



ORYZON

A GLOBAL LEADER IN EPIGENETICS

INVESTOR PRESENTATION

MADX: ORY

SEPTEMBER 2018

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COMPANY HIGHLIGHTS

- ✓ MADX: ORY A **publicly traded** company on the Spanish Stock Exchange (*)
- ✓ A **clinical stage** biopharmaceutical company developing innovative therapies in the field of Epigenetics
- ✓ A competitive **EPIGENETIC PLATFORM** validated scientifically and clinically
- ✓ Three therapeutic programs in LSD1 in development with multiple indication opportunities
 - ✓ In CNS → in 3 Phase IIAs
 - ✓ in Oncology → in 2 Phase IIAs
 - ✓ In an orphan disease → ready to start Phase I
- ✓ Large IP portfolio with technology fully developed in-house



BOLSA DE MADRID

ORYZON GENOMICS SA
BALANCE SHEET DATA (AUDITED)
 (Amounts in thousands US \$)

- ✓ **Raised €32M** in 2015-2016. Additional **€18.2M** raised from blue chip investors in the US and Europe **in March 2017**
- ✓ 34.1M Shares outstanding. Fully diluted.
- ✓ Loss/Earnings from Operations 1H2018: **-€1.5M**
- ✓ **Cash runway** expected till **1Q2020**
- ✓ One of the most **liquid** companies in the MicroCap group in the Spanish Stock Market
 - ✓ +585.854 daily volume (*90 Day Avg Traded Volume*. as per 24.09.2018).
 - ✓ +72M shares negotiated in 2018

	June 30th, 2018	June 30th, 2017
Cash and cash equivalents	30.986	41.493
Marketable securities	165	1.303
Total Assets	68.352	70.932
Deferred revenue	0	0
Total Stockholders' equity	40.697	41.972

⁽¹⁾ €26.579 M. Audited by Deloitte

* Spanish Automated Quotation System (Continuous Market) that includes Madrid, Barcelona, Bilbao and Valencia Stock Exchanges

ORYZON: A UNIQUE COMPANY

EPIGENETICS

- ✓ One of the global leaders in Epigenetics with an efficient platform
- ✓ Highly specialized in LSD1, one of the most promising targets in the field (GSK, Takeda, Celgene, Incyte,...)
- ✓ Leading the field in clinics and exploring a variety of development possibilities

BROAD PRODUCT PIPELINE

- ✓ World class science and a broad patent portfolio
- ✓ A diverse and promising Pipeline: 2 Programs in Clinic and another ready to start
- ✓ 5 trials in Phase IIa. Additional indications under exploration. Strong science-driven decisions to position our drugs in clinical trials
- ✓ A Program in CNS with a strong transformation potential

PROVEN TRACK RECORD

- ✓ Skilled & Resilient team in a highly capital efficient company (~€50m raised in equity since inception)
- ✓ First ever University Start-Up to become public in Spain
- ✓ A leading licensing deal signed in Spain by a Biotech (ROCHE \$21m Upfront).

SOLID SITUATION

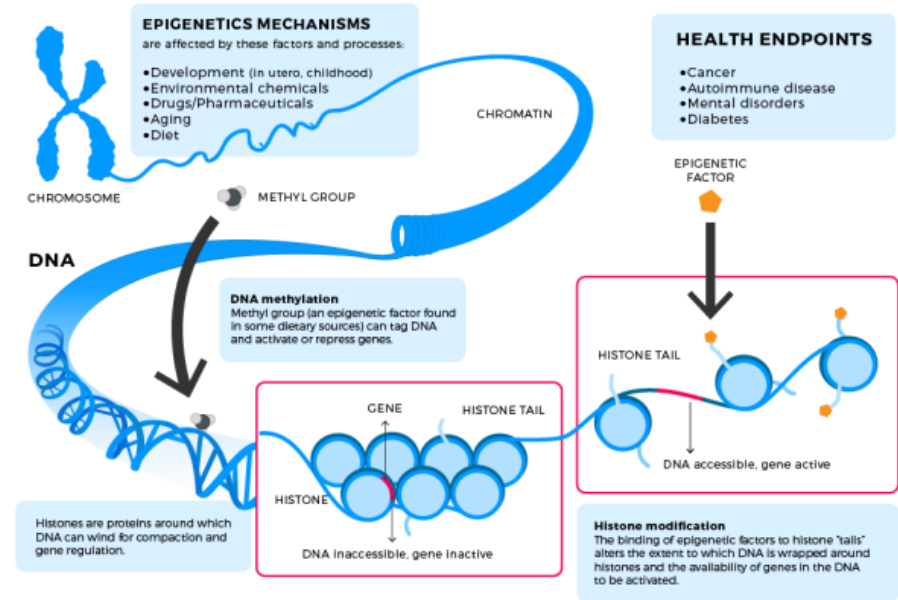
- ✓ Expected Cash Runway beginning of 2020
- ✓ Compact Human team
- ✓ Clinical Programs approved and launched

INVESTMENT PROPOSAL

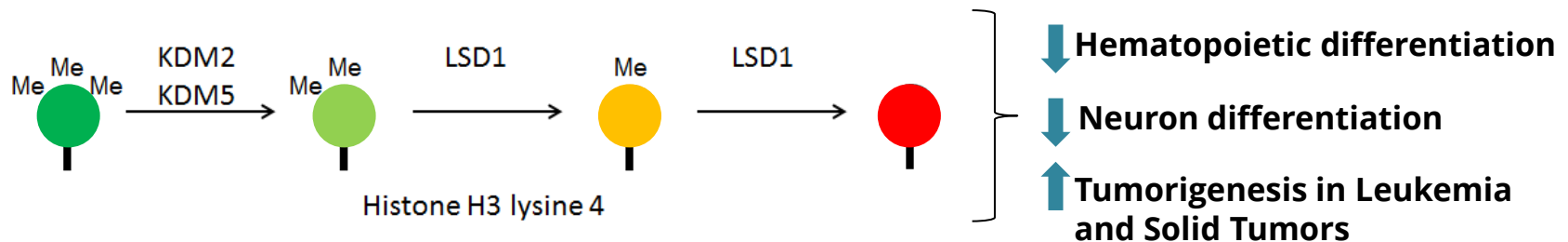
- ✓ Company is at an important inflection point and will consider a potential Dual Listing in Nasdaq in the future
- ✓ Rich flow of catalysts in 9-12m
- ✓ Currently undervalued compared with its natural peers

LSD1 an Epigenetic target

- ✓ Lysine specific histone demethylase 1 (LSD1), also known as KDM1A, removes methyl marks at mono- and dimethyl-H3K4 (histone H3 lysine 4) and H3K9 (histone H3 lysine 9)
- ✓ “Erasing” methyl marks (demethylation) regulates the expression of genes that are important in the onset and progression of certain diseases as cancers and others
- ✓ Aberrant expression of LSD1 has been shown in many types of cancers, such as bladder, SCLC, colorectal, AML, ALL, some breast cancers, prostate and aggressive brain cancers
- ✓ LSD1 plays a very important role in the development and function of the CNS



