A GLOBAL LEADER IN EPIGENETICS

INVESTOR PRESENTATION

MADX: ORY

JUNE 2016

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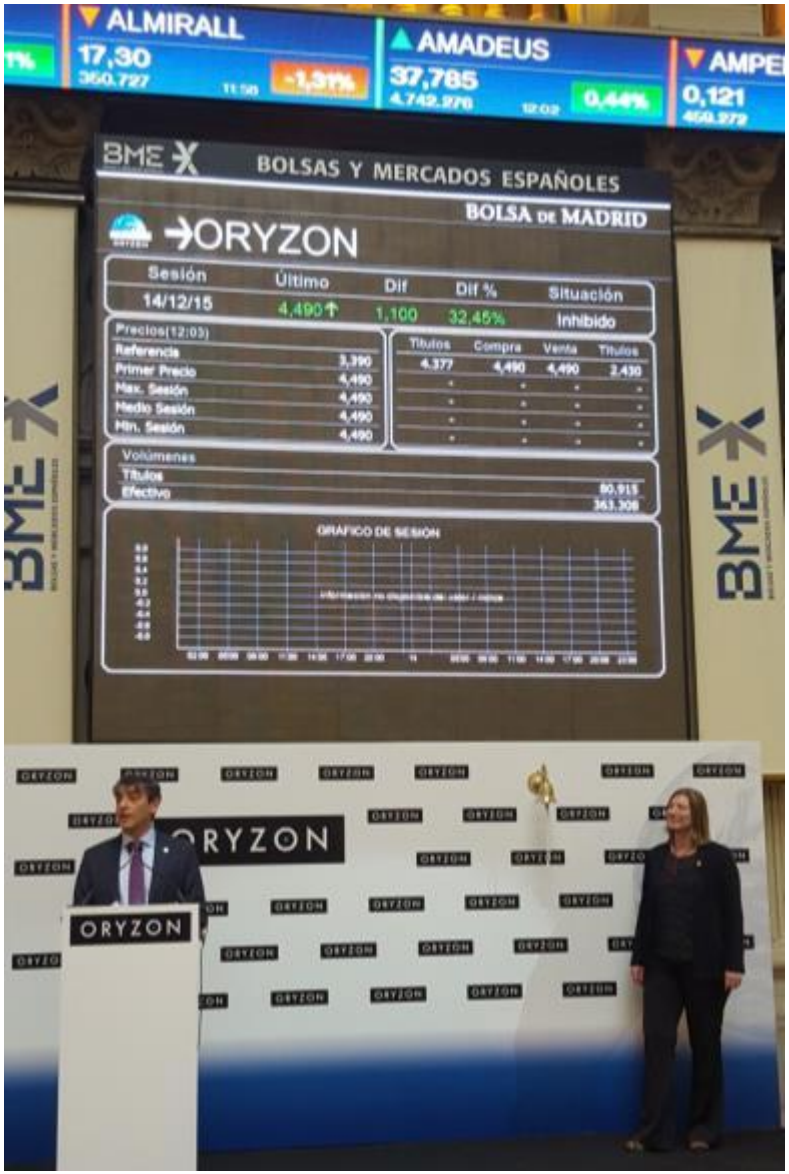
COMPANY HIGHLIGHTS



- MADX: ORY A publicly traded company in the Madrid Stock Exchange
- A clinical stage biopharmaceutical company developing innovative therapies in oncology and neurodegeneration leading the field of Epigenetics
- A competitive EPIGENETIC Platform with a first program that validates scientifically and clinically the platform.
  - Two therapeutic programs in clinical development with multiple indication opportunities.
  - Additional assets in preclinical development to be progressed quickly
- Signed global strategic partnership with ROCHE for ORY-1001 valued at 500M USD
- Strong IP portfolio with technology developed in-house
- Raised €27m in the last 12 months. Cash runway till 1H2018

