A GLOBAL LEADER IN EPIGENETICS

INVESTOR PRESENTATION

MADX: ORY

New York City February 2016

LEGAL NOTICE

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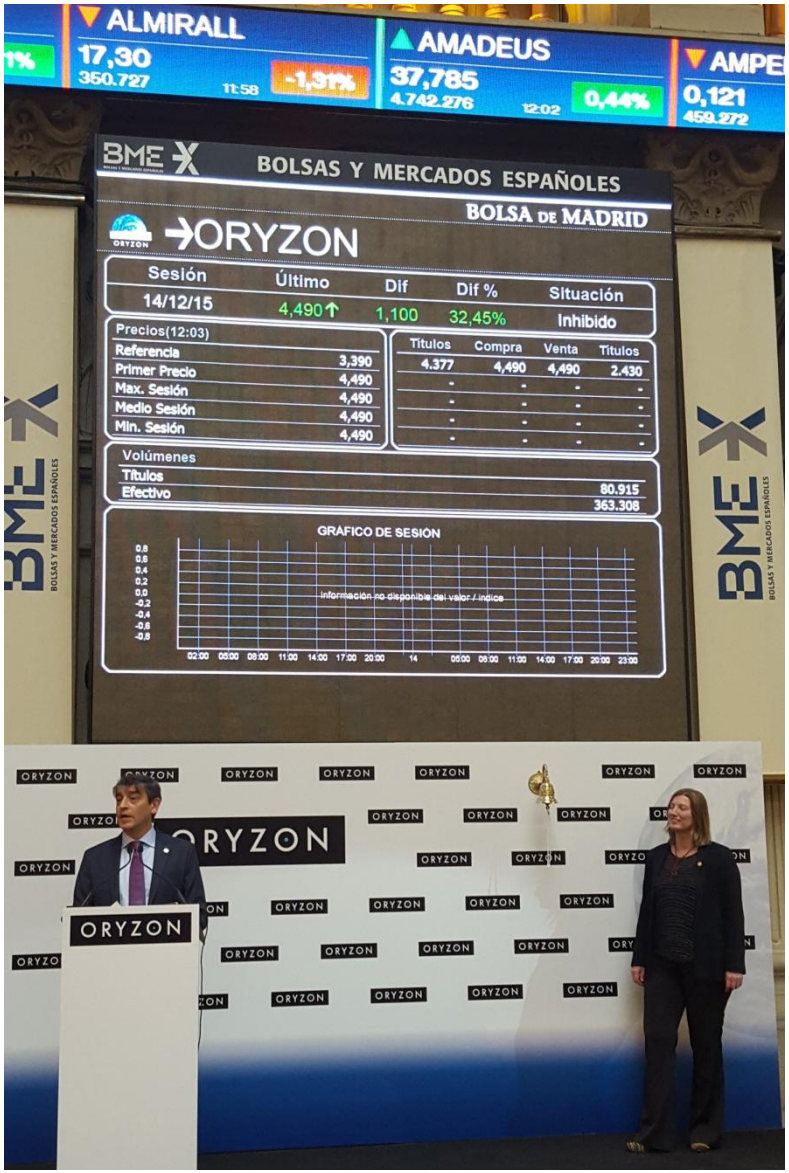
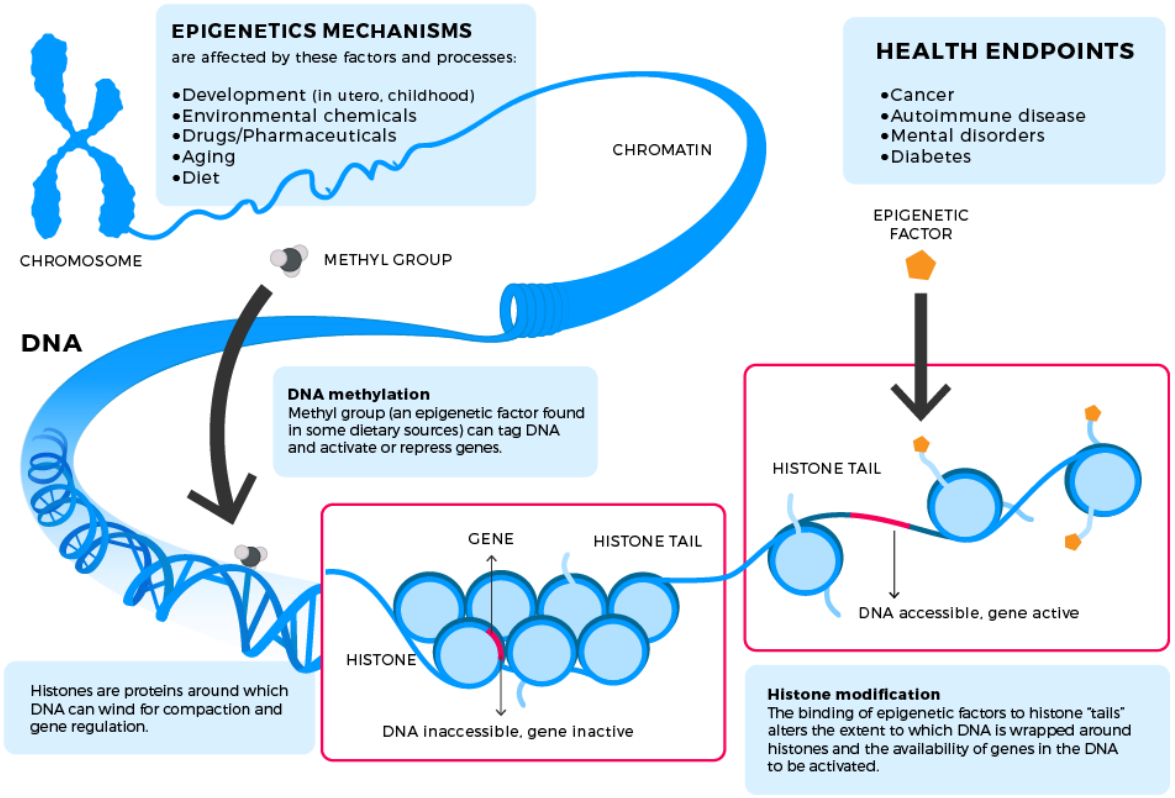
COMPANY HIGHLIGHTS



- MADX: ORY A publicly traded company in the Madrid Stock Exchange since December 14th 2015
- Trading started at €3,39 = €96,5M Market Cap
- A clinical stage biopharmaceutical company developing innovative therapies in oncology and neurodegeneration leading the field of Epigenetics
- Two therapeutic programs in clinical development with multiple indication opportunities & additional assets in preclinical development
- Signed global strategic partnerships with ROCHE for ORY-1001 valued at 500M USD
- Strong IP portfolio with technology developed in-house
- Strong financial profile with €+20M cash on balance sheet with runway till 2018
- Experienced management team

EPIGENETICS: THE CRITICAL ROLE OF HISTONE CODING

- **Epigenetics** − the study of heritable changes in genome function that occur without a change in DNA sequence
- These changes mainly occur due to variations in the structure of chromatin that silence or activate whole regions of the chromosome and all the genes that reside in this region
- These variations are caused by post-translational modifications on histones, the proteins that serve as scaffold for the DNA to conform the chromatin
- Lysine methylation and demethylation is one of the key epigenetic modifications of the Histone tails



EPIGENETICS COMPETITIVE LANDSCAPE

- **EPIGENETICS** is a new Space being explored by the Pharma Industry: Clinical Programs are still in Early Phases.
- ORYZON, Epizyme and Constellation are the only Biotechs developing more than one compound.
- GSK, Roche, Merck, Pfizer, Celgene and other Big Pharmas are also entering in the field either through their own programs or through alliances.