LSD1 Overexpression Leads to:



EXTENSIVE PIPELINE : 2 PROGRAMS IN CLINIC WITH MULTIPLE INDICATIONS

- ✓ A Productive Epigenetic Platform
- ✓ A strong focus on LSD1
- ✓ 3 Different LSD1 inhibitors in development
- ✓ Additional programs on other targets

INDICATION	STUDY	RESEARCH	PRECLINICAL	PHASE I	PHASE IIA	PHASE IIB
VAFIDEMSTAT (ORY-2001) - dual LSD1-MAO B inhibitor						
Alzheimer's disease (Mild Moderate)	ETHERAL monotherapy ⁽¹⁾					
Multiple Sclerosis (Relapse Remitting & Secondary Progressive)	SATEEN monotherapy ⁽¹⁾					
CNS Basket Trial Aggression	REIMAGINE monotherapy ⁽²⁾					
IADADEMSTAT (ORY-1001) - selective LSD1 inhibitor						
AML (Elderly Unfit)	ALICE Combo w Aza ⁽²⁾					
SCLC (First Line Relapsed)	CLEPSIDRA Combo w Platinum/Etoposide ⁽³⁾					
ORY-3001 - selective LSD1 inhibitor						
Non Oncological	Preclinical finished					
OTHER PROGRAMS						
Undisclosed						

⁽¹⁾ Approved. Recruitment ongoing

⁽²⁾ Approved

⁽³⁾ CTA submitted

Solid evidence of an Epigenetic axis in CNS diseases

In neurodegenerative disorders

- ✓ Historic results with HDACi's
 - ✓ HDACi improves HD symptoms in animal models
 - ✓ HDAC2 inhibition recovers memory on the AD bi-tg CK-p25 Tg mouse model
 - ✓ HDAC inhibition improves FTD
 - ✓ HDAC inhibition improves MS in EAE models
- ✓ See “The emerging field of epigenetics in neurodegeneration and neuroprotection” by Jee-Yeon Hwang, et al., Nature Reviews Neuroscience vol18, p 347–361 (2017)
- ✓ See “Epigenetic Alterations in Alzheimer’s Disease” by JV. Sanchez-Mut & J. Gräff. Front Behav Neurosci. 2015; 9: 347.

In Psychiatric disorders

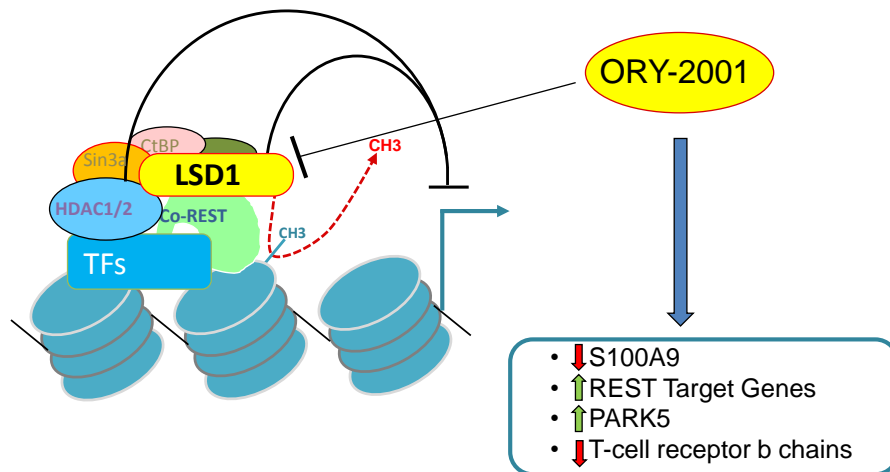
- ✓ HDAC inhibition suggested also to work in Major depression
- ✓ Histone methylation is also implicated in depression.
- ✓ See “Epigenetic Signaling in Psychiatric Disorders” by Peña et al., J Mol Biol. 2014 Oct 9; 426(20): 3389–3412.



- Identical twins (monozygotic)
- Same DNA with GBA risk mutation
- Discordant for symptoms of Parkinson's
- Up to 20 years difference in onset
- Patient derived iPSCs: difference in MAO-B levels

Epigenetics MoA in CNS is often exercised through transcription control

- ✓ Most of the Epigenetics enzymes have a dual role:
 - ✓ Enzymatic → As Chromatin remodelers
 - ✓ **Scaffolding → Interacting with a variety of Transcription Factors and other epigenetic modulators through protein-protein interactions that results in Transcriptional Complexes and super-enhancers controlling the expression of key genes for cellular function (see example below)**
- ✓ HDACs are difficult targets for chronic use in non-life threatening diseases:
 - ✓ The different HDACs are quite pleiotropic → Many signaling pathways will always be affected
 - ✓ The different HDACs are highly conserved → So far it has been impossible to produce real selective inhibitors



- ✓ **LSD1 is a key component of different CNS Transcriptional complexes** interacting with different Transcription Factors and very often with HDAC1 and HDAC2
- ✓ **LSD1 is not a very pleiotropic target**
- ✓ **Different to what happens in HDACs, it has been proven that it is possible to develop extremely selective LSD1 inhibitors with excellent pharmacological properties**

A new experimental drug for the global treatment of Neurodegenerative and Psychiatric Disorders

VAFIDEMSTAT acts in a holistic way on the different domains that are presented in human CNS indications



VAFIDEMSTAT (ORY-2001), a “NEURON-FIXER”. Summary

- ✓ A small molecule that selectively inhibits LSD1 and MAO-B
- ✓ Excellent Pharmacology.
- ✓ Safe in 6 and 9 months PC regulatory toxicological studies.
- ✓ Positive results in many different animal models and in many in-vitro models:
 - ✓ Cognition Improves cognition in SAMP8 AD model and in R6/1 HD model
 - ✓ Locomotion Improves locomotion and motility signals in the EAE and Thyler’s MS models and in the R6/1 HD model
 - ✓ Neuroprotection Produces axonal protection in the Thyler’s MS model, and in IV glutamate excitotoxic challenging
 - ✓ Neuroinflammation Reduces neuroinflammation in SAMP8 AD model and in the EAE and Thyler’s MS models
 - ✓ Social Withdrawal / Apathy Reverts social avoidance in the rat isolation model, increases sociability in the TCT in the SAMP8 AD model
 - ✓ Aggression/Agitation Reverts severe aggressiveness in SAMP8 AD model
 - ✓ Others Protection in the rat OH-dopamine and mouse MPTP challenges
- ✓ MoA: Reset the Gene expression program → Strong anti-neuroinflammatory activity and enhances synaptic plasticity
- ✓ Biomarkers identified in animals that show promise for use in human clinics
- ✓ Capable of acting in all the processes that manifest in neurodegenerative disease patients
- ✓ Safe in humans in a Phase I trial. Oral once daily
- ✓ Crosses the BBB and engages the target in humans

In Phase IIa (in MS, AD and in a basket trial in aggression)