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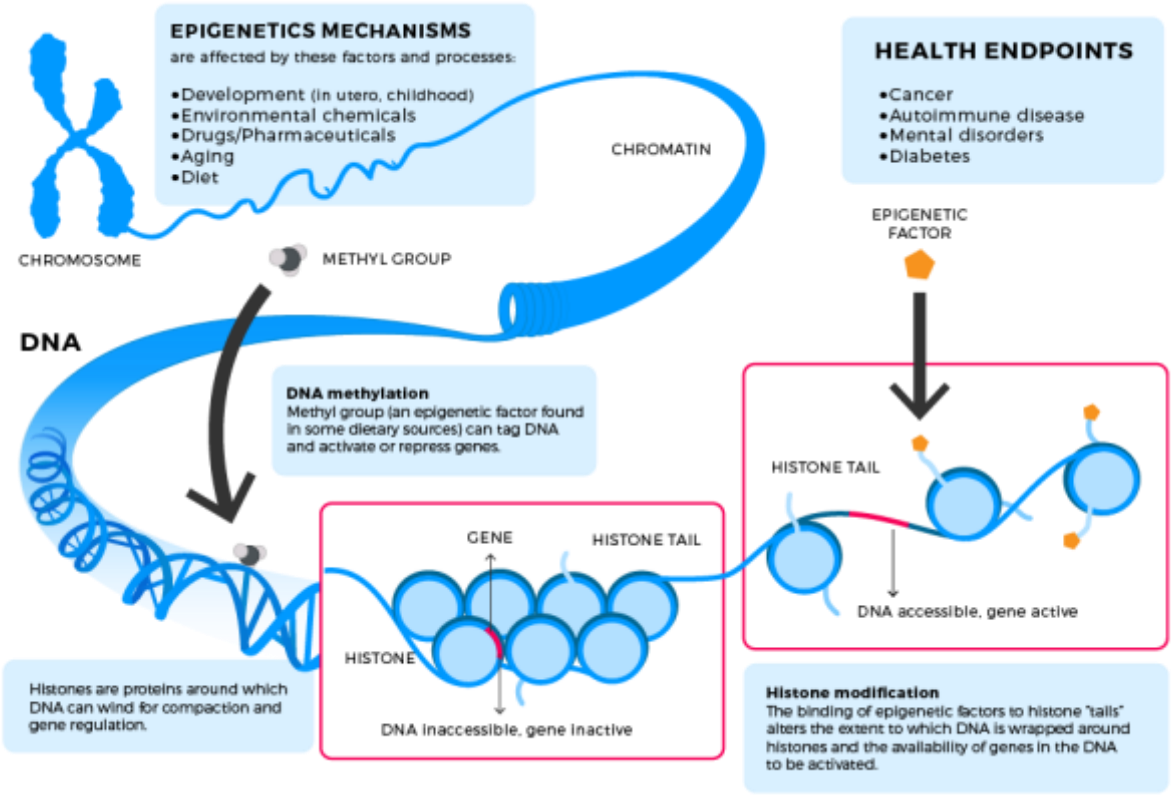
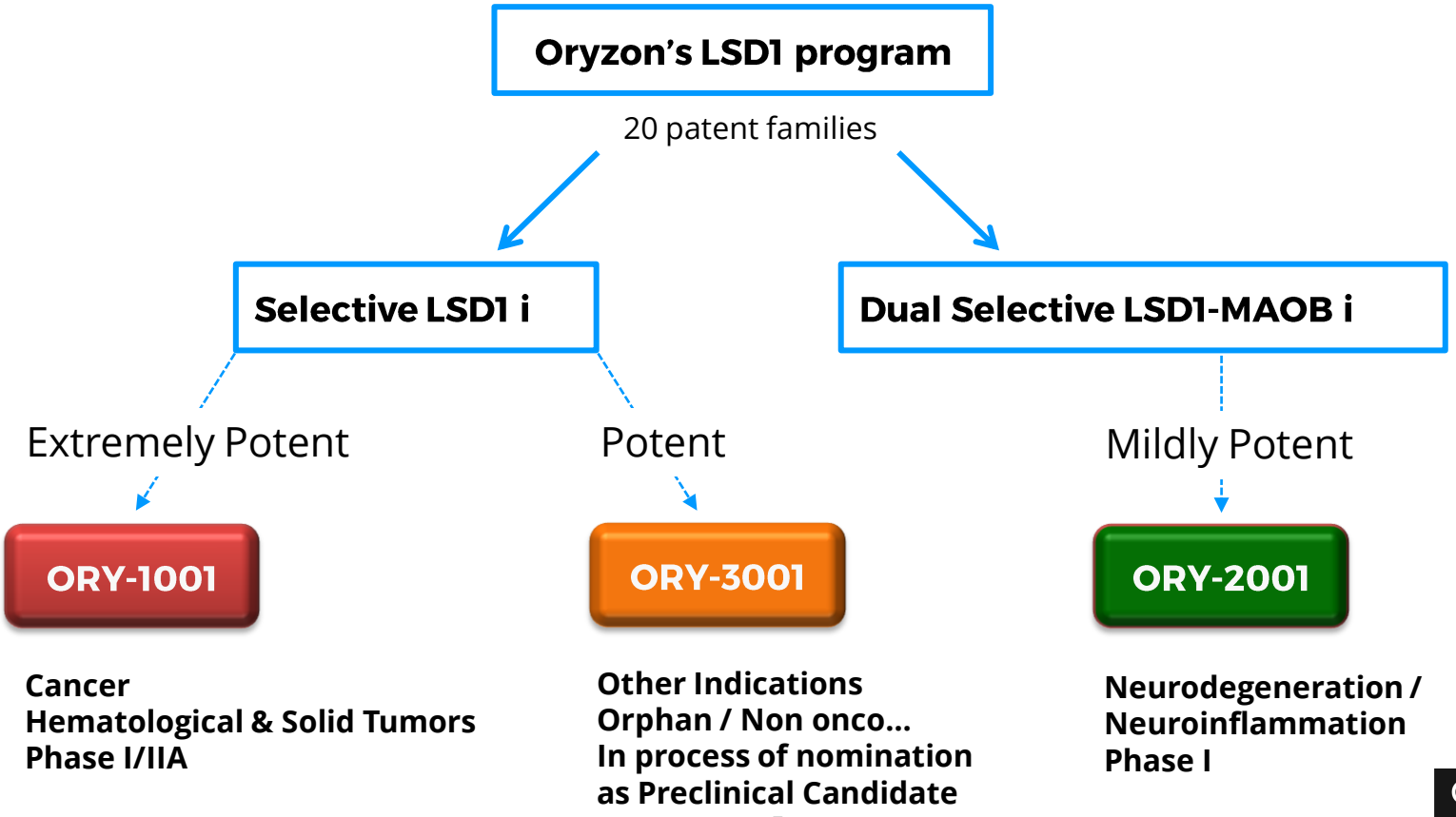
EPIGENETICS: THE CRITICAL ROLE OF HISTONE CODING