COMPANY	COMPOUND	DESCRIPTION	INDICATION	STATUS
Reverlogix	RVX-208	BET bromodomain inhibitor	Atherosclerosis -Diabetes	Phase II b
Acetylon Pharmaceuticals	(ACY-1215) lic to Celgene	Oral selective HDAC6 inhibitor	Multiple myeloma (MM)	Phase I/II
Oryzon Genomics	**ORY-1001 lic. to Roche**	**Lysine-specific demethylase 1 (LSD1) inhibitor**	**Acute myelogenous leukemia (AML)**	**Phase I/IIa**
	ORY-2001	**LSD1-MAOB dual inhibitor**	**Alzheimer's Disease Other Neurodegenerative disorders**	**Phase I**
Constellation Pharmaceuticals	CPI-1205	EZH2 inhibitor	lymphoma	Phase II
	CPI-0610	BET bromodomain inhibitor	Progressive Lymphoma AL, MDS, myeloproliferative neoplasms Multiple myeloma	Phase I
Epizyme	EPZ 6438 Tazemetostat	EZH2 inhibitor	non-Hodgkin B-cell lymphoma Synovial Sarcoma	Phase I/II IND / Phase I
	EPZ-5676 lic. to Celgene	HMT DOT1L inhibitor	MLL- AML	Phase I/II
Tensha Therapeutics	TEN-010	BET bromodomain inhibitor	Cancers including NUT midline carcinomas	Phase I

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EXTENSIVE PIPELINE : 2 PROGRAMS IN CLINIC WITH MULTIPLE INDICATIONS

INDICATION	TARGET	MOLECULE	DISCOVERY	H2L	LEAD OPTIMIZATION	PRECLINICAL	PHASE I-IIA	PHASE IIB	PHASE III	PARTNER
CANCER Leukemia Solid Tumors	LSD-1	ORY-1001								Roche
DEMENTIAS Alzheimer's Disease Parkinson's Disease Other Dementias	LSD-1-MAOB	ORY-2001								
ORPHAN Huntington's Disease Other Orphan Diseases	LSD-1-MAOB	ORY-2001								
OTHER INDICATIONS	LSD-1									
CANCER	Other KDMs									
CANCER	Other Epigenetic Targets									

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LSD1 PROGRAM: AN EPIGENETIC "ERASER"

- Lysine-specific histone demethylase 1 (LSD1 or KDM1A) is an enzyme that demethylates histones (removes methyl groups), specifically mono and di-methylated H3K4 and H3K9
- LSD1 belongs to the family of FAD dependent amine oxidases, which include known drug targets such as MAO-A and MAO-B
- LSD1 is located in the nucleus, unlike MAOs
- LSD1 expression has a high correlation in many solid tumors
- In some aggressive Leukemia, Leukemia Stem Cells are addicted to LSD1 activity
- The pan-MAO inhibitor tranylcypromine: a chemical starting point to design covalent LSD1 inhibitors.
- **Protected by 19 patent families filed globally with 10 granted in US**

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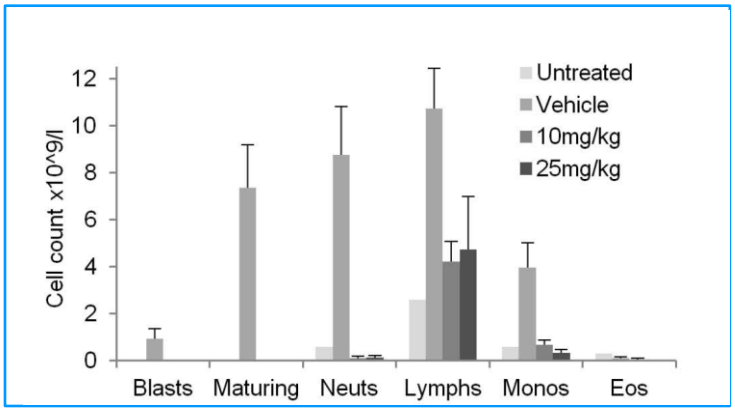
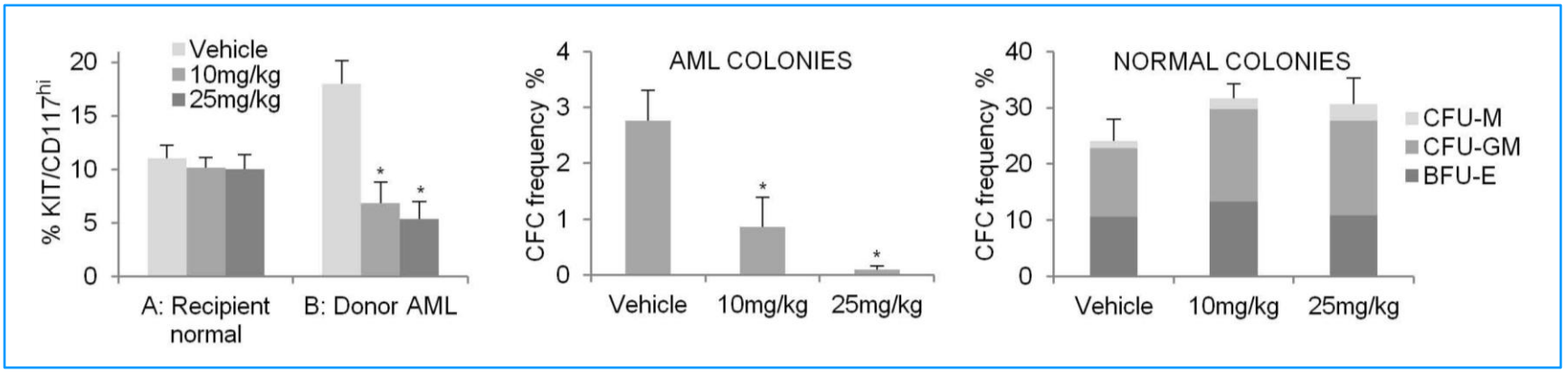
ORYZON's CLINICAL ONCOLOGY PROGRAM: **ORY-1001**

- KDM1A is a key effector of the differentiation block in MLL leukemia
- KDM1A sustains expression of the MLL-AF9 oncogenic program
- Nanomolar KDM1A inhibitor concentrations induce differentiation of human AML cells
- KDM1A inhibition in vivo targets MLL-AF9 cells, but spares normal repopulating cells.