VAFIDEMSTAT (ORY-2001), a “NEURON FIXER”. Wide Clinical Options

- ✓ LSD1i. activity is the driving effector in Vafidemstat . MAO-B component is a synergizing-or-helper component
- ✓ Capable of acting in most of the processes that manifest in patients with different neurodegenerative and psychiatric diseases

ORY-2001 Results in PC models		Relevance in some CNS disorders							
		Neurodegenerative space				Psychiatric space			
		AD	MS	PD	HD	ADHD	BPD	ASD	Depression
+	Cognition / Memory	+	+	+	+			+	
+	Neuroprotection	+	+	+	+	+	+	+	+
+	Neuroinflammation	+	+	+	+	+	+	+	+
+	Social Withdrawal / Apathy	+	+	+	+	+	+	+	+
+	Sociability					+	+	+	+
+	Aggression/Agitation	+	+	+	+	+	+	+	+

These data may sustain a broader clinical development of ORY-2001 beyond the current indications of AD and MS



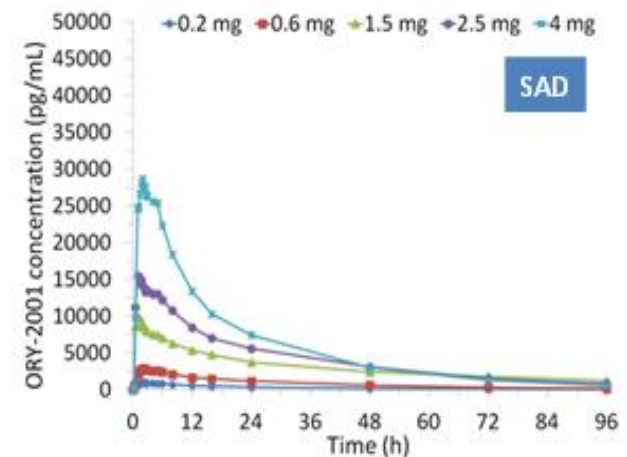
VAFIDEMSTAT (ORY-2001)

**An epigenetic drug that enhances
Neuronal recovery allowing a broad
clinical development**

CLINICAL DEVELOPMENT

VAFIDEMSTAT (ORY-2001) Phase I: Safety and hematology

- ✓ **Safe and well tolerated in the conditions tested in +100 healthy volunteers**
- ✓ **ORY-2001 efficiently crosses the BBB:**
 - ✓ ORY-2001 concentrations measured in CSF at 2, 6 and 12 h after a single oral 2 mg or 4 mg dose
 - ✓ CSF levels comparable to corresponding unbound plasma concentrations (CSF/plasma_u ratio ≈ 0.7-0.9)
- ✓ **ORY-2001 efficiently inhibits the brain human LSD1**
 - **PK** Oral PK T_{1/2} ≈ 22h allowing once daily oral
 - **PK/PD** data allow to select Phase II doses



VAFIDEMSTAT (ORY-2001) is in Phase II in humans in AD and MS where we expect to have the first read outs in 2H-2019

ETHERAL: Epigenetic **THER**apy in **AL**zheimer's Disease

CLINICAL STUDY PROTOCOL

A multicentre, multinational, randomised, double-blind, placebo-controlled, 3-arm, 24-week parallel-group study to evaluate the safety, tolerability and preliminary efficacy of ORY-2001 in patients with mild-moderate Alzheimer's Disease. **ETHERAL Study**

- ✓ **Mild to Moderate patients**
- ✓ N° of patients: 150
- ✓ Primary Objective: SAFETY & Tolerability
- ✓ Secondary Objectives :
 - ✓ Cognition/Agitation/Apathy/QoL
 - ✓ CSF Biomarkers
 - ✓ Volumetric MRI



- ✓ 125 in EU. 17 sites
- ✓ Actively recruiting in SP, UK and FR



- ✓ A Twin study in US: around 25 patients
- ✓ IND submission October
- ✓ IND expected approval November
- ✓ FPI expected 1Q2019

Already approved in Spain, France and UK
First Patients enrolled in May

Why a study in Mild and Moderate AD patients?

- VAFIDEMSTAT (ORY-2001) fully restores cognition to normal levels in SAMP8 AD model

- Changes Behavior in various models

- Reverts Aggressiveness
- Reverts social withdrawal
- Enhances sociability

- Easier to recruit patient target population

More than 340 SAMP8 mice treated with ORY-2001 or veh. in 10 different experiments a schematic overview below

MILD

MODERATE

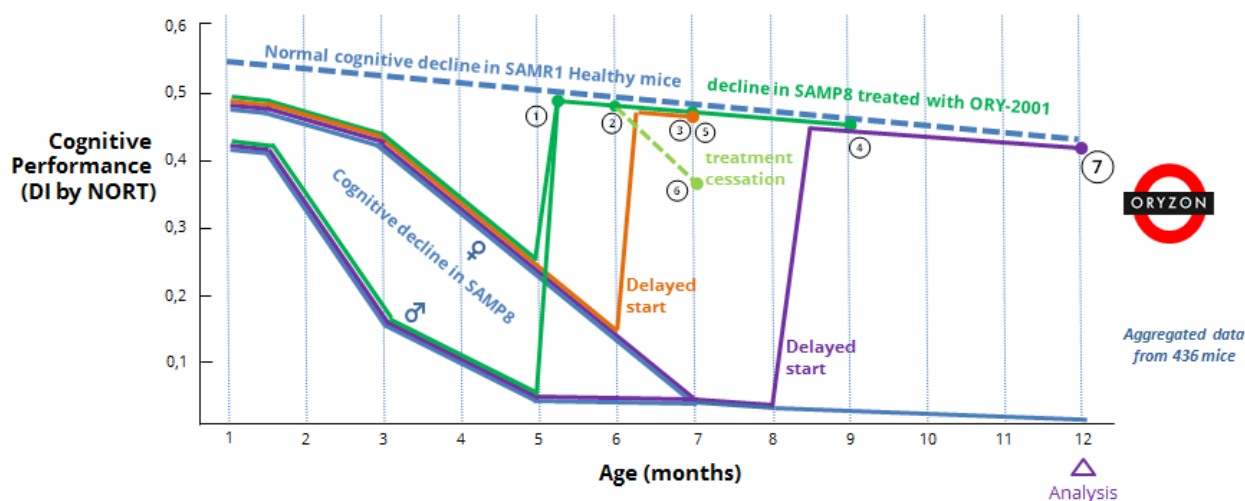
SEVERE

Treatment from month 5 during 1 week (1), 1 month (2), 2 months (3), 4 months (4)

Treated from month 6 during 1 month (Delayed start-1) (5)

Treatment from month 5 during 1 month, tested at month 7 (1 month after treatment cessation) (6)

Treatment from month 8 during 4 months (Delayed start-2) (7)



Preclinical results suggestive of Disease modifying potential

VAFIDEMSTAT (ORY-2001) reduces aggression in mice Alzheimer's Disease model

Following unplanned observations that SAMP8 male mice treated with ORY-2001 (bottom mouse) presented a better condition than untreated animals (top mouse) suggesting that ORY-2001 might reduce the aggressions between males caged together. Later we confirmed this in proper *Resident-intruder* aggression tests.



