED rate hikes
- War in Ukraine
- Food / Cereal Crisis
- Bank Bailouts/rescues (SVB, First Republic Bank, Credit Suisse)
- New regulations (IRA, EU pharmaceutical legislation)

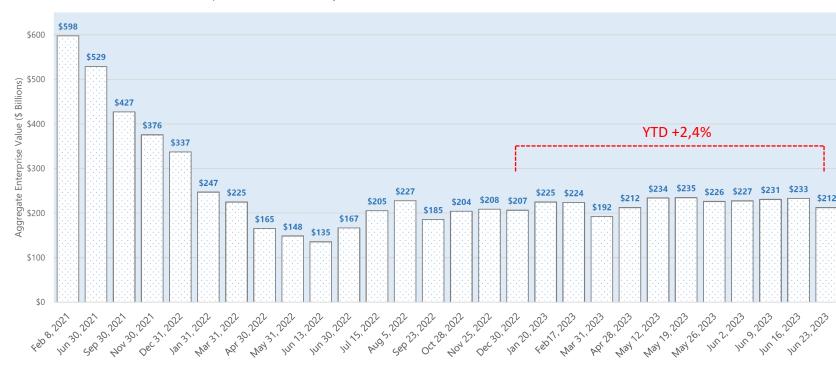


CREDIT SUISSE

The financial crisis affects especially the biotech funding ecosystem

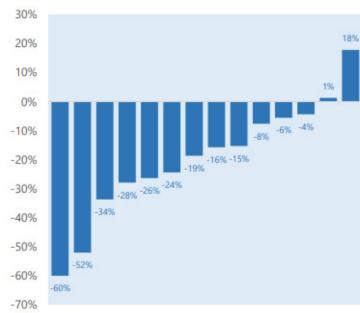
In the last two years, the Biotech Sector has been affected by the negative market sentiment





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

Change in Aggregate EV Since Feb 8, 2021 Market Peak



Source: CapitallQ



After 2022 interest rate hikes spook investors, pharma M&A to resurge in late 2023

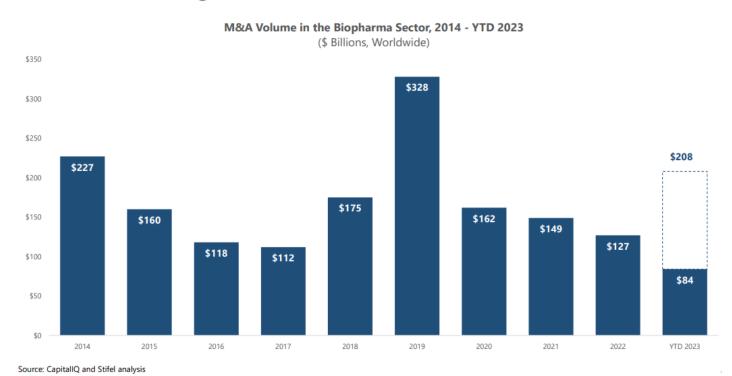


Comment | May 26, 2023

Pharma company merger and acquisition (M&A) activity will increase later in 2023.

Experts at PWC, Goldman Sachs, and Morgan Stanley agree that pharmarelated M&A is expected to pick up in 2023.

We are Tracking to a \$208 Billion M&A Year



Source: Biopharmaceutical Sector Market Update. May 29 Stifel



In a very adverse market, Oryzon has obtained several positive clinical results

Despite the positive results and the good fundamentals, the general market conditions have resulted in a mixed performance





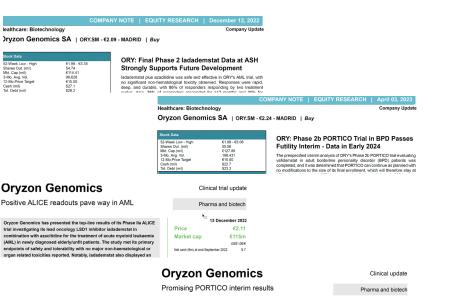
Must-haves in current market for Biotech companies to succeed