- **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



The LSD1 PROGRAM: A demonstration of the productivity of our Epigenetic platform

- LSD1 is an enzyme that demethylates histones: specifically mono and dimethylated H3K4 and H3K9
- LSD1 belongs to the family of FAD – dependent amine oxidases, which include known CNS drug targets, such as MAO-A and MAO-B
- The general MAO inhibitor tranylcypromine is a chemical starting point to design LSD1 inhibitors



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	ORY-3001								
CANCER	Other KDMs									
CANCER	Other Epigenetic Targets									

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ORY-1001: ONCOLOGY PROGRAM

- LSD1 is a key effector of the differentiation block in MLL leukemia
- MLL Leukemic stem cells are addict to LSD1 activity
- ORY-1001 a highly potent and selective LSD1 inhibitor with orphan drug status granted by the European Medicines Agency (EMA)
- 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 in solid tumors

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PHASE I HIGHLIGHTS: ORY-1001 LEUKEMIA

Licensed to ROCHE in 2014

- $23m received in 2014-15
- +$500m in future contingent milestones
- Tiered royalties up to double digit.
- Clinical development and all related investments beyond the ongoing Phase I/IIA trial are the responsibility of ROCHE

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

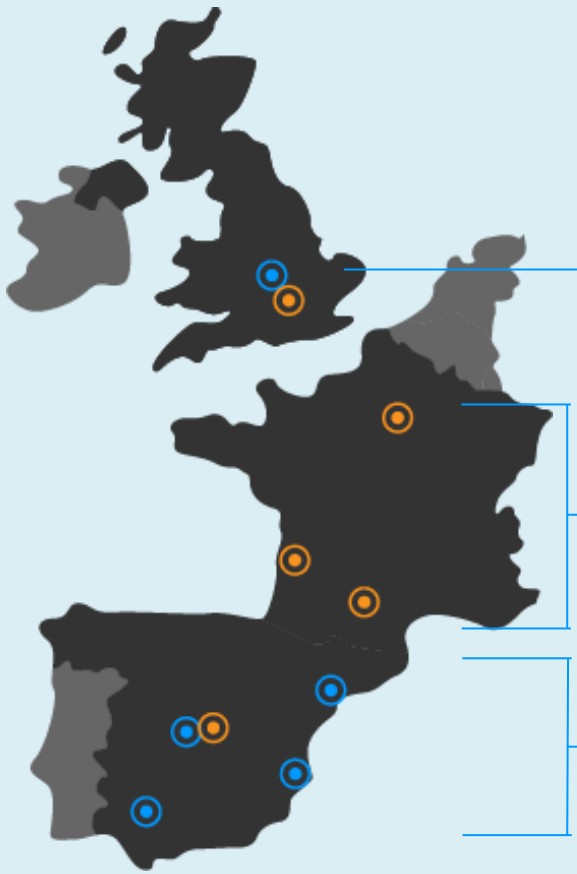
SECONDARY ENDPOINTS		
Characterize PK	Assess Responses (CR/Cri/PR), particularly for rMLL gene	Evaluate surrogate PD markers for target engagement

PRELIMINARY RESULTS
Excellent safety profile
Demonstrated impact on pharmaceutical target
PD clear readings several biomarkers
Good PK
Established maximum recommended dose

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



- ✓ 14 Patients enrolled
- ✓ Status: Enrollment closed. 3 patients still under treatment
- ✓ Completion Date: 3Q16

Expected Report Preliminary Data in ASH 2016

10 Hospitals in 3 Countries

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

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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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

Lines of evidence supporting a role of epigenetics in etiology and pathogenesis of specific NDGs