SAMP8 MICE treated with Vehicle
Resident Intruder test



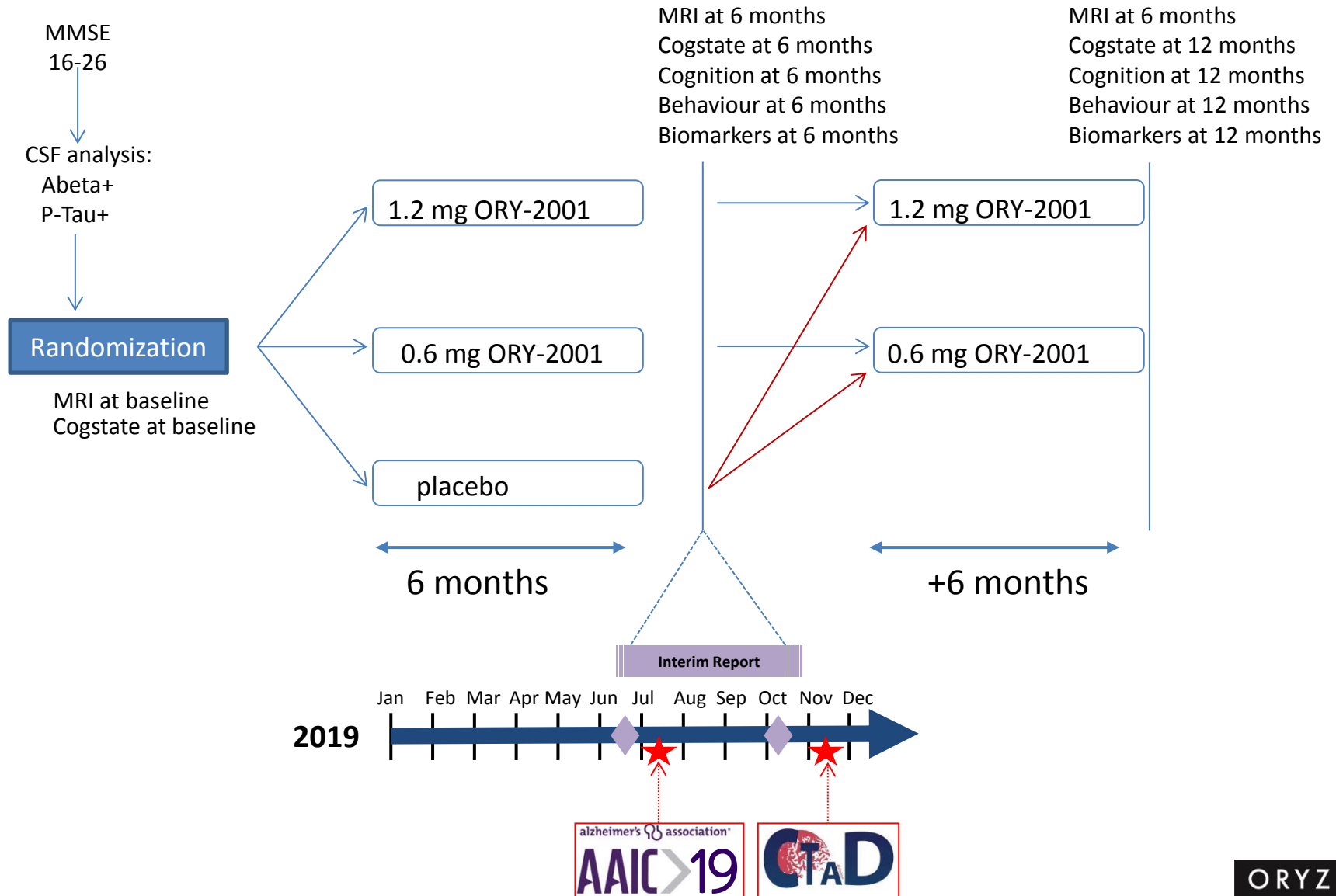
SAMP8 MICE treated with ORY-2001 0,32mg
Resident Intruder test

VAFIDEMSTAT (ORY-2001) does not produce sedation

ORYZON

ETHERAL: Epigenetic **THER**apy in **AL**zheimer's Disease

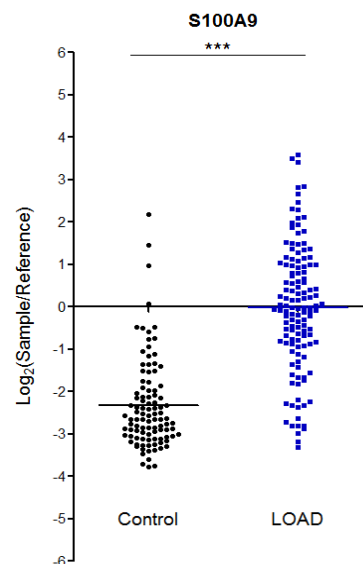
Expected First Clinical read outs in mid-2019



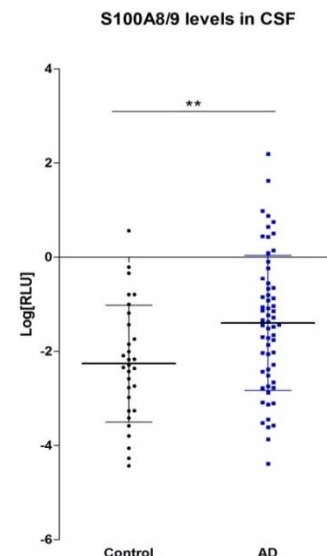
S100a9 was one of the TOP10 up-regulated genes in LOAD dataset

- ✓ S100A9 PROTEIN levels are significantly increased in CSF from AD patients compared to age-matched controls
- ✓ S100A9 CSF PROTEIN levels will be monitored in ETHERAL AD trial
 - ✓ S100A9 and inflammation have a correlation with the disease
 - ✓ Inflammation plays a mechanistic role in the progression of the disease
 - ✓ ORY-2001 reduces S100A9 in animals

Human PFC (RNA)



Human CSF (protein)



if +



Will it be accepted by regulatory agencies as a surrogate for activity?
May it be the basis for a fast track?