In a difficult market, access to financing has become increasingly hard for biotech companies. Several must-haves are critical to achieving this. Oryzon is well-positioned to attract the attention of investors and corporate partners

Well-endorsed & cutting-edge science.	YES; LSD1 class validation; CRADA NCI-NIH Agreement. Ample Independent evidence in CNS
Focused on an undisputed high-unmet medical need with a relevant market opportunity.	YES; BPD and negative symptoms in SCZ are high-unmet medical needs with huge markets AML and SCLC are high-unmet medical needs with significant markets
Critical clinical read-outs in the short term with potential to change the company's magnitude.	YES; BPD Phase 2b to be read in the next 6-9 months. AML to be read over the next 12-18 months
Pipeline maturity enabling Licensing Agreeements or M&A	YES;
Cash-runway sufficient to go till the next clinical read-outs.	YES;
Management team with proven industry and clinical experience.	YES;. A US-EU team with proven clinical development and FDA interaction experience
Strong IP protection.	YES;
Proper company size.	YES; Company Market value has oscillated between ~\$130-200m in the last 24 months
Good corporate governance	YES; Independent Board & Big-4 Auditing Firm
Liquidity	YES; Oryzon is one of the most liquid biotech values among the small-midcap segment in the European stock Markets. ~38 million shares traded in the last 12 months, ~44 million in 2022 and ~53 million in 2021
US presence	YES; Strong US team. Plans to list in Nasdaq

Oryzon has continued its efforts in communicating its progresses to the markets

- To improve investors and potential corporate partners awareness of Oryzon's progress, we maintain an ongoing communication effort
- Oryzon's scientists and executives have attended 49 International Conferences and Events in the last 12 months and 21 in YTD2023



Oryzon has announced promising results from an interim analysis of the Phase IIb PORTICO study, a trial evaluating validemstat as a treatment for

borderline personality disorder (BPD). An independent data monitoring

ny modifications to the design. These interim results, along with positive

committee (IDMC) conducted an analysis of the first 90 patients who

€135m

Expansión

Oryzon avanza en su principal ensayo

Gabriel Trindade. Barcelona

Oryzon Genomics anunció ayer resultados positivos en un análisis provisional del ensayo clínico Portico, su principal proyecto de I+D. Tras el anuncio, las acciones de la biotecnológica se revalorizaron un 6,92% en la sesión de ayer en Bolsa.

La compañía presidida por Carlos Buesa ha obtenido resultados positivos en un análisis preliminar de su fase IIb con el fármaco Vafidemstat en 188 pacientes para la indicación de trastorno límite de la personalidad. "Tras com-

pletar el 60% del reclutamiento, ha quedado claro que esta investigación no es fútil", explica Buesa.

Este tipo de análisis preliminares se realiza para evitar suministrar tratamientos no efectivos si el fármaco no presenta ningún tipo de respuesta. "No se obtiene información detallada del comité independiente, sino simplemente un visto bueno de que la investigación tiene interés", comenta.

Vafidemstat tiene un potencial de 2.400 millones de dólares en su pico de ventas.

Oryzon presenta datos positivos en fase II en leucemia

G. Trindade, Barcelona

Oryzon Genomics sufrió un importante revés en 2017 cuando Roche le devolvió el fármaco oncológico Isdademotat I a multipocional

CincoDías

IDUSTRIA FARMACÉLITICA

El laboratorio español Oryzon logra resultados positivos en su terapia frente a la leucemia

Despeja la senda a la firma catalana para una alianza con una gran farma. El mercado al que se dirige ronda los 1.000 millones anuales

INDUSTRIA FARMACÉU

Oryzon obtiene 20 millones en bonos convertibles del fondo Nice & Green

El fondo suizo se guarda una opción para participar en una ampliación si Oryzon cotiza en el Nasdaq

invertia EL®AESPAÑOL

OBSERVATORIO DE LA SANIDAD

Oryzon Genomics reduce un 9,7% sus pérdidas en 2022 y las sitúa en 4,2 millones

Los ingresos al cierre del tercer trimestre del año ascendieron a 15,6 millones de euros.

