ORYZON

A GLOBAL LEADER IN EPIGENETICS

INVESTOR PRESENTATION
MADX: ORY
JANUARY 2017
LEGAL NOTICE

DISCLAIMER
This document has been prepared by Oryzon Genomics, S.A. exclusively for use during the presentation. Oryzon Genomics, S.A. does not assume liability for this document if it is used with a purpose other than the above. The information and any opinions or statements made in this document have not been verified by independent third parties; therefore, no express or implied warranty is made as to the impartiality, accuracy, completeness or correctness of the information or the opinions or statements expressed herein. Oryzon genomics, S.A. does not assume liability of any kind, whether for negligence or any other reason, for any damage or loss arising from any use of this document or its contents. Neither this document nor any part of it constitutes a contract, nor may it be used for incorporation into or construction of any contract or agreement. Information in this document about the price at which securities issued by Oryzon Genomics, S.A. have been bought or sold in the past or about the yield on securities issued by Oryzon Genomics, S.A. cannot be relied upon as a guide to future performance.

IMPORTANT INFORMATION
This document does not constitute an offer or invitation to purchase or subscribe shares, in accordance with the provisions of Law 24/1988, of 28 July, on the Securities Market, Royal Decree-Law 5/2005, of 11 March, and/or Royal Decree 1310/2005, of 4 November, and its implementing regulations. In addition, this document does not constitute an offer of purchase, sale or exchange, nor a request for an offer of purchase, sale or exchange of securities, nor a request for any vote or approval in any other jurisdiction. The shares of Oryzon Genomics, S.A. may not be offered or sold in the United States of America except pursuant to an effective registration statement under the Securities Act of 1933 or pursuant to a valid exemption from registration.

FORWARD-LOOKING STATEMENTS
This communication contains forward-looking information and statements about Oryzon Genomics, S.A., including financial projections and estimates and their underlying assumptions, statements regarding plans, objectives and expectations with respect to future operations, capital expenditures, synergies, products and services, and statements regarding future performance. Forward-looking statements are statements that are not historical facts and are generally identified by the words “expects,” “anticipates,” “believes,” “intends,” “estimates” and similar expressions. Although Oryzon Genomics, S.A. believes that the expectations reflected in such forward-looking statements are reasonable, investors and holders of Oryzon Genomics, S.A. shares are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Oryzon Genomics, S.A., that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include those discussed or identified in the documents sent by Oryzon Genomics, S.A. to the Comisión Nacional del Mercado de Valores, which are accessible to the public. Forward-looking statements are not guarantees of future performance. They have not been reviewed by the auditors of Oryzon Genomics, S.A. You are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date they were made. All subsequent oral or written forward-looking statements attributable to Oryzon Genomics, S.A. or any of its members, directors, officers, employees or any persons acting on its behalf are expressly qualified in their entirety by the cautionary statement above. All forward-looking statements included herein are based on information available to Oryzon Genomics, S.A. on the date hereof. Except as required by applicable law, Oryzon Genomics, S.A. does not undertake any obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.
COMPANY HIGHLIGHTS

✓ MADX: ORY  A **publicly traded** company on the Madrid Stock Exchange

✓ A **clinical stage** biopharmaceutical company developing innovative therapies in the field of Epigenetics

✓ A competitive **EPIGENETIC Platform** with a first program that validates the platform scientifically and clinically
  
  ✓ 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** valued at $500M

✓ Strong IP portfolio with technology developed in-house (+20 patent families)

✓ **Raised €32M** in the last 12 months. **Cash runway till 2018**

✓ **+32%** stock evolution on the last 12 months
**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**
A LSD1 focused company
LSD1 is an enzyme that demethylates histones: specifically mono and dimethylated H3K4 and H3K9