Changes in S100A9 in patient's CSF may have important clinical development implications

SATEEN A pilot study in MS

SAfety, **T**olerability and **E**fficacy in an **E**PIGEN**E**TIC approach to treat Multiple Sclerosis

Randomised, double-blind, placebo-controlled, 3-arm, 36 weeks parallel-group study to evaluate the safety and tolerability of ORY-2001 in patients with Relapsing-Remitting Multiple Sclerosis (RRMS) and Secondary Progressive Multiple Sclerosis (SPMS)

APPROVED by the AEMPS in 4Q-2017

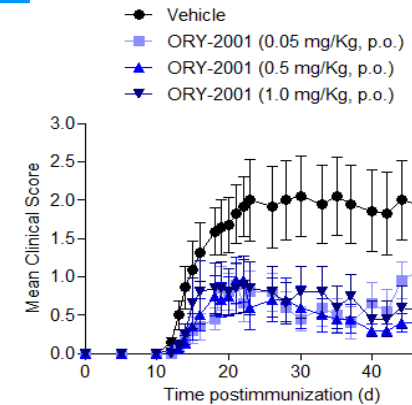
Spain only; 8 Hospitals; 24 patients (RR & SP);

FPI January 2018

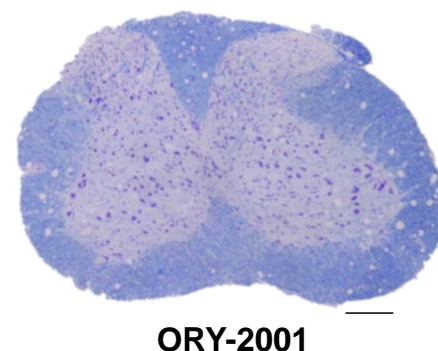
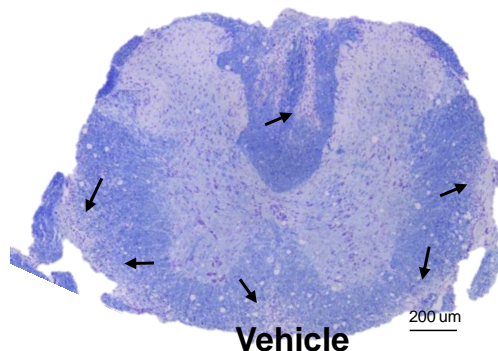
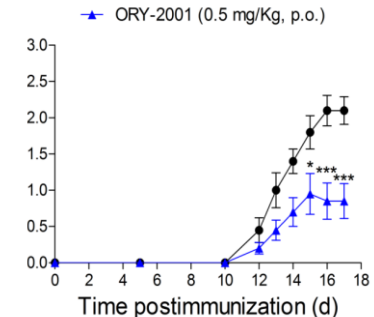
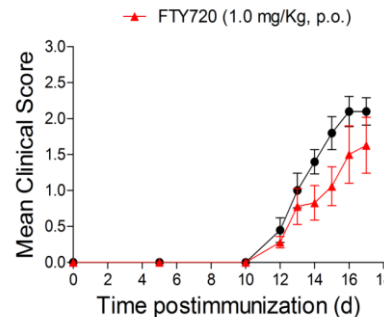
expected LPO 2H-2019

Why did we start a trial in RR and SP MS with VAFIDEMSTAT (ORY-2001)?

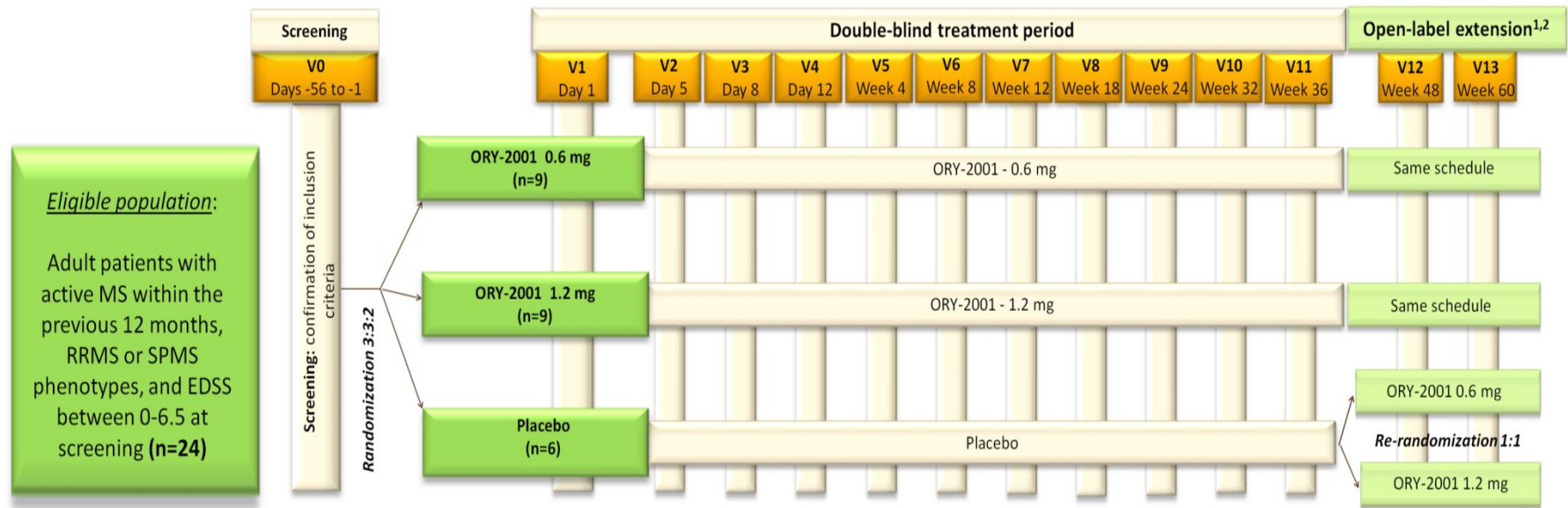
- ✓ VAFIDEMSTAT strongly reduced neuro-inflammation in a fast manner in various MS models
- ✓ The effect is long-lasting after treatment
- ✓ The effect is stronger and faster than Fingolimod (Gilenya® , Novartis)
- ✓ The MoA has similitudes with Fingolimod but has differential hallmarks
- ✓ Results are suggestive of neuro-protection in the Thyler's MS model (increased axonal protection)



therapeutic treatment (p.o.)



SATEEN Study



Primary objective:

✓ Evaluate safety - tolerability of 2 ORY-2001 doses compared to placebo.

Secondary objective:

✓ Assess effect of 2 ORY-2001 doses on MRI measures compared to placebo.

Exploratory objectives:

✓ Assess effect of 2 ORY-2001 doses on focal tissue damage MRI measures compared to placebo.

✓ Assess effect of 2 ORY-2001 doses on diffuse tissue damage MRI measures compared to placebo.

✓ Assess effect of 2 ORY-2001 doses on inflammation MRI measures compared to placebo.

✓ Assess effect of 2 ORY-2001 doses on Optical Coherence Tomography (OCT) derived measures compared to placebo.