Oryzon's LSD1 inhibitor (OG-86) blocks progression of leukemia cells into the circulation MLL-AF9 mice model

Oryzon's LSD1 inhibitor (OG-86) targets leukemia stem cells but spares normal hematopoietic stem cells



Modified from Harris et al., Cancer Cell. 2012: 21(4):473-87)

ORY-1001: ONCOLOGY PROGRAM

- ORY-1001 a highly potent and selective LSD1 inhibitor with orphan drug status granted by the European Medicines Agency (EMA)
- Pharmacological Properties
  - High druggability
  - Optimal ADMET and PK profiles
  - Orally bioavailable once daily
  - Easy to scale up
  - Good pharmaceutical properties
- Currently in Phase I/IIA
  - Completed Part 1 of the study (Phase I) in acute leukemia
  - Extension Arm (Phase II-A) ongoing
- Potential for additional indications, such as solid tumors (like SCLC) and sickle cell disease
- Global strategic collaboration with ROCHE valued >500M USD

ORY-1001: ROCHE PARTNERSHIP

- In April 2014, Oryzon and ROCHE entered into a global collaboration to research, develop and commercialize LSD1 inhibitors, including ORY-1001, for oncology, hematology and non-malignant conditions
- Licensed compounds are covered by 2 patents in the Oryzon IP portfolio
- Remaining LSD1 inhibitors in Oryzon's LSD1 IP portfolio are not part of the ROCHE license agreement
- Clinical development and all related investments beyond the ongoing Phase I/IIA trial are the responsibility of ROCHE
- Parties will collaborate on R&D through the ROCHE Translation Clinical Research Center (TCRC)

- Development and sales milestones total >**500M USD**
- Payment at contract signing plus near term milestone total **21M USD**
- Sales royalty rates tiered up to mid-teens.

Roche

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PHASE I HIGHLIGHTS: ORY-1001 LEUKEMIA

TRIAL DESIGN		
Refractory & Relapsed Acute Leukemia	Multi-Center (5)	Multiple Ascending Dose (8 Cohorts)

PRIMARY ENDPOINT
Evaluate Safety (hematological and non-hematological toxicities) and Tolerability

SECONDARY ENDPOINTS		
Characterize PK	Assess Responses (CR/Cri/PR), particularly for rMLL gene	Evaluate surrogate PD markers for target engagement

PRELIMINARY RESULTS
Excellent safety profile with no SAEs
Demonstrated impact on pharmaceutical target
PD clear readings several biomarkers
Good PK
Established maximum recommended dose

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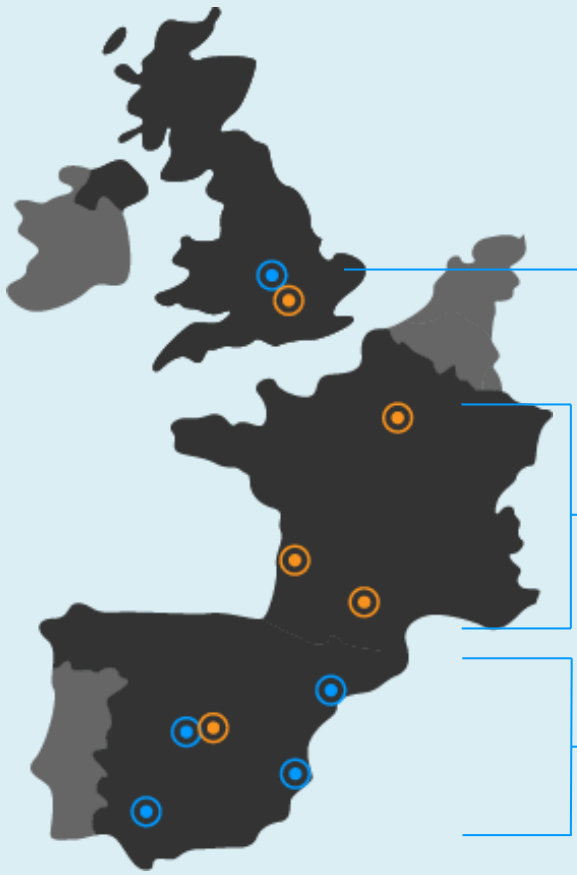
PHASE IIA: ORY-1001 LEUKEMIA

After the MRD , an Expansion arm (Phase II-A) to include patients with target mutations (MLL and others) to evaluate preliminary signs of efficacy

CENTERS



- 9 Patients to be included
- Status: 6 patients enrolled and actively recruiting
- Completion Date: 2Q-2016

10 Hospitals in 3 Countries

UK
- Christie Hospital, Manchester
- University College London hospitals NHS, London

FRANCE
- Gustave Roussy, Paris
- CHU Hopitaux, Bordeaux
- Hôpital Purpan - (CHU), Toulouse

SPAIN
- Valle de Hebron, Barcelona
- La Fe, Valencia
- Virgen del Rocío, Sevilla
- 12 de Octubre, Madrid
- Gregorio Marañón, Madrid

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LSD1 Additional indications

Beyond onco-hematology there are a number of growing additional indications for LSD1i:

- Specific solid tumors are a growing field for the clinical expansion of LSD1 inhibition and ORY-1001
  - **Small Cell Lung Cancer** GSK is in Phase I with a LSD1 inhibitor (A DNA Hypomethylation Signature Predicts Antitumor Activity of LSD1 Inhibitors in SCLC, Mohammad et al, Cancer Cell 28(1), 57–69, July 13, 2015)
  - **Triple Negative Breast Cancer** (10%-15% of all breast cancer, in the United States): orthotopic mouse xenograft: BALB / c (nu / nu) injected with MDA-MB-231 cells and treated with LSD1i in combo with paclitaxel show a better efficacy than Paclitaxel alone. (Beijing Institute of Genomics (Chinese Academy of Sciences) , 2016)
- Non Malignant Indications
  - **Sickle cell disease (SCD).** LSD1i induces High levels of Fetal Hemoglobin in Anemic Baboons models. SCD is a common inherited blood disorder in the United States, affecting an estimated 70,000 to 100,000 Americans ((56th ASH, Rivers et al 2014. Univ of Illinois; and The LSD1 inhibitor RN-1 induces fetal hemoglobin synthesis and reduces disease pathology in sickle cell mice, Cui et al, Blood 2015 Jul 16;126(3):386-96)

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ORY-1001 market capture opportunity above $1.8 billion

A number of scientific reports point out the potential of LSD1 inhibition as a target in a number of solid tumors

Non oncological diseases as SCD and others may also be a CDP option

Acute Myeloid Leukemia

12% of all Blood Cancers
18.860 new cases in US in 2014 [1,2]

Global Mk Potential of $932 million in 2024,
CAGR of 10.5% [4]

Small Cell Lung Cancer

15% of all Lung Cancers
32.420 new cases in US in 2014 [1,3]

Global Mk Potential of $684 million in 2017 [5]

Sickle Cell Disease

SCD Epidemiology
US/EU Prevalence ~150K

US Mk Potential of $200 million in 2017,
(Market to grow at 17% CGAR till 2019)

NOTE: ROCHE is the sole responsible for the further Clinic Development Plan for ORY-1001. The indications and markets mentioned above are only presented on its likelihood based on the development of competitors or published scientific reports

1. ACS, Cancer Facts & Figures 2014
2. www.hematology.org
3. www.lungcancer.org
4. Global Data 2015
5. Decision Resources 2015

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ROLE OF EPIGENETICS: NEURODEGENERATIVE DISORDERS

- Studies suggest epigenetic modifications that induce alterations in gene expression programs contribute to neurodegenerative disorders:
  - Alzheimer's Disease (AD)
  - Parkinson's Disease (PD)
  - Huntington's Disease (HD)
- Epigenetic alterations on related genes may also result in neurodegeneration, partially accounting for the etiology
- Epigenetic drugs target the proteins responsible for modifications on DNA or histone
  - HDAC inhibitors (HDACi)
  - HAT modulators
  - DNA methyltransferase inhibitors
  - Histone demethylase inhibitors