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>TARGET</th>
<th>MOLECULE</th>
<th>DISCOVERY</th>
<th>H2L</th>
<th>LEAD OPTIMIZATION</th>
<th>PRECLINICAL</th>
<th>PHASE I</th>
<th>PHASE IIA</th>
<th>PHASE IIB</th>
<th>PHASE III</th>
<th>PARTNER</th>
</tr>
</thead>
<tbody>
<tr>
<td>CANCER</td>
<td>LSD1</td>
<td>ORY-1001 (*) (RG6016)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Roche</td>
</tr>
<tr>
<td>Leukemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CANCER</td>
<td>LSD1</td>
<td>ORY-1001 (RG6016)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Roche</td>
</tr>
<tr>
<td>Small Cell Lung Cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNS DEMENTIAS</td>
<td>LSD1-MAOB</td>
<td>ORY-2001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Roche</td>
</tr>
<tr>
<td>Alzheimer’s Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parkinson’s Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Dementias</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNS INFLAMMATION</td>
<td>LSD1-MAOB</td>
<td>ORY-2001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Autoimmune</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNS ORPHAN</td>
<td>LSD1-MAOB</td>
<td>ORY-2001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Roche</td>
</tr>
<tr>
<td>Huntington's Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Orphan Diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OTHER INDICATIONS</td>
<td>LSD1</td>
<td>ORY-3001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CANCER</td>
<td>Other KDMs</td>
<td>ORY-2001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CANCER</td>
<td>Other Epigenetic Targets</td>
<td>ORY-2001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(*) Phase I / IIA in Acute Leukemia has been done in the same trial
ORY-1001: ONCOLOGY PROGRAM

- LSD1 is a target in some cancers
- LSD1 is a key effector of the differentiation block in MLL leukemia
- MLL Leukemic stem cells are addicted to LSD1 activity
- ORY-1001 a highly potent and selective LSD1 inhibitor with orphan drug status granted by the European Medicines Agency (EMA)
- Finishing Data Analysis of Phase I/IIA study:
  - Completed Part 1 of the study (Phase I) in acute leukemia
  - Extension Arm (Phase IIA) completed
- Potential for additional indications in solid tumors

Licensed to ROCHE in 2014

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

A $2+ billion market potential
Well tolerated and has been administered to 41 patients in total up to a maximum of three cycles. Excellent oral bioavailability in humans and excellent pharmacokinetic parameters

Pharmacodynamic biomarkers S100A12, VCAN, ITGAM, LY96, CD86, GPR65, CRISP9, ANXA2 and LYZ permit monitoring of response to ORY-1001 treatment in M4/M5 AML patients

Promising clinical responses were observed in the Phase IIA arm (14 patients, 4M6, 6MLL gene fusion and 4 MLL other mutations) mandating further clinical research and investigation

Taking the four M6 patients together, there was no significant rise in blast cell count after two cycles of therapy – suggesting disease stabilization

4/6 patients with MLL leukemia showed evidence of morphological blast cell differentiation

2 of these exhibited a differentiation syndrome

100% (5/5) of patients with MLL gene Fusion with evaluable PD samples showed evidence of blast differentiation by qRT-PCR analysis in PD analyses

23% of BM responses (3/13)
ORY-1001 (RG6016): Next Steps

ORY-1001 has demonstrated Biological Proof of Mechanism as a highly active LSD1 inhibitor with strong differentiation-inducing activity in patients with MLL leukemia. It has shown an excellent safety profile in acute leukemia patients, and also displayed excellent oral bioavailability and pharmacokinetic parameters.

Pharmacodynamic biomarkers identified for M4-M5 leukemias, as well as for Small Cell Lung Cancer (SCLC; Milleti et al., 2016, AACR: “Neuroendocrine gene transcript expression is associated with efficacy to lysine-specific demethylase-1 inhibitor RG6016 in small cell lung cancer-derived cell lines”) and other subtypes of malignancies.

ORY-1001 might be a potential combinatorial therapeutic option in the treatment of several types of acute myeloid leukemia.

As a potent and safe LSD1 inhibitor, ORY-1001 is also of potential interest in the treatment of solid tumors such as small cell lung cancer, and possibly others in the future.

Roche now has sole responsibility of developing ORY-1001 (Roche’s ID codes RO7051790 and RG6016) and has recently initiated its first clinical trial with ORY-1001 in extensive-stage disease SCLC (ED SCLC). The trial is an open-label, multi-centre (4 countries) study with an estimated 70 ED SCLC patients to be treated with ORY-1001. Safety/tolerability is the primary endpoint, while secondary endpoints will include preliminary efficacy (overall survival, progression-free survival, objective response) and PK/PD data. The estimated completion date is H2 19. See https://clinicaltrials.gov/ for more details (Study identifier NCT02913443).
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
**LSD1 in the CNS**