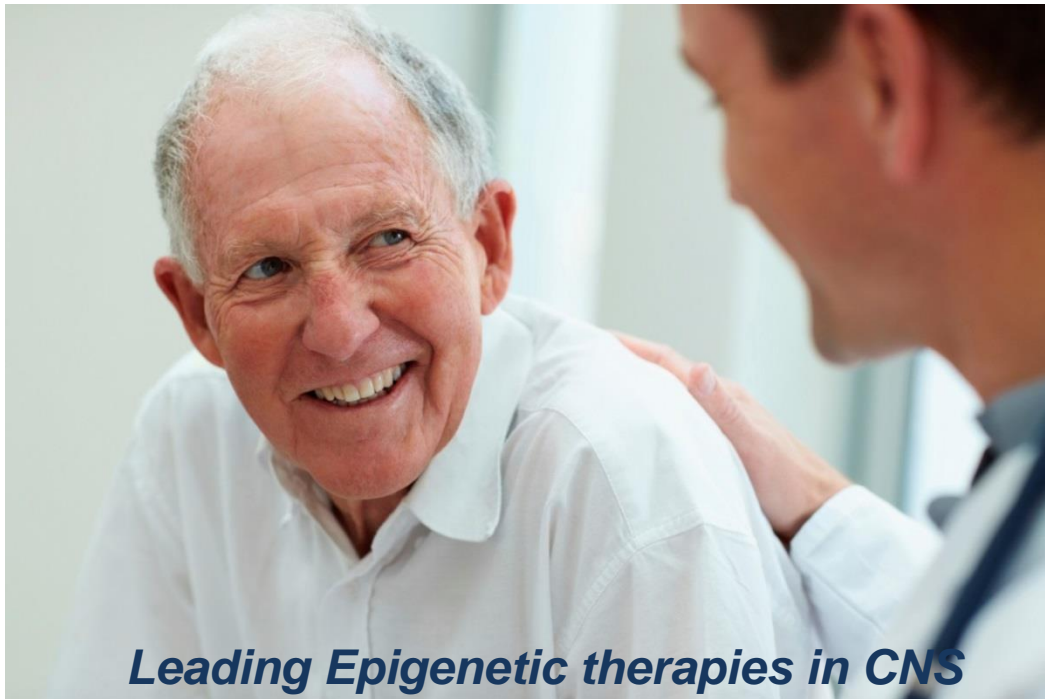
✓ Evaluate pharmacokinetics (PK) of ORY-2001.

✓ Assess the effect of 2 ORY-2001 doses on body fluid biomarkers of tissue damage compared to placebo. LSD1 Target Engagement (TE), Plasma Neurofilament Light Chain (NLC) and Th1/Th2 cytokines (IL2, IFN γ , IL4 and IL10) in serum.

VAFIDEMSTAT (ORY-2001) in Psychiatric disorders:

Produces profound changes in animal behavior

VAFIDEMSTAT reduces aggression, enhances sociability and diminishes social withdrawal



VAFIDEMSTAT (ORY-2001): REIMAGINE: A Basket trial in aggression

ORY-2001 REIMAGINE Study

- ✓ An open label exploratory basket trial to assess the effect of ORY-2001 in reducing aggression in patients with the following neurodegenerative or neuropsychiatric diseases:

✓ AD
✓ DLB *Neurodegen.*

✓ ADHD
✓ ASD
✓ BPD *Psychiatric*

- ✓ 6 patients per indication. 8 weeks of treatment
- ✓ Single arm of ORY-2001 (1.2 mg)
- ✓ No placebo control. 1 single site
- ✓ FPI 2H2018
- ✓ Expected LPO 1Q2019



SYNOPSIS

Name of the Sponsor/Company: Oryzon Genomics S. A.	Study Code:
Name of Investigational Medicinal Product: ORY-2001	EudraCT No.:
Development Phase of the Study: Phase IIa	Trial under an IND: TBD Not applicable
TITLE OF THE STUDY: An unicentre, opened-labelled, 1-arm, 8-week study to evaluate the efficacy, safety and tolerability of ORY-2001 in adult patients with Alzheimer dementia (AD), Borderline Personality Disorder (BPD),	



CTA approved by AEMPS

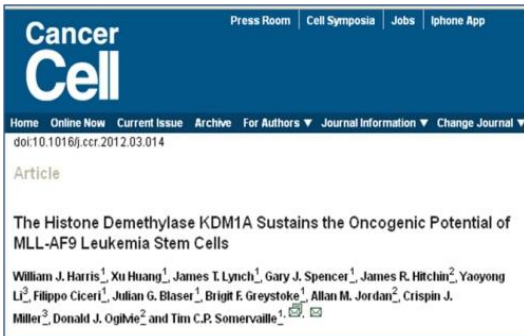


**IADADEMSTAT
(ORY-1001)
LSD1 inhibitors in Cancer
SUMMARY**

ORYZON LSD1 inhibitors are a potential therapeutic approach for Acute Leukemias

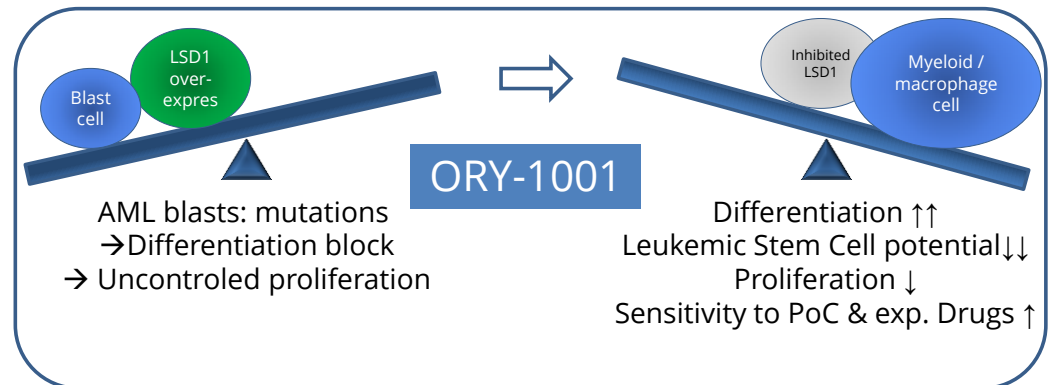
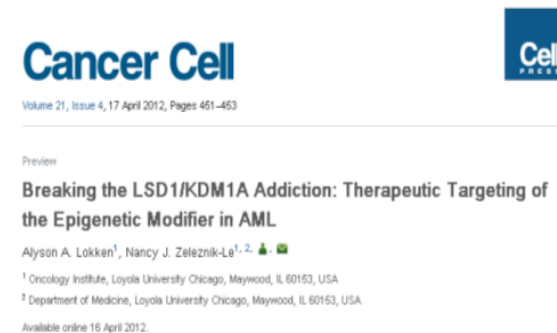


LSD1 is a target for HEMATOLOGICAL CANCERS, and in particular, for a subset of acute myeloid leukemia: *mixed lineage leukemia* MLL-AML



✓ **Oryzon's LSD1 inhibitors block progression of leukemia into the circulation in mice with experimentally initiated MLL-AF9 AML**

✓ **Oryzon's LSD1 inhibitors target Leukemia Stem Cells but spare normal HSPCs**



ORY-1001, a Potent and Selective Covalent KDM1A Inhibitor, for the Treatment of Acute Leukemia

Tamara Maes,^{1,6,*} Cristina Mascaró,¹ Iñigo Tirapu,¹ Angels Estiarte,¹ Filippo Ciceri,¹ Serena Lunardi,¹ Nathalie Guibourt,¹ Alvaro Perdonés,¹ Michele M.P. Lufino,¹ Tim C.P. Somervaille,² Dan H. Wiseman,² Cihangir Duy,³ Ari Melnick,^{3,4} Christophe Willekens,⁵ Alberto Ortega,¹ Marc Martinell,¹ Nuria Valls,¹ Guido Kurz,¹ Matthew Fyfe,¹ Julio Cesar Castro-Palomino,¹ and Carlos Buesa¹