LAVANGUARDIA

MPRESAS ORYZON

Oryzon inicia una colaboración con la CMT Research Foundation

Inicio > Programas > Capital Intereconomía

Oryzon Genomics espera avances positivos en su fármaco para el TLP y mantiene sus planes para cotizar en el Nasdaq

Planta Doce.

Oryzon Genomics recibe 400.000 euros de la UE para un proyecto oncológico



Salud

Oryzon ultima una terapia con 1.000 millones de mercado



ORYZON

A unique dual EPIGENETIC proposition in CNS and ONCOLOGY

- A validated approach with multiple shots on goal
- One and only epigenetic company in CNS
- 2 Phase II programs
- Differentiated pipeline of first- and potentially best-in-class LSD1 therapies
- Derisked: Safety proven in 400+ subjects dosed

Value Creation in 2023-24

Multiple inflection points

- Top Line Read Out in BPD PORTICO e4Q2023-1H2024
- 2L AML FRIDA trial preliminary readouts in 2024 (EHA & ASH)
- 2L NET trial preliminary readouts in 2024
- Kabuki Syndrome Phase I/II trial IND & initiation
- 1L ED-SCLC with potential to support accelerated development IND & initiation



Evolución de la solvencia financiera (2012-2022)

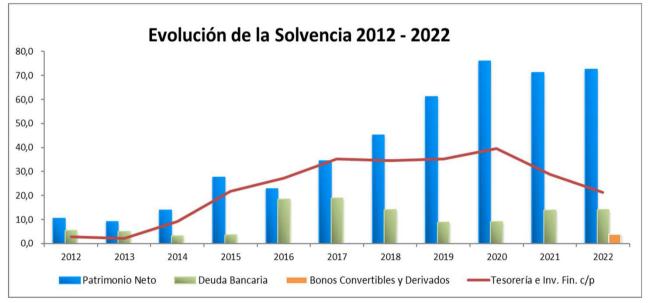
Patrimonio Neto → 72,6 M€

Tesorería e inv. financieras c/p → 21,3 M€

Endeudamiento financiero → 23,3 M€



Patrimonio Neto \rightarrow 70% Recursos permanentes \rightarrow 82% Exigible a corto plazo \rightarrow 18%



Millions /€	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Patrimonio Neto	10,3	9,0	13,9	27,6	22,7	34,4	45,1	61,1	75,9	71,3	72,6
Tesorería 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
Deuda Bancaria	5,3	4,9	3,1	3,6	18,5	18,9	14,1	8,9	9,1	13,8	14,0
Bonos Convertibles y Derivados	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	3,9
Arrendamiento Financiero	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	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
Deuda CDTI	1,0	1,0	1,0	0,8	0,7	0,6	0,7	0,6	1,5	1,2	2,2
Project Funding	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	1,1

FINANCIACION BANCARIA

- 60% de participación en la deuda financiera
- 14,0 M€ de financiación viva
- Sin garantías ni avales

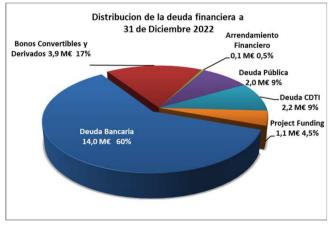
FINANCIACION PUBLICA y OTROS

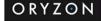
- 23% de participación en la deuda pública y otros
- 5,4 M€ de financiación viva