- **LSD1 is a key component of different CNS Transcriptional complexes** interacting with different Transcription Factors and very often with HDAC1 and HDAC2.
- In the Brain one of these TFs is REST. The LSD1-REST-CoREST-HDAC1/2 repressor complex is involved mainly in controlling developmental programs and modulating neuronal morphology in the CNS. 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 known to be an important regulator in the maintenance of pluripotency and in specification of neuronal commitment of pluri- or multipotent cells.
- In C. elegans, Drosophila and mammalian cells, LSD1 suppression has been reported to significantly enhance the removal of misfolded proteins with a critical role on neurodegeneration like SOD1, TDP-43, FUS, and polyglutamine-containing proteins, indicating a general improvement in protein quality control.
Pharmacological Properties

- A selective dual LSD1-MAO-B inhibitor
- 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

Preclinical Proof of Concept

Achieved in different animal models of:
- Alzheimer’s Disease
- Huntington’s Disease
- Multiple Sclerosis
- 2 Additional CNS disorders

Additional indications being explored preclinically

Clinical development → In Phase I:

LVO expected in early 2017
- Alzheimer’s Disease is lead indication → Phase IIB Planned
- Additional indications: MS and HD → Phase IIA Planned
SAMP8 mouse: A model for Alzheimer’s Disease

The senescence accelerated mouse (SAM) as a model for oxidative stress and Alzheimer’s disease

John E. Morley, Harvey James Ambrichter, Susan A. Farr, Vijaya B. Kumar

The senescence accelerated mouse (SAM) is a spontaneous animal model of oxidative stress and Alzheimer’s disease. It develops early memory disturbances and changes in the brain–behavioral profiles resulting in decreased efficiency of amyloid-β protein, suggesting a role for amyloid-β in the pathogenesis of Alzheimer’s disease. This review focuses on the role of oxidative stress and neuroinflammation in Alzheimer’s disease.

Nodes and biological processes identified on the basis of network analysis in the brain of the senescence accelerated mice as an Alzheimer’s disease animal model

Xiao-ri Chong, Xi-lu Bao, Yel-ling Zhang, Gui-tong Zhang, Peng Li, Huang Huang, Yu-ying Zhao, Xiao-chen Bo, Sheng-qiu Wang, Wen-xia Zhou, and Yong-xiang Zhang

1 Department of Neuroimmunomorphology, Beijing Institute of Psychology and Neurology, Beijing, China
2 Department of Neuroimmunomorphology, Beijing Institute of Psychology and Neurology, Beijing, China

These authors have contributed equally to this work.

Habiting the behavioral and histopathological hallmarks of Alzheimer’s disease (AD), senescence accelerated mouse prone 8 (SAMP8) mice are currently considered a robust model for studying AD. However, the underlying mechanisms, prioritized pathways, and genes in SAMP8 mice linked to AD remain unclear. In this study, we provide a biological interpretation of the molecular underpinnings of SAMP8 mice. Our results were derived from differentially expressed genes in the hippocampus and cerebral cortex of SAMP8 mice compared to age-matched SAMR1 mice at 2, 6, and 12 months of age using cDNA microarray analysis. On the basis of PPI, MetaCore, and the co-expression network, we constructed a distinct genetic sub-network in the brains of SAMP8 mice. Next, we determined that the regulation of synaptic transmission and apoptosis were disrupted in the brains of SAMP8 mice. We found abnormal gene expression of RAIF, MAPT, PGS2, CDKN2A, CAMK2A, NTRK2, ACE2, ADRB1, MCM10, and ST18, which may have induced the dysfunction of biological processes in the brains of SAMP8 mice. Specifically, we found microRNAs, including mir-10a, mir-12, mir-34a, mir-15, mir-18a, mir-22, mir-28a, mir-101, mir-106b, and mir-128a, that might regulate the expression of nodes in the sub-network. Taken together, these results provide new insights into the biological and genetic mechanisms of SAMP8 mice and add an important dimension to our understanding of the neuro-pathogenesis in SAMP8 mice from a systems perspective.