ENVIRONMENT

GENES EXPERIENCE

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

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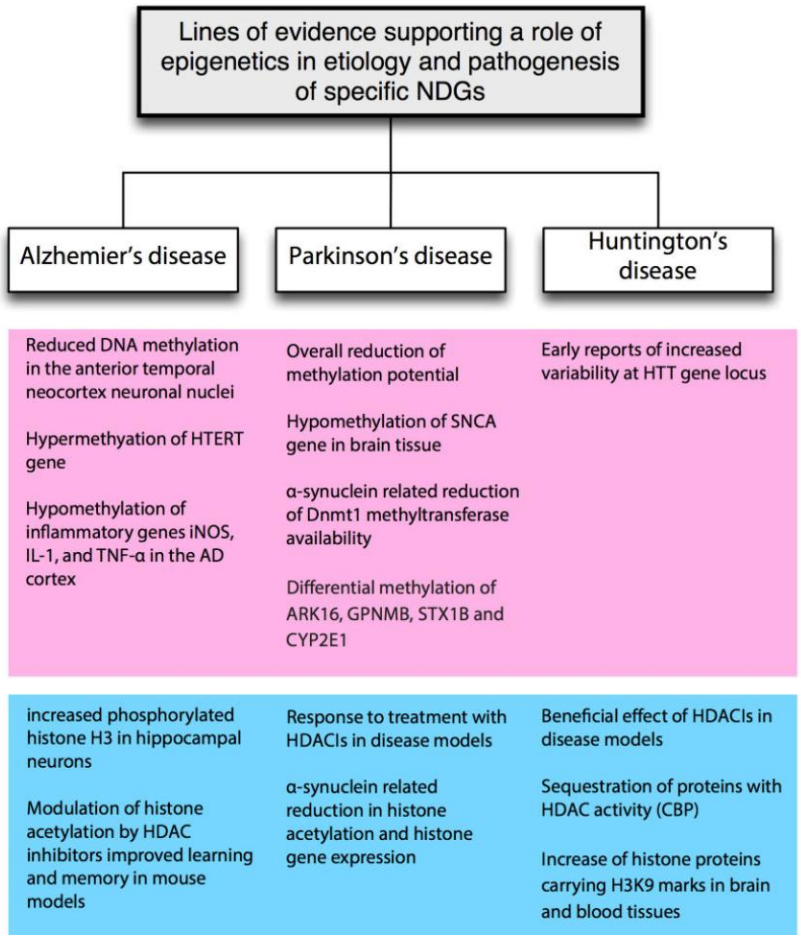
ROLE OF EPIGENETICS: NEURODEGENERATIVE DISORDERS



Luca Lovrečić, et al., 2013 The Role of Epigenetics in Neurodegenerative Diseases

- ✓ HDACi improves HD symptoms in animal models
- ✓ HDAC2 inhibition recovers memory on the bi-transgenic CK-p25 Tg mouse model
- ✓ HDAC inhibition improves FTD

Efforts to develop Selective HDACi

rodin THERAPEUTICS

Selective HDAC2 i in Alzheimer's Disease
Program in Preclinical

Acetylon Pharmaceuticals, Inc.

HDAC-6 i in neurodegeneration and autoimmunity.
Program in Preclinical

Pan-HDAC inhibitors have demonstrated preclinical proof of concept that inhibition of HDACs improves cognitive function, however, these drugs have dose limiting side effects that make them unsuitable for the chronic settings needed in neurological indications.

Developing more selective HDAC inhibitors is not an insignificant challenge as HDACs are highly conserved proteins

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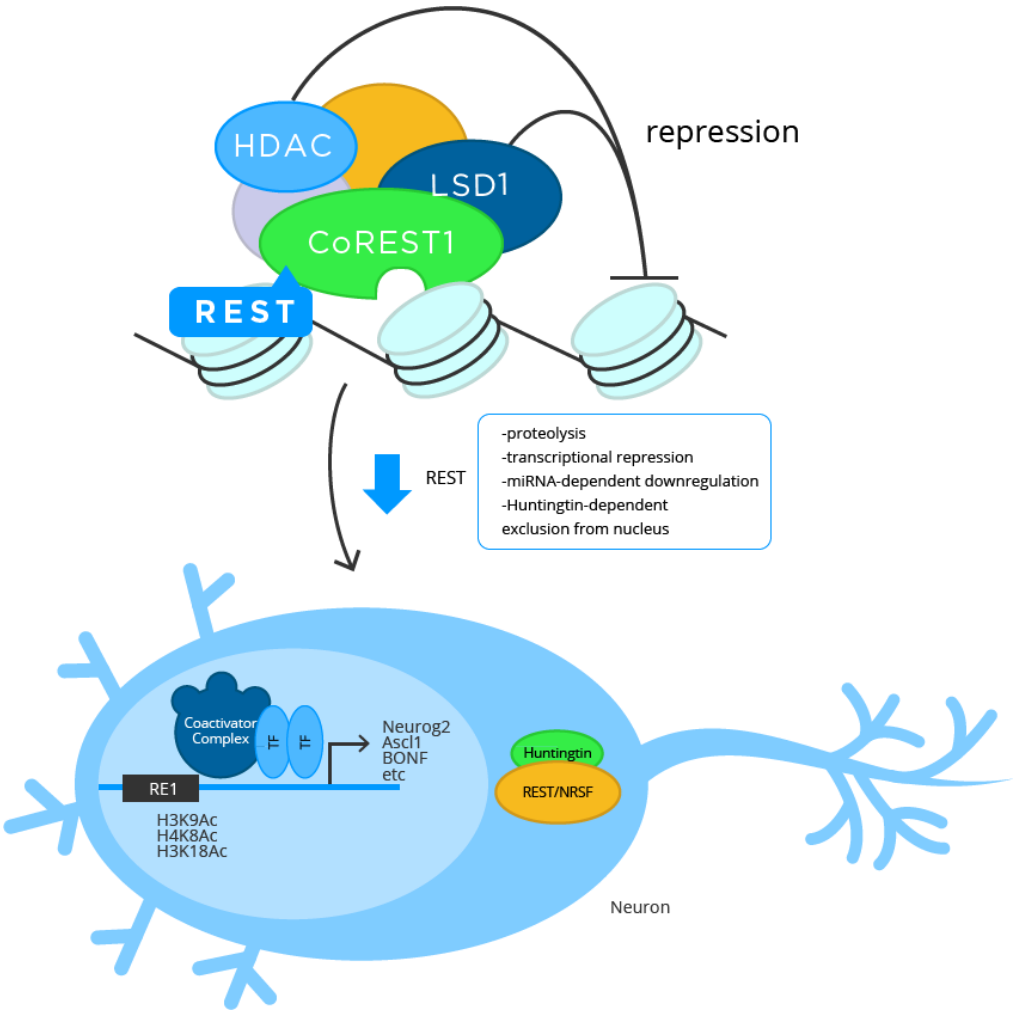
LSD1 IN THE NERVOUS SYSTEM