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<https://doi.org/10.1016/j.ccell.2018.02.002>



Cancer Cell
Previews

ORY-1001: Overcoming the Differentiation Block in AML

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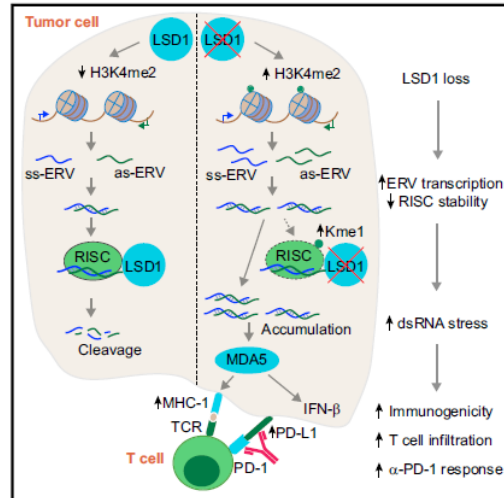
<https://doi.org/10.1016/j.ccell.2018.02.014>

In this issue of *Cancer Cell*, Maes and colleagues report *in vitro* and *in vivo* findings with ORY-1001—an oral, highly potent and selective covalent small-molecule inhibitor of lysine-specific demethylase 1 (LSD1)—in development for acute myeloid leukemia (AML), as well as correlative data from two AML patients receiving ORY-1001.

Cell

LSD1 Ablation Stimulates Anti-tumor Immunity and Enables Checkpoint Blockade

Graphical Abstract



Highlights

- ERV induction and RISC reduction activate dsRNA-IFN pathway upon LSD1 inhibition
- LSD1 loss in tumor cells stimulates anti-tumor T cell immunity
- LSD1 ablation enhances tumor immunogenicity and T cell infiltration
- LSD1 inhibition overcomes resistance to anti-PD-1 therapy in a mouse melanoma model

Authors

Wanqiang Sheng, Martin W. LaFleur, Thao H. Nguyen, ..., Housheng Hansen He, Arlene H. Sharpe, Yang Shi

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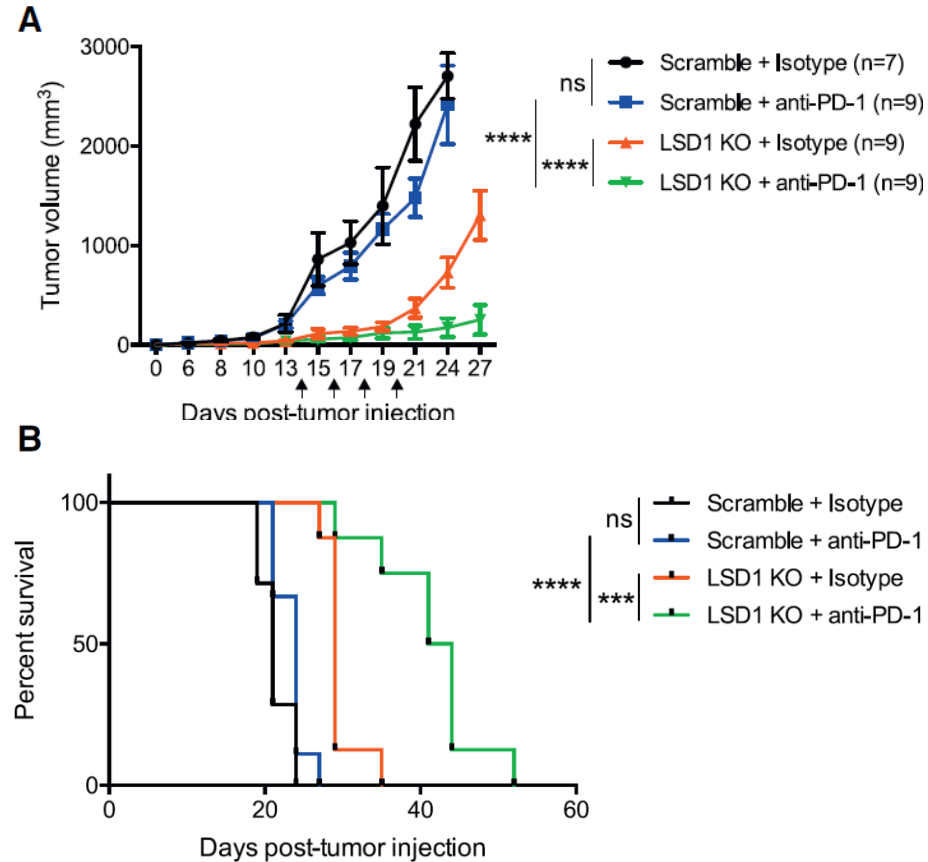
In Brief

Ablating the histone demethylase LSD1 genetically or pharmacologically enhances tumor immunogenicity by stimulating endogenous retrovirus expression and downregulating RNA-induced silencing complex, supporting the promise of LSD1 inhibition in overcoming resistance to checkpoint blockade in cancer treatment.

Data resources

GSE112230

Article



(A and B) Tumor growth (A) and survival curves (B) of immunocompetent mice inoculated with 250 k B16 melanoma cells, and treated with anti-PD-1 or isotype control. Arrows indicate time points of anti-PD-1 injection.

IADADEMSTAT (ORY-1001) PHASE I/IIa in Acute Leukemia relapsed-refractory patients:

✓ *Manuscript under preparation.*



- ✓ Iadademstat (ORY-1001) was administered to **41 patients**
- ✓ **Excellent oral bioavailability** in humans and excellent PK parameters
- ✓ **Pharmacodynamic biomarkers (MLLr)** permit monitoring response to iadademstat (ORY-1001) in M4/M5 AML patients
- ✓ **22% (6/27) response rate in the dose finding part of phase 1, including one CRi** (complete remission with incomplete blood count recovery)
- ✓ **46% (6/13) of relapsed/refractory AML patients showed anti-leukemic clinical activity** in the extension arm (Phase IIa)
- ✓ Partial bone marrow remission in 50% (2/4) M6 patients, **suggesting disease stabilization**
- ✓ 100% (5/5) of MLL gene fusion patients with evaluable PD samples showed evidence of blast differentiation by qRT-PCR analysis
- ✓ 67% (4/6) of MLL leukemia patients showed evidence of morphological blast cell differentiation (2 patients experienced a differentiation syndrome)
- ✓ 15% (2 (M6)/13) partial bone marrow responses and 1 MLL patient with 3 month hematologic improvement
- ✓ **From all patients in the Phase I/IIa study, antileukemic activity observed in 29% of patients (12/41), including one CRi**

IADADEMSTAT (ORY-1001) Current Clinical Development Plan

Oryzon licensed ORY-1001 global rights to Roche (2014). After regaining control of the asset (January 2018), Oryzon has continued its clinical development in AML and SCLC. Lori Kunkel MD has been appointed as Scientific Advisor in Oncology

ALICE: An AML trial with LSD1i in Combination with azacitidine in the Elderly

A Phase IIa study to evaluate safety, tolerability dose finding and efficacy of IADADEMSTAT (ORY-1001) in combination with azacitidine in older patients with AML in first line therapy

36 patients. Open label.