Keywords: Alzheimer’s disease, senescence accelerated mouse prone 8, molecular network, hippocampus, cerebral cortex, differentially expressed genes, synaptic transmission, apoptosis

Table 1
Comparison of Alzheimer’s disease, SAMP8 mouse and transgenic models

<table>
<thead>
<tr>
<th></th>
<th>Alzheimer’s disease</th>
<th>SAMP8</th>
<th>Transgenic models</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overproduction of amyloid-β</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Amyloid plaques</td>
<td>Yes</td>
<td>Late*</td>
<td>Yes</td>
</tr>
<tr>
<td>Phosphorylated tau</td>
<td>Increased</td>
<td>Increased</td>
<td>In some models</td>
</tr>
<tr>
<td>Cerebral amyloid angiopathy</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Neuron loss</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Synaptic dysfunction</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Dendritic spine loss</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Glossis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Cholinergic deficit</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Learning and memory impaired</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Circadian rhythm disturbances</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Oxidative damage</td>
<td>Yes</td>
<td>Yes</td>
<td>4 months - 8 months</td>
</tr>
</tbody>
</table>

*= uncertain.

* Occur at 16 to 18 months.
ORY-2001: A possible disease modifier drug

- 2 or 4 months of oral treatment with ORY-2001 produce a marked cognitive improvement in SAMP8 animals measured by NORT memory tests
- +150 animals tested

**ORY-2001 restores the discrimination index in SAMP8 mice**

Meta-analysis of cognitive deficit of untreated SAMP8 mice (historical data)
PoC studies in SAMP8 mice

- 2 or 4 months of oral treatment with ORY-2001 produce a marked cognitive improvement in SAMP8 animals measured by NORT memory tests

- ORY-2001 provides a dose dependent protective effect in the medium-term memory of mice, compared to age-matched SAMP8 mice
PoC studies in SAMP8 mice - **BIOMARKERS**

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

<50 genes up or down-regulated by > 2-fold female SAMP8 vs SAMR1 (see also Carter *et al.* )

Chr 4 cluster including *Ccl19* and *Ccl27* is amplified and over-expressed SAMP8 vs SAMR1 mice

Inflammation genes upregulated in SAMP8 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 SAMP8 mice

✔ **ORY-2001** up-regulated genes associated with improved cognitive function, neuroplasticity and memory
S100A9 and Alzheimer’s disease

- S100A9 downregulation improves memory in different AD Tg mice models
- S100A9 has been involved in the A-Beta deposition dynamics

CT-Tg mice
Mutant APP(V717I)
CT100 (London mutation)

Tg2576 mice
mutant APP (isoform 695);
Swedish mutation (KM670/671NL)

sh S100a9 RNA lentiviral brain injection

Tg2576 S100a9-/- mice have improved memory, reduces amyloid pathology
(Kim et al., 2014)

APP/PS1 mice
mutant APPswe
PSEN1dE9

S100a9 upregulated in hippocampus, memory impairment
(Kummer et al., 2012)

APP/PS1 S100a9-/- mice have increased phagocytosis of fibrillar amyloid β (Aβ) in microglia cells, improved memory
(Kummer et al., 2012)

S100a9 markedly increased in cortex and hippocampus, memory impairment
(Ha et al., 2010)

S100a9 Knockdown attenuates learning and memory impairment in Tg2576 mice / reduces amyloid plaques in Tg2576 brains
(Ha et al., 2010)

Tg2576 mice
mutant APP (isoform 695);
Swedish mutation (KM670/671NL)

S100a9-/- knock-out mice

Tg2576 S100a9-/- mice have improved memory, reduces amyloid pathology
(Kim et al., 2014)

S100a9 marked increased in cortex and hippocampus, memory impairment
(Ha et al., 2010)

S100a9 upregulated in hippocampus, memory impairment
(Ha et al., 2010)

APP/PS1 mice
mutant APPswe
PSEN1dE9

S100a9-/- knock-out mice

APP/PS1 S100a9-/- mice have increased phagocytosis of fibrillar amyloid β (Aβ) in microglia cells, improved memory
(Kummer et al., 2012)
ORY-2001 also a possible approach to treat Multiple sclerosis?

- ORY-2001 downregulates S100A9 in the Hc of SAMP8 animals
- Complexes of S100A8 and S100A9 (S100A8/A9) are expressed and released at inflammatory sites
- A correlation between serum levels of S100A8/A9 and disease activity has been observed in many inflammatory disorders
- Quinoline-3-carboxamides (Q compounds) that target S100A9 have been explored as treatments for autoimmune/inflammatory diseases in humans. And one of these, Laquinimod is being currently explored for Multiple Sclerosis treatment
- There are additional models/diseases in which S100A9 has been found to be both overexpressed and deleterious. One of these models is EAE, a Multiple Sclerosis model
ORY-2001 a possible approach to treat Multiple sclerosis?