BONOS CONVERTIBLES y DERIVADOS

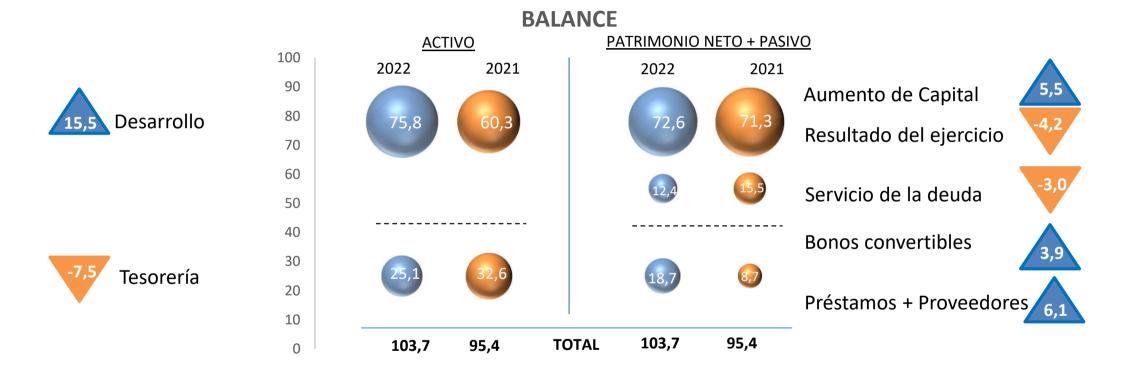
- 17% de participación en Bonos Convertibles y derivados
- 3,9 M€ de financiación viva

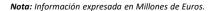






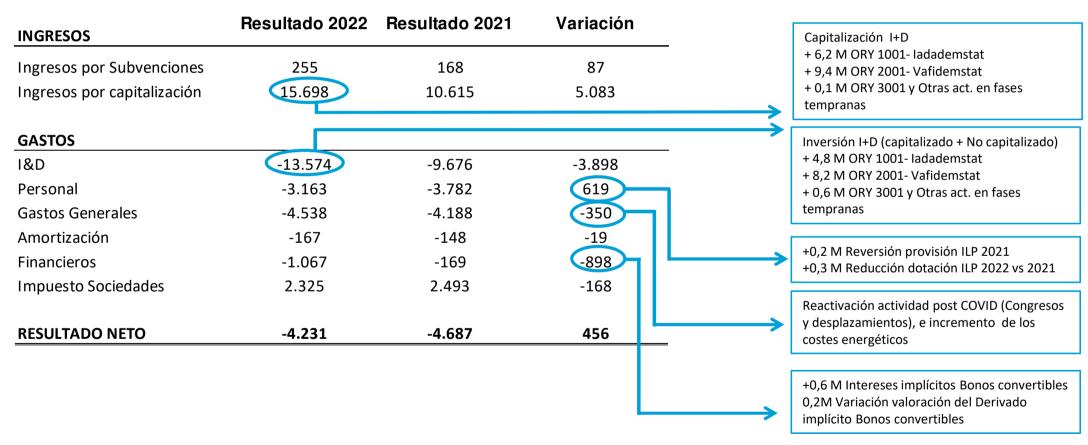
Evolución del Balance







Estados Financieros – Ejercicio 2022 - Resultado



Nota: Información expresada en Miles de Euros.



Estado de Cambios en el Patrimonio Neto

PATRIMONIO NETO A 31.12.2021	71.262
Resultado del ejercicio	-4.231
Ampliaciones de Capital	5.500
Subvenciones (Neto de efecto fiscal)	714
Otras variaciones del patrimonio neto	-718
PATRIMONIO NETO A 31.12.2022	72.527



Estado de Flujos de Efectivo

	TOTAL	ACTIVIDADES DE EXPLOTACIÓN Y TIPOS DE CAMBIO	ACTIVIDADES DE INVERSIÓN	ACTIVIDADES DE FINANCIACIÓN
TESORERÍA A 31.12.2021	28.725			
Cash In				
Subvenciones	144			144
Bonos Convertibles	7.878			7.878
Préstamos	5.114			5.114
Cash back	2.483	2.483		
Cash Out				
Préstamos	-4.426			-4.426
CAPEX	-14.271		-14.271	
Costes financieros netos	-306	-306		
Gastos Ordinarios	-4.024	-4.024		
TESORERÍA A 31.12.2022	21.317	-1.847	-14.271	8.710

Nota: Información expresada en Miles de Euros.