	Alzhemier's disease	Parkinson's disease	Huntington's disease
Methylation	Reduced DNA methylation in the anterior temporal neocortex neuronal nuclei Hypermethyation of HTERT gene Hypomethylation of inflammatory genes iNOS, IL-1, and TNF-α in the AD cortex	Overall reduction of methylation potential Hypomethylation of SNCA gene in brain tissue α-synuclein related reduction of Dnmt1 methyltransferase availability Differential methylation of ARK16, GPNMB, STX1B and CYP2E1	Early reports of increased variability at HTT gene locus
Histone modifications	increased phosphorylated histone H3 in hippocampal neurons Modulation of histone acetylation by HDAC inhibitors improved learning and memory in mouse models	Response to treatment with HDACIs in disease models α-synuclein related reduction in histone acetylation and histone gene expression	Beneficial effect of HDACIs in disease models Sequestration of proteins with HDAC activity (CBP) Increase of histone proteins carrying H3K9 marks in brain and blood tissues

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

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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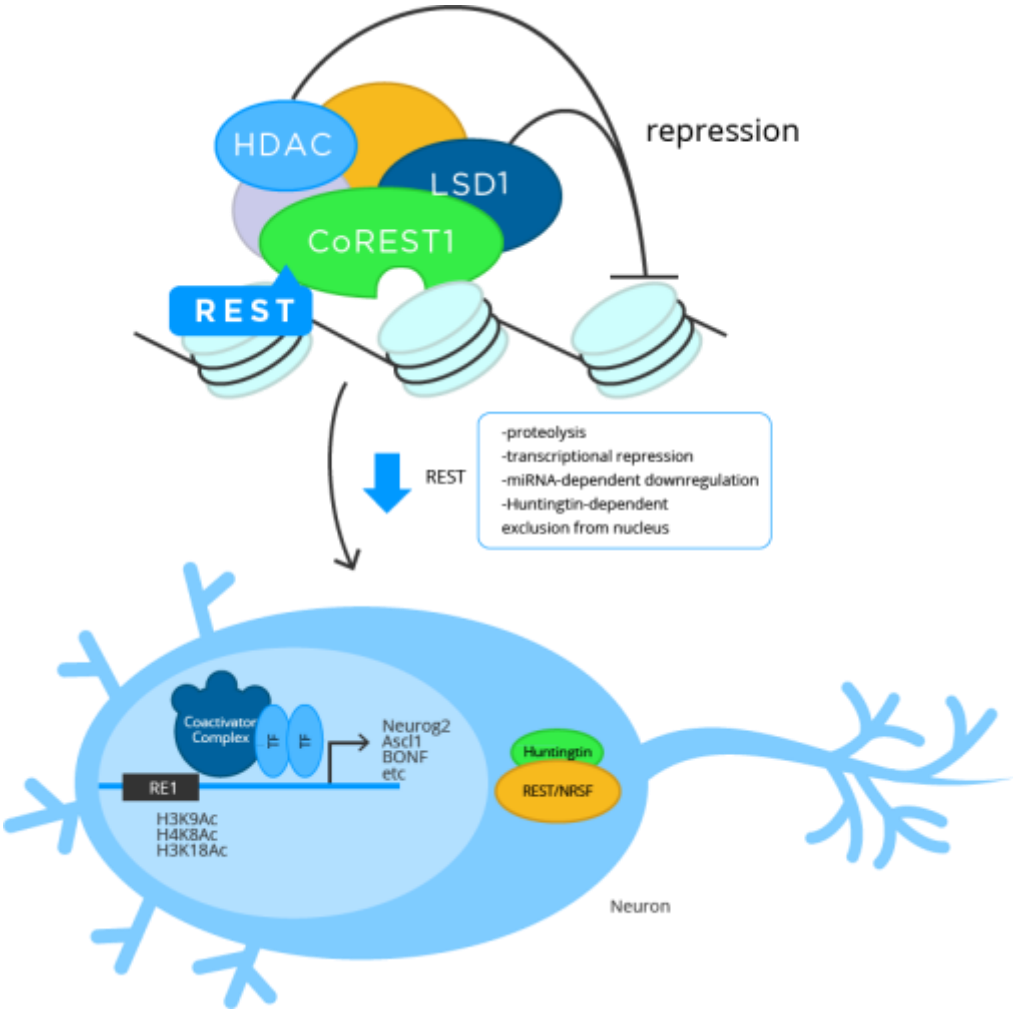
LSD1 IN THE NERVOUS SYSTEM

- Different to what happens in HDACs, it has been proven that it is possible to develop extremely selective LSD1 inhibitors with excellent pharmacological properties
- 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
- Oryzon has the wider IP portfolio in the LSD1 space with drug candidates specially suitable to be developed in neurological indications



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ORY-2001 – A COMPOUND FOR CNS ready for Phase II in 1H2017