- LSD1 is a key component of the LSD1-REST-CoREST-HDAC1/2 repressor complex involved mainly in controlling developmental programs and modulating neuronal morphology in the CNS
- LSD1 is known to be an important regulator in the maintenance of pluripotency and in specification of neuronal commitment of pluri- or multipotent cells
- Different to what happens in HDACs, it has been proven that it is possible to develop extremely selective LSD1 inhibitors with excellent pharmacological properties
- Oryzon has the wider IP portfolio in the LSD1 space with drug candidates specially suitable to be developed in neurological indications



ORY-2001: CNS PROGRAM

- ORY-2001 is a highly selective dual LSD1-MAO-B inhibitor
- Preclinical Proof of Concept: LSD1 Against AD and HD
- Clinical development
  - Phase I in Healthy Volunteers
- Alzheimer's Disease is lead indication
- Potential for additional indications: PD, HD and others
- Exclusively owned by Oryzon
- Pharmacological Properties
  - Optimal ADMET and PK profiles
  - Crosses efficiently the BBB
  - Once daily oral bioavailable
  - Good pharmaceutical properties
  - Selectivity against MAO-A demonstrated in-vitro and in-vivo
  - High therapeutic window in animals

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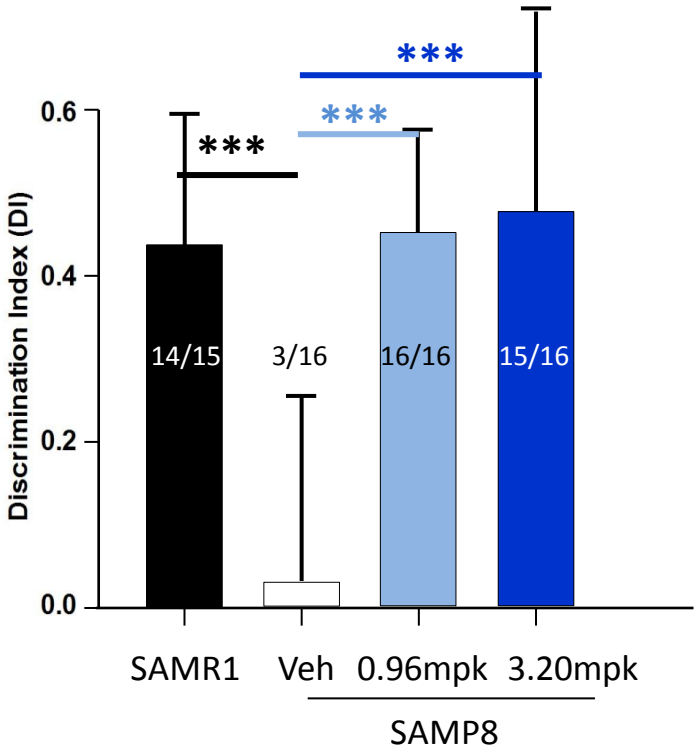
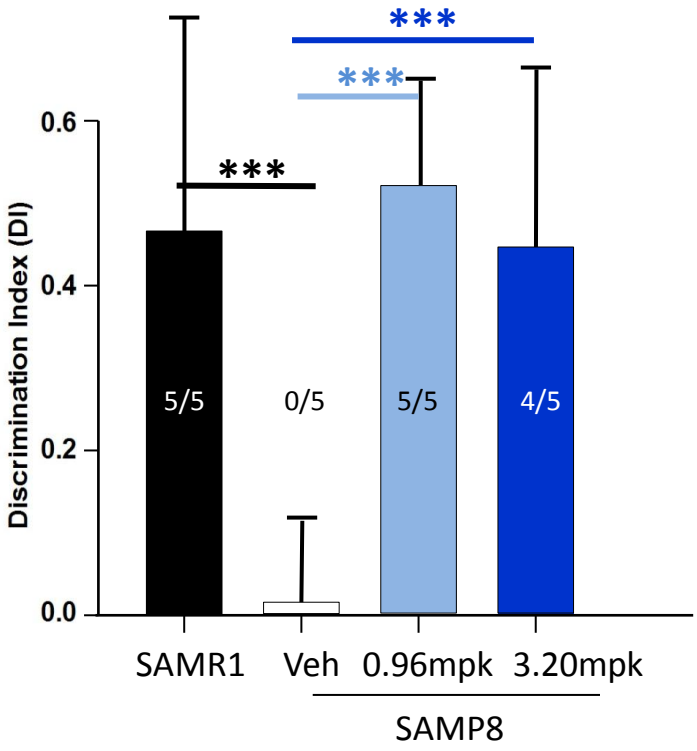
PoC studies in SAMP8 mice

- The SAMP8 mouse is an excellent model to examine the pathophysiology of early defects seen in Alzheimer's disease. They develop accelerated aging and senescence and show deficits in learning and memory as well as other similarities to pathology of AD
- ORY-2001 cognitive effect tested by NORT in five different studies
- After 2 and 4 month of oral treatment, ORY-2001 provides a robust protective effect in the medium and long-term memory of female mice, compared to age-matched SAMP8 mice
- We lowered dose in males (Study #2)



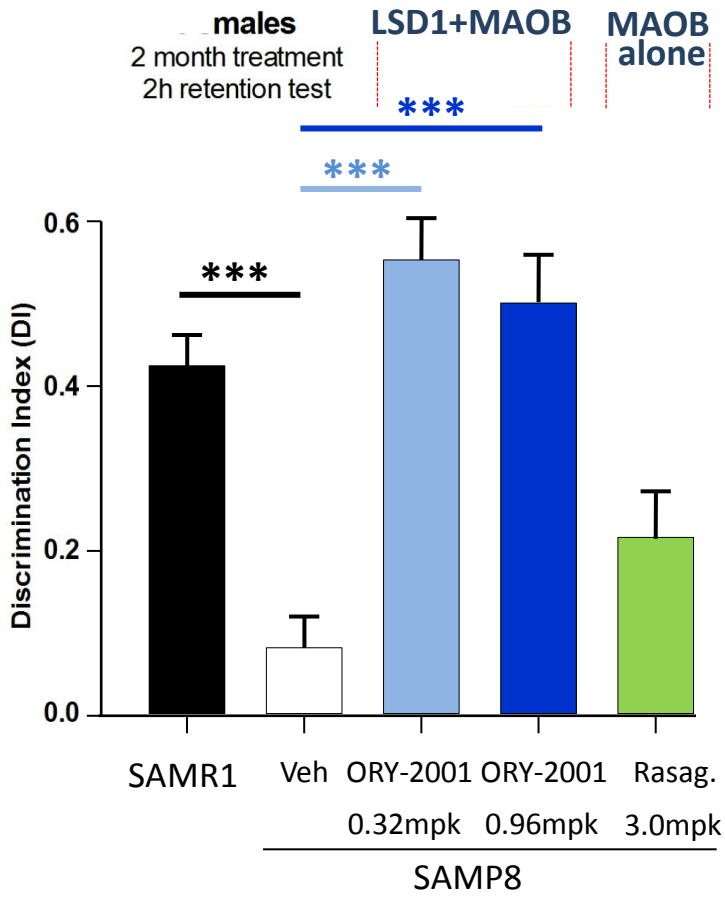
2 months treatment
Tested 2 h after training