2 sites in Spain

The study is organized in two parts.

The objective of Part 1 is to determine the recommended doses of ORY-1001 in elderly unfit AML patients

The objective of Part 2 is to evaluate the clinical activity of ORY-1001 in first line elderly unfit AML patients in combination with Azacitidine

Primary end point: safety

Secondary endpoints: responses; time to responses; duration of response; and overall survival

Expected Clinical Study Time Frame:

First patient in: 3Q 2018

Last patient first visit: 3Q 2019

Last patient last visit: 3Q 2020

Clinical Study Report: 4Q 2020

CTA approved by AEMPS

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 MINISTERIO
DE SANIDAD, SERVICIOS SOCIALES
E IGUALDAD

ORYZON

CLEPSIDRA: A **C**ombination trial of **L**SD1 and **E**top-**P**latinum in **S**mall Cell Lung Cancer in **B**iomarker-**ID** Relapsed p**A**tients

A Phase IIa study to assess the safety, tolerability, dose finding and efficacy of ladademstat (ORY-1001) in combination with platinum-etoposide chemotherapy in patients with relapsed, extensive-stage disease small cell lung cancer

36 patients ⁽¹⁾. Open label.

4 sites in Spain

The study is organized in two parts.

The objective of Part 1 is to determine the recommended doses of ORY-1001 in combination with platinum-etoposide chemotherapy

The objective of Part 2 is to evaluate clinical activity of ORY-1001 in combination with platinum-etoposide chemotherapy

Primary end point: safety

Secondary endpoints: RECIST responses; time to responses; duration of response; and overall survival

Expected Clinical Study Time Frame:

First patient in: 4Q 2018

Last patient first visit: 4Q 2019

Last patient last visit: 4Q 2020

Clinical Study Report: 1Q 2021

**CTA requested to AEMPS in
July 2018**

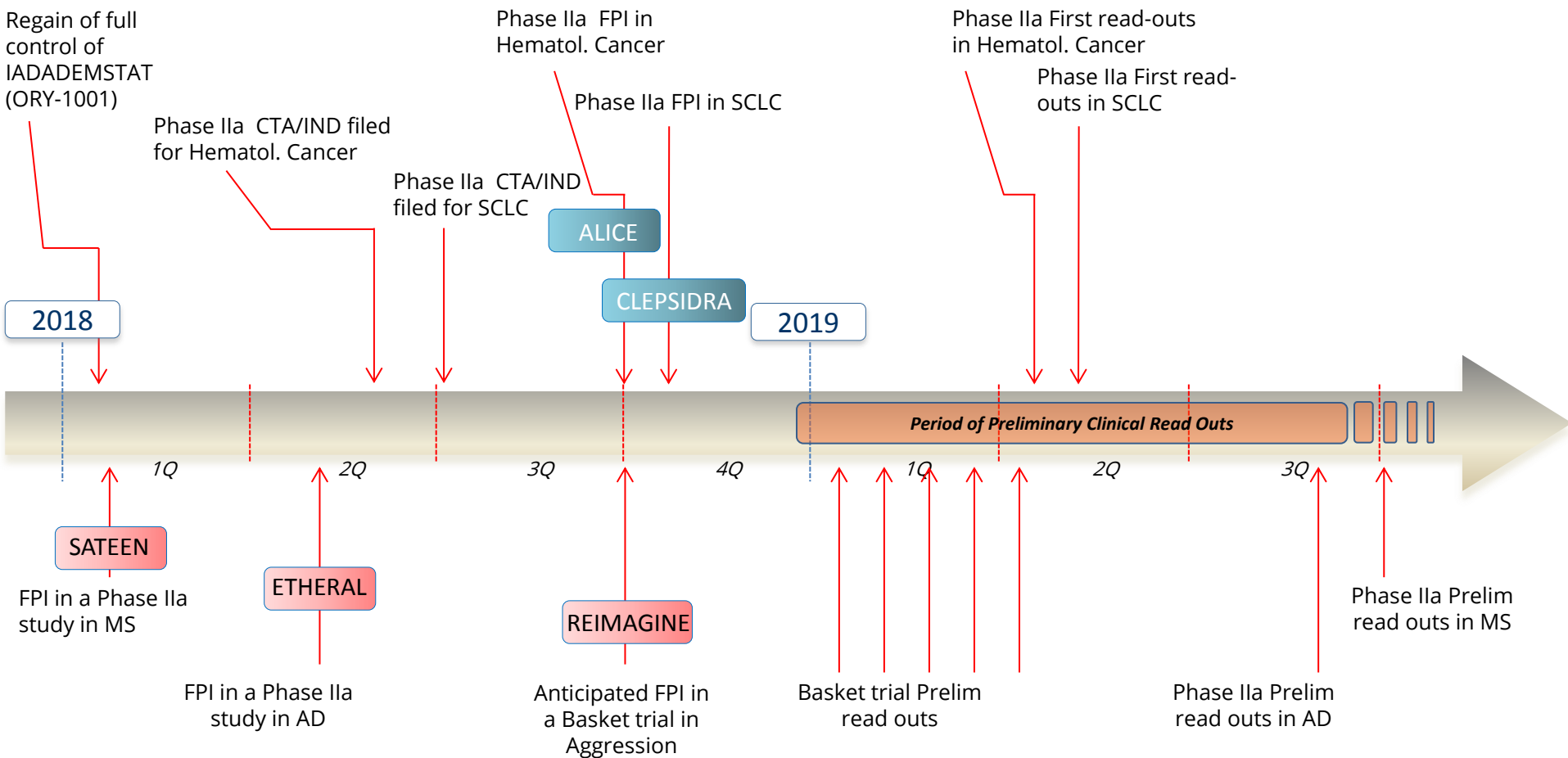
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⁽¹⁾ Relapsed but platinum sensitive, extensive-stage disease small cell lung cancer who are positive to candidate predictive biomarkers.

RECENT & ANTICIPATED ORYZON MAIN CATALYSTS

IADADEMSTAT (ORY-1001): lead CANCER asset



VAFIDEMSTAT (ORY-2001): lead CNS asset

ORYZON a Unique Case

- ✓ One of the global leaders in Epigenetics with an efficient platform
- ✓ Highly specialized in LSD1, one of the hottest targets in the field (GSK, Takeda, Celgene, Incyte,...)
- ✓ World class science and a broad patent portfolio
- ✓ A diverse and promising Pipeline
- ✓ Public in Europe with an experienced management and BoD
- ✓ Robustly financed
- ✓ Catalysts in 9-12m
- ✓ Currently undervalued compared with its natural peers
- ✓ Dual Listing in Nasdaq expected in the future

ORYZON
A GLOBAL LEADER
IN EPIGENETICS



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