- ✓ Highly selective dual LSD1-MAO-B inhibitor
- ✓ Preclinical Proof of Concept: LSD1 Against AD and HD
- ✓ A third indication (still confidential)
- ✓ Other additional indications being explored preclinically
- ✓ Clinical development : In Phase I - LPO expected in Dec2016
  - ✓ Alzheimer's Disease is lead indication
  - ✓ Potential for additional indications: PD, HD and others
- ✓ 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: a safe drug for chronic settings
  - ✓ Target engagement demonstrated in vivo
- ✓ Biomarkers identified
- ✓ Exclusively owned by Oryzon

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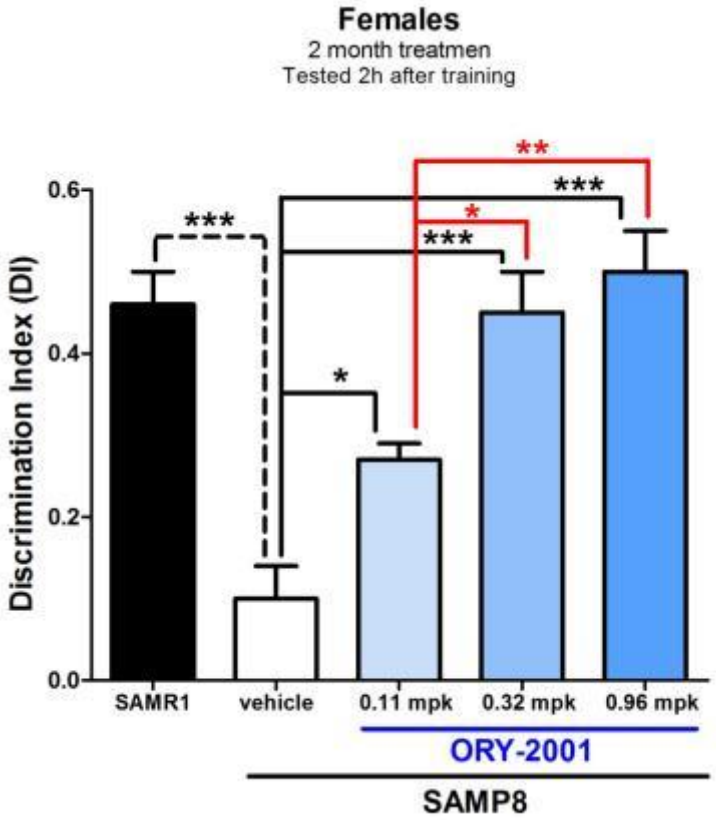
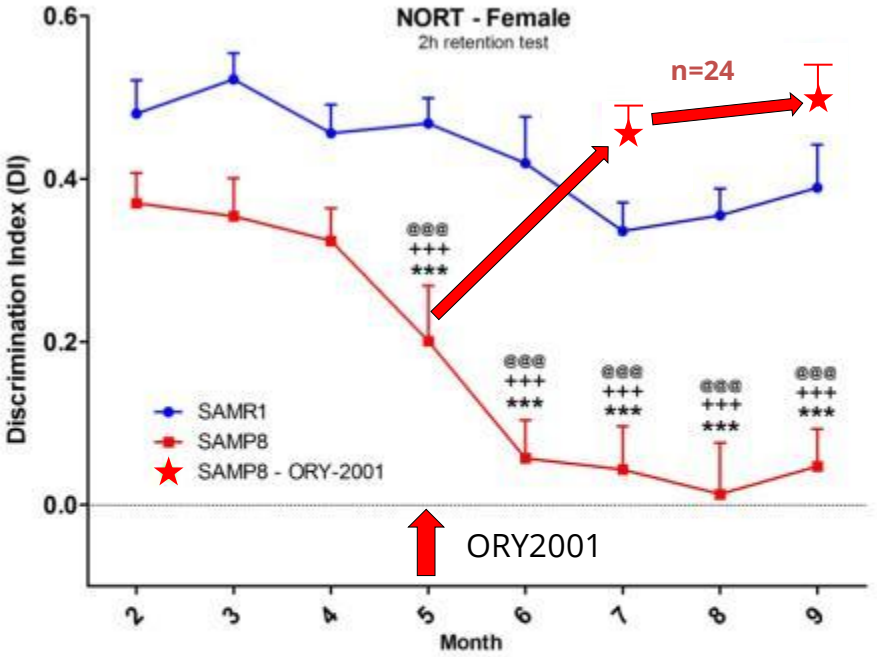
PoC studies in SAMP8 mice

- ✓ ORY-2001 provides a dose dependent protective effect in the medium-term memory of female mice, compared to age-matched SAMP8 mice