4 months treatment
Tested 2 h after training

Dissecting the LSD1 and MAOB components

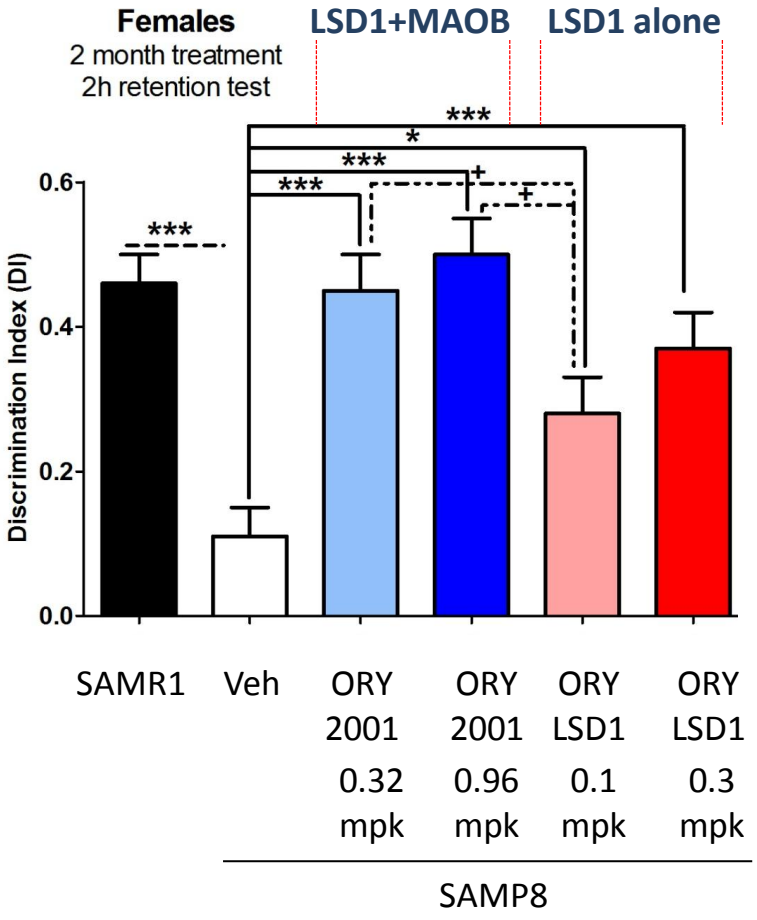
- MAOB inhibition alone shows a trend on cognitive improvement on the SAMP8 animals but it is not significant
  - p=0.12 at 2h
  - p=0.22 at 24h
- LSD1 inhibition is therefore crucial to obtain the recovery on cognitive improvement on the SAMP8 animals



SAMP8 male animals (n=8 per group)

Dissecting the LSD1 and MAOB components

- ORY-2001 provides a robust protective effect in the medium and long-term memory of mice, compared to age-matched SAMP8 mice
- LSD1 inhibition alone is also able to produce an effect but less pronounced
- Protection is driven by the LSD1 inhibition and not by MAO-B, **but the combination with MAO-B inhibition (i.e. a dual compound,ORY-2001) enhances the effect**

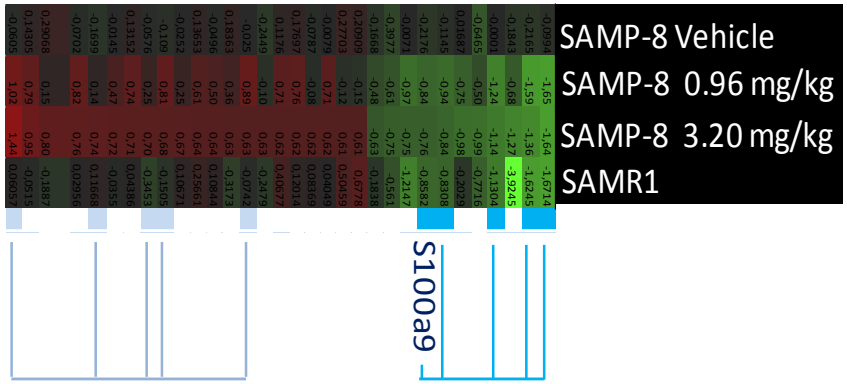


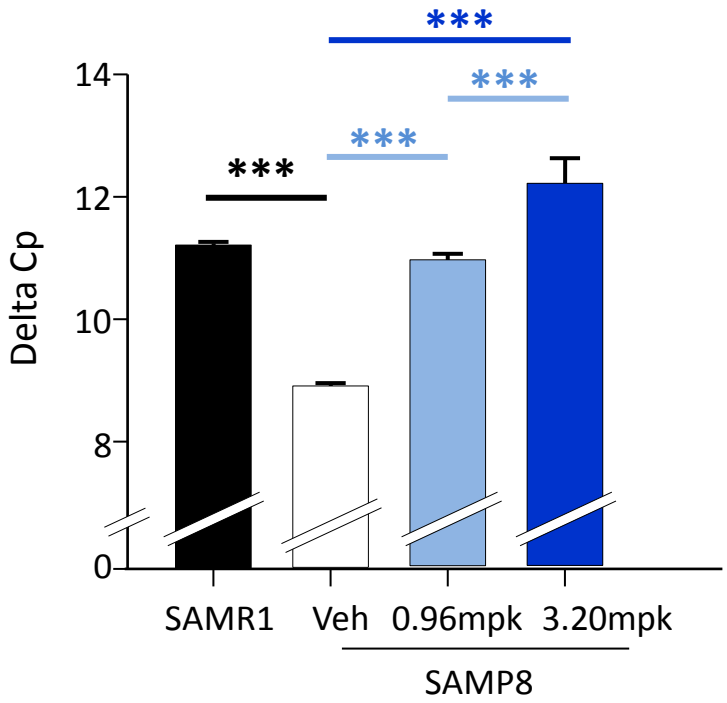
SAMP8 female animals (n=8 per group)