ORY-2001: A possible disease modifier drug

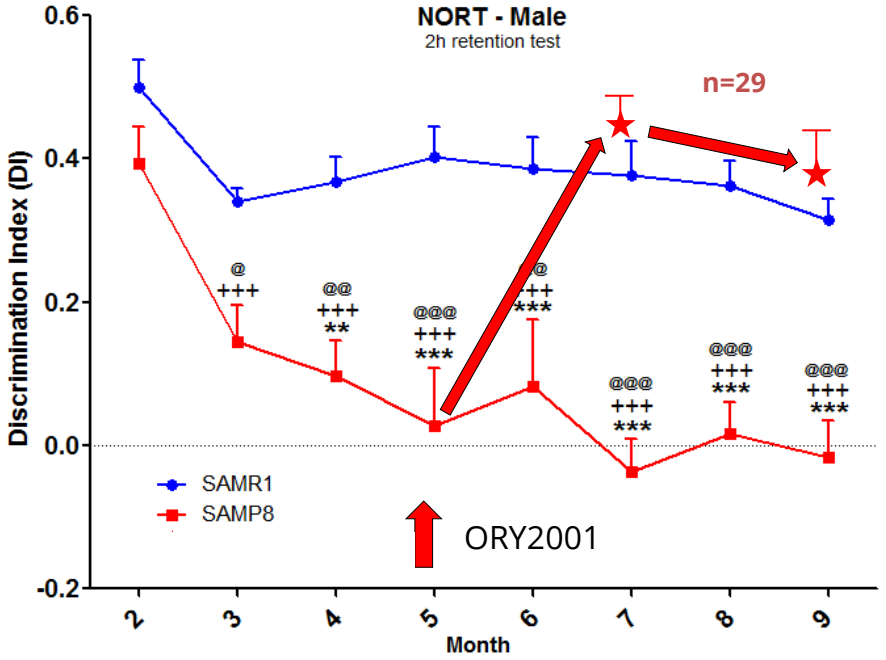
Meta-analysis of cognitive deficit of untreated SAMP-8 mice (historical data)



SAMP8 cognitive deficit compared to SAMR1 start to be significative from month 5. *** p <0.001 two-way ANOVA (Genotype vs. Age; n = 15 genotype/month)

SAMP8 animals treated with ORY-2001 for 2 months have restored cognitive function compared to control SAMP8 of 5-9 months. +++ p < 0.001 two-way ANOVA (Treatment vs control; treated group n = 24)

SAMP8 animals treated with ORY-2001 for 4 months have restored cognitive function compared to control SAMP8 of 5-9 months. @@@ p < 0.001 two-way ANOVA (Treatment vs contro; treated group n = 10)



SAMP8 cognitive deficit compared to SAMR1 start to be significative from month 4. ** p < 0.01; *** p <0.001 two-way ANOVA (Genotype vs. Age; n = 15 genotype/month)

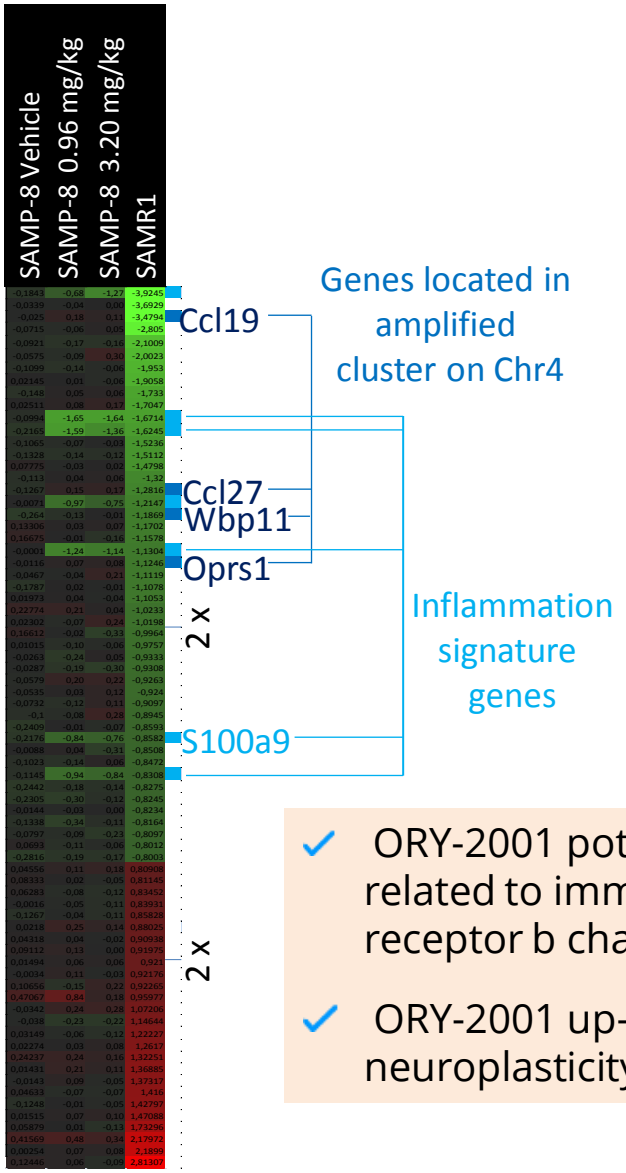
SAMP8 animals treated with ORY-2001 for 2 months have restored cognitive function compared to control SAMP8 of 3-9 months. +++ p < 0.001 two-way ANOVA (Treatment vs control; treated group n = 29)

SAMP8 animals treated with ORY-2001 for 4 months have restored cognitive function compared to control SAMP8 of 3-9 months. @ p < 0.05; @@ p < 0.01; @@@ p < 0.001 two-way ANOVA (Treatment vs contro; treated group n = 10)

ORY-2001 restores the discrimination index in SAMP-8 mice

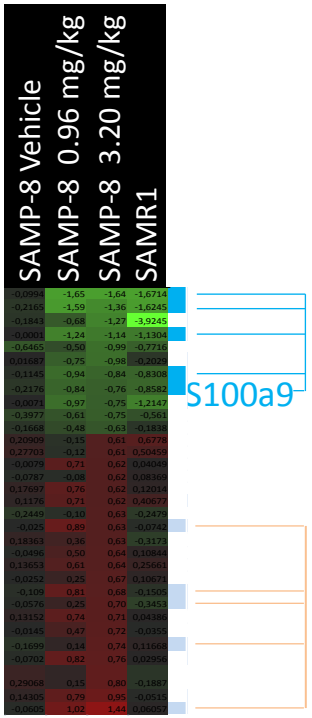
PoC studies in SAMP8 mice - **BIOMARKERS**

We have identified different Hippocampal **biomarkers** upon ORY-2001 treatment:



Genes located in amplified cluster on Chr4

Inflammation signature genes



Inflammation signature genes

Cognitive function, neuroplasticity and memory

<50 genes up or down-regulated by > 2 fold female SAMP-8 vs SAMR1 (see also Carter *et al.*).

Chr 4 cluster incuding *Ccl19* and *Ccl27* is amplified and over-expressed SAMP-8 vs SAMR1 mice.

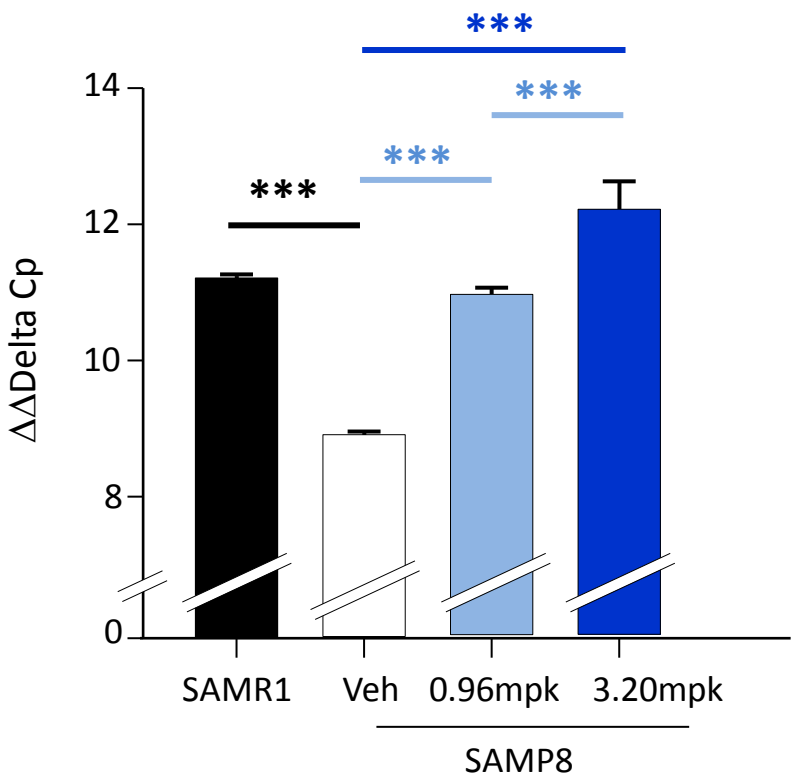
Inflammation genes upregulated in SAMP-8 vs SAMR1 mice

- ✓ ORY-2001 potently down-regulated the expression of a subset of genes related to immune reaction and inflammation, including S100A9 and T-cell receptor b chains in SAMP-8 mice
- ✓ ORY-2001 up-regulated genes associated with improved cognitive function, neuroplasticity and memory

ORY-2001 - PROOF OF CONCEPT IN SAMP8 MICE

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

- 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).
- 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