ORY-2001 - PROOF OF CONCEPT IN SAMP8 MICE

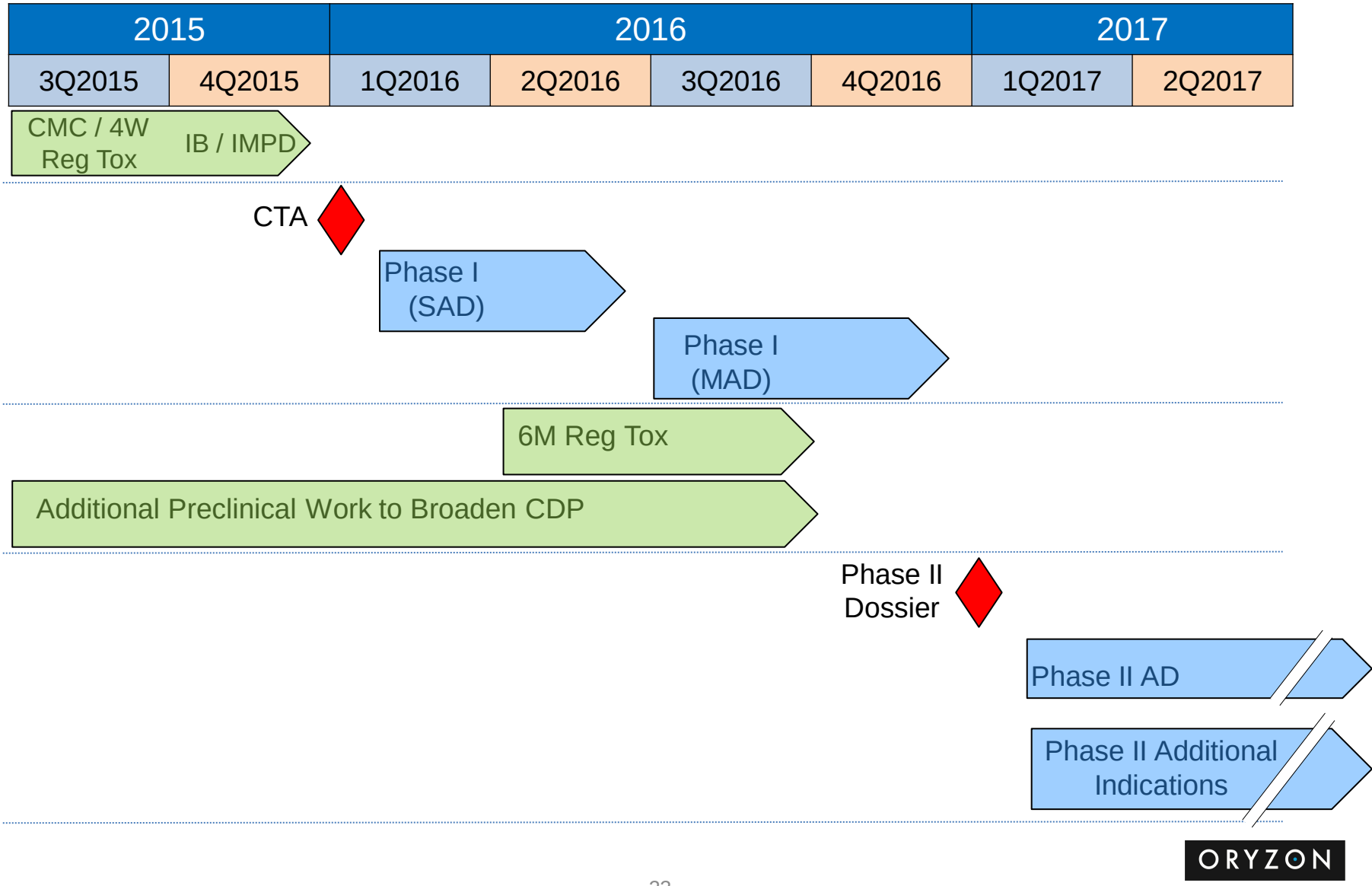
BIOMARKERS : We have identified different biomarkers upon ORY-2001 treatment:

- ORY-2001 has a pleiotropic effect on the hippocampal gene expression pattern and increases memory associated genes and reduces levels of inflammatory genes.
- Down-regulation of the pro-inflammatory S100A9 protein by ORY-2001 is particularly interesting, since S100A9 is emerging as an important contributor to inflammation-related neurodegeneration. S100A9 was found to be increased in patients with AD, postoperative cognitive dysfunction (POCD) and traumatic brain injury (TBI). In addition, knockout or knockdown of S100A9 has been shown to be beneficial to memory in APP/PS1 and Tg2576 models of Alzheimer's disease





ORY-2001 DEVELOPMENT TIMELINE



ORY-2001 DEVELOPMENT TIMELINE

A Phase I study with 88 healthy volunteers, young and elderly.

Phase I, single center, double blind, parallel, ascending single and multiple dose trial.

TITLE: A Study to Assess the Safety, Tolerability and Pharmacokinetic of Single and Multiple Oral Doses of ORY-2001 in Healthy Male, Female Subjects and Elderly Population
STUDY CODE: CL01-ORY-2001
EUDRACT NUMBER: 2015-003721-33

Phase I Clinical Trial in young and elderly healthy volunteers

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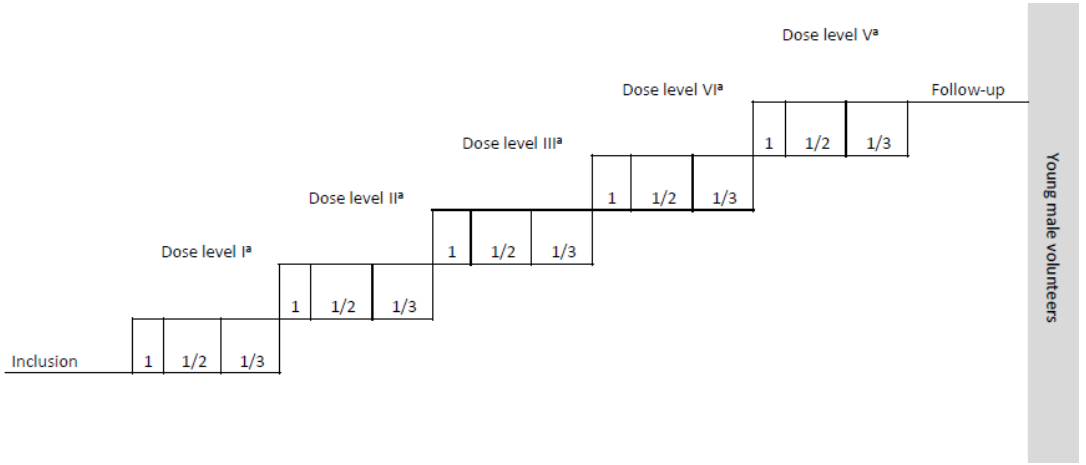
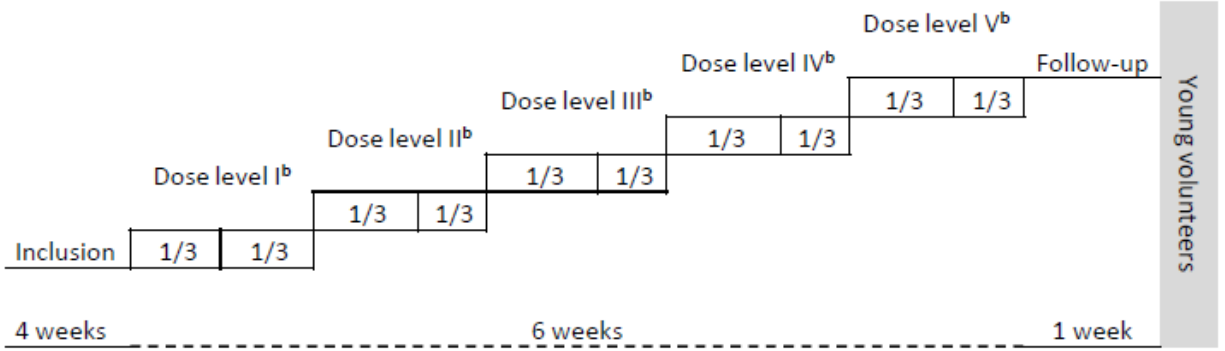
ORY-2001 DEVELOPMENT TIMELINE

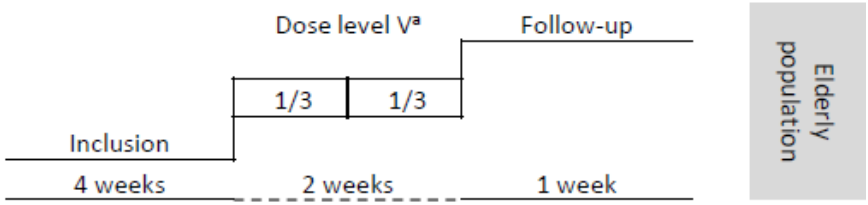
A Phase I study with 88 healthy volunteers, young and elderly.