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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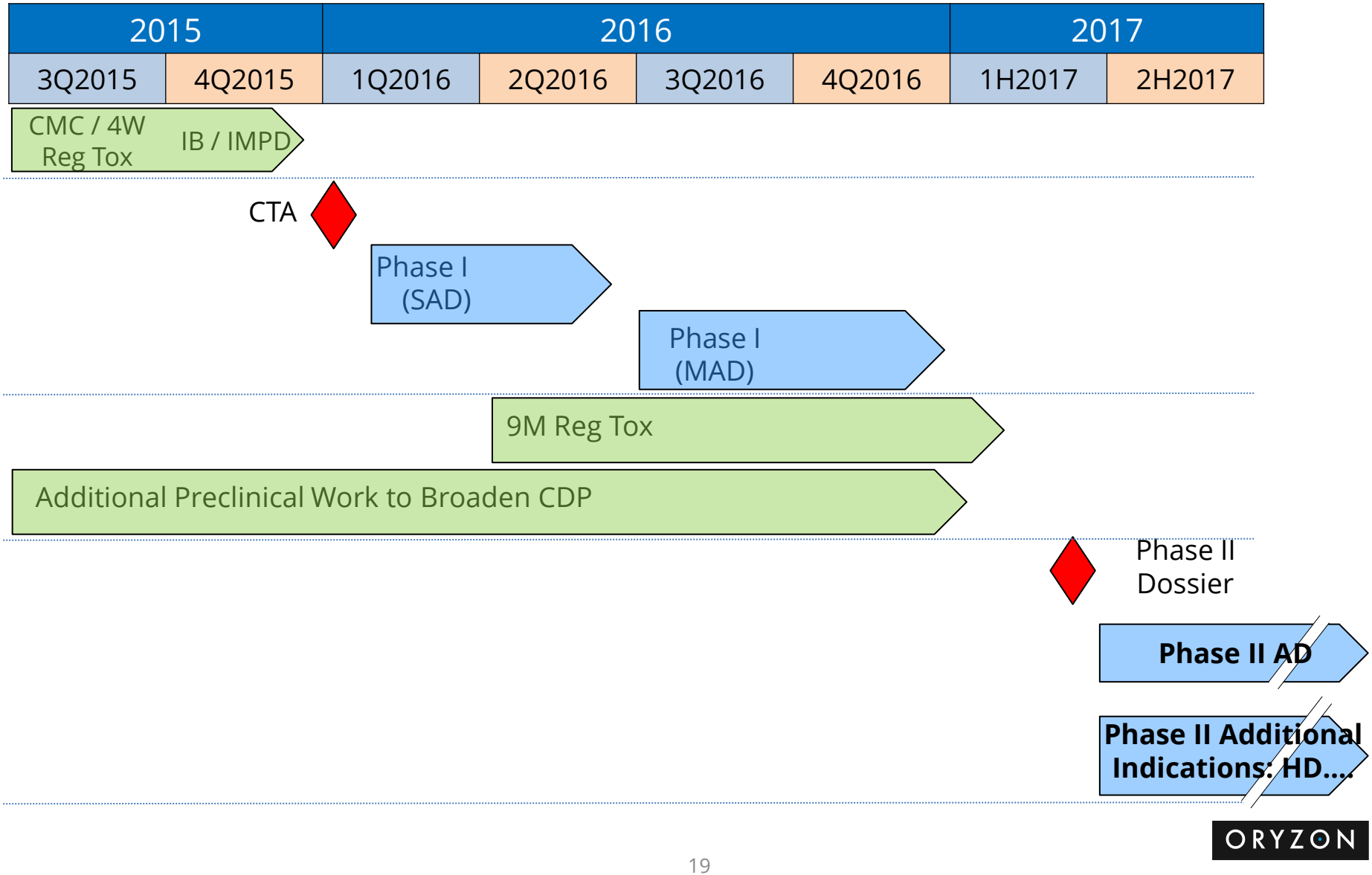
ORY-2001 DEVELOPMENT TIMELINE



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

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FINANCIAL HIGHLIGHTS

- €27m raised in the last 12 months (equity+debt)
- Strong balance sheet with €+29m in cash at the end of Q1-2016
- $5 million payment from ROCHE in 2015 ($23m total in the period 2014-15)
- Secured €2.6M in public aids in 2015
- €20M 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%)
  - 1Q-2016: 10.5M non-senior, non-secured debt in 1Q 2016 4-5y term at rates between 1.5%-3.5%
- Expected cash burn of €10-12M annually for next 2 years
- Raised €31 M since inception
- Spanish GAAP rules adapted to IFRS and ready for Nasdaq
- Accounts audited by Grant Thornton since 2003
- 35 employees (40 expected by the year's end)

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CATALYSTS 2016

- ✓ ORY-1001: LEAD CANCER ASSET
  - Complete Phase IIA and report target efficacy
  - Roche execute ongoing clinical development plan
- ✓ ORY-2001: LEAD CNS ASSET
  - ✓ Begin Phase I patient enrolment
  - Complete Phase I dosing safety study in healthy volunteers
  - Layout of a multiple Phase II clinical study including potential additional indications
- ✓ ORY-3001: Nomination of Preclinical Candidate
- ✓ CORPORATE
  - Prepare to Dual List on the NASDAQ in the future

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THANK YOU VERY MUCH!

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