CL01-ORY-2001
SAD



CL01-ORY-2001
MAD





ORY-2001 CLINICAL & MARKET POTENTIAL

ORY-2001 market capture opportunity above $3 billion.

Further development may include Neuro- inflammatory disorders

ALZHEIMER'S DISEASE

5.4 M people currently affected in US. By 2025 the number of patients will rise to 7.1 million in USA[1]

8.7 million Europeans are also affected [2] and in Asia another potential 10 to 12 million people are diagnosed or suspected to suffer AD.

Drug market projected to reach US $9.5 billion by 2017 [6]

PARKINSON'S DISEASE

Around 6.3 million people have the condition worldwide[3]

It affects over 1 million people in the US, with nearly 60,000 people newly diagnosed every year. [4]

Drug market projected to reach US $2.6 billion in 2020 in the 7MM

HUNTINGTON'S DISEASE

Worldwide prevalence of HD is 5–10 cases per 100,000 persons. There are around 30,000 symptomatic Americans and more than 200,000 at-risk of inheriting the disease [5]

Up to 71,000 patients in Europe.

Drug market projected to reach US$1.3 billion by 2020 [7]

1. Alzheimer's association www.alz.org
2. Alzheimer Europe www.alzheimer-europe.org
3. European Parkinson's Diesease Association http://www.epda.eu.com/
4. American Parkinson Disease Association http://www.apdaparkinson.org/ , http://www.ninds.nih.gov/
5. http://www.huntington-assoc.com/
6. http://www.fiercebiotech.com/
7. http://www.strategyr.com

ORYZON

FINANCIAL HIGHLIGHTS

- Strong balance sheet with €+20m in cash
- $5 million payment from ROCHE in 2015
- Secured €2.6M in public aids in 2015
- Unused credit line of €6 M from commercial banks
- €10M in debt with low interest rates
  - Repayment terms over either 3-4y or 8-10y (commercial loans or Public R&D loans)
  - Rates from 0-3% (average cost of debt 1,3%)
- Expected cash burn of €10-12M annually for next 2 years
- Raised €31 M since inception
- Spanish GAAP rules adapted to IFRS
- Accounts audited by Grant Thornton since 2003 and through 2014
- Audited in 1H 2015
- 35 employees

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KEY INVESTMENT HIGHLIGHTS

EPIGENETICS

- Global leader in Epigenetics, an emerging field recognized by the pharmaceutical industry as a novel approach to varying diseases and personalized medicine

EXTENSIVE PIPELINE

- 2 programs in clinical development
- Both clinic programs can expand in multiple indications
- An Epigenetic platform with additional assets

PROVEN TRACK

- Collaborative agreement with ROCHE valued at $500 million
- Cutting edge science endorsed by international agencies

SOLID IP

- Strong patent portfolio with19 patent families and10 granted in US
- All patented technology developed in-house with no owed royalties

LEADERSHIP

- Highly experienced management team

FINANCIALS

- €+20M on balance sheet with runway till 2018
- Plan to grow as a public company in Europe and dual list on NASDAQ in the future

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CATALYSTS 2015 - 2016

- ✓ ORY-1001: LEAD CANCER ASSET
  - ✓ Conclude Phase I dosing study
  - ✓ Receive recommended dose milestone payment from Roche
  - ✓ Phase IIA first patient-in
  - Complete Phase IIA and report target efficacy
  - Roche execute ongoing clinical development plan
- ✓ ORY-2001: LEAD CNS ASSET
  - ✓ Complete preclinical toxicology package
  - ✓ File CTA/IND
  - Begin Phase I patient enrolment
  - Complete Phase I dosing safety study
  - Layout of a multiple Phase II clinical study including potential additional indications
- ✓ CORPORATE
  - ✓ €16.5M cross over funding in Spain
  - ✓ List on the Spanish Main Market
  - Prepare to List on the NASDAQ in the future

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INTERNATIONAL RESEARCH NETWORK

Our research has been partly funded by competitive grants

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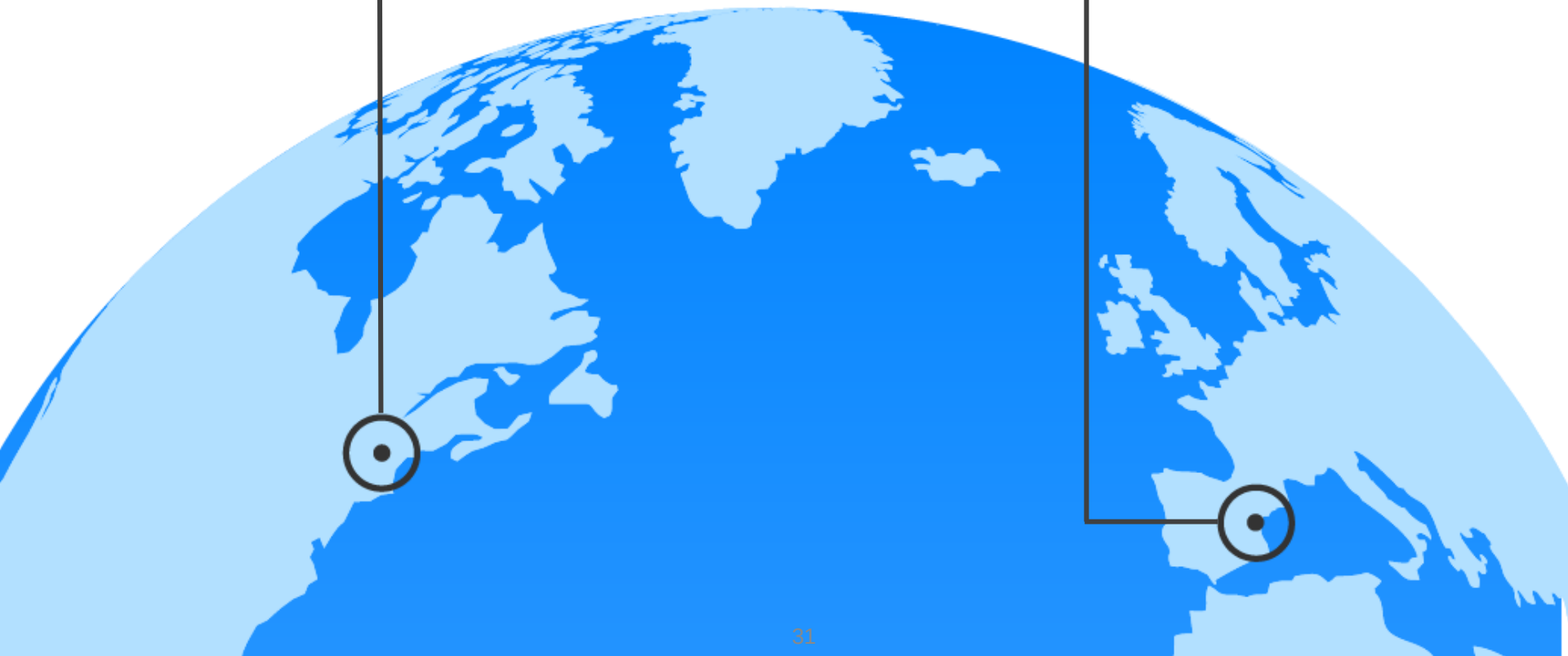

THANK YOU VERY MUCH!

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