**Experimental Autoimmune Encephalitis (EAE)** mice model is a model in which S100A9 has been described to be upregulated. This model is considered a meaningful model for Multiple Sclerosis.

To determine the efficacy of ORY-2001 following oral gavage administration for 2 consecutive weeks in mice.

**Method:**
Female C57BL/6 mice
G1: Vehicle Control
G2: ORY-2001 1.0 mg/Kg, p.o.
G3: ORY-2001 3.0 mg/Kg, p.o.

**Parameter to assess:**
- Body weight
- Clinical score
- Inflammatory response
- Autoimmune response

**Clinical score:**
- 0.0, no clinical signs
- 0.5, partial loss of tail tonicity
- 1.0, complete loss of tail tonicity
- 2.0, flaccid tail and abnormal gait
- 3.0, hind leg paralysis
- 4.0, hind leg paralysis with hind body paresis
- 5.0, hind and fore leg paralysis
- 6.0, death

**Onset of clinical signs**
C57BL/6 mice (Six-week old)

**Early onset reactive treatment**
100 µg MOG35-55 sc. In CFA

**Days**
0 10 11 15 19 24 60
ORY-2001 is a possible approach to treat Multiple sclerosis

Multiple Sclerosis (Experimental Autoimmune Encephalitis (EAE) mice model)

- Treatment with ORY-2001 during the effector phase of the disease greatly inhibited the development of EAE and reduced disease incidence and severity.
- Animals treated with ORY-2001 show more cellularity on the lymphoid organs indicating that the T cell immune response against oligodendrocytes did not occur.

**Mean Clinical Score**

**Cell number (x 10^6)**

**Spleen**

**Lymph nodes**

***p < 0.001

ORY-2001 is protective in the EAE model
ORY-2001 has a Multi-Modal Mechanism of Action

A neuroprotective component + antiinflammatory component

LSD1 plays a role in expression of neuronal genes thru demethylation of H3K4 and H3K9
A Phase I study with 88 healthy volunteers, young and elderly

- **Single Ascending Dose (SAD):** all cohorts were safe. No hematological effects nor any other relevant/significant side effects observed in any cohort

- **Additional arm** to determine CSF ORY-2001 levels after a Single Dose

- **Multiple Ascending Dose (MAD):** five dose levels tested so far in young volunteers, no hematological effects nor any other relevant/significant side effects observed
ORY-2001 DEVELOPMENT TIMELINE

- ORY-2001 will be Phase II ready in 2Q-2017
- The Phase I in healthy volunteers enables us to go for Phase II’s in different indications
- The company envisages to perform three different Phase II in AD, MS and HD

**PLANNED ORY-2001 CDP**

- Phase II-B in AD
- Phase II-A in MS
- Phase II-A in HD

A multibillion market potential
ORYZON, A UNIQUE OPPORTUNITY

Corporate Strategy: Epigenetics Momentum, IP & First in Class Clinical Assets

- Epigenetics is one of the hottest spots in the Pharma Industry with high appetite from Pharma Companies (2016 acquisitions Roche–Tensha; Celgene–Acetylon) and from Specialized Investors (Imago, Constellation)
- ORYZON has World class Science and a broad patent portfolio on LSD1, one of the hottest targets in this area (GSK, Celgene, Incyte, Takeda...). Excellent Patent Position and FTO. +20 patent families, many already granted in USA
- ORYZON is a Global Champion in Epigenetics: We pioneer

Platform + Broad Product Pipeline: Three different assets in Clinic (5-6 trials) by 2017

- We developed the first ever LSD1 inhibitor reaching clinical trials in the world. We have reported the first human data in oncology with ORY-1001 (RG-6016)
- A dual LSD1-MAOB inhibitor finishing Phase I and with PoC in in several human disease animal models
- Three Phase IIA-IIB clinical trials ready to start in 2H 2017
- A third LSD1 inhibitor being developed for an Orphan disease and Phase I ready in 2017
- Other epigenetic programs in development

Financials and Governance: Strong balance sheet

- A dynamic and capital efficient company with excellent know-how (40 people)
- €29M in cash at the end of 3Q-2016: Cash runway until 2018, but wanting to invest more to capture the upside of our Phase IIB in ORY-2001 and other clinical programs
- An experienced Public Company Board with Top Executives with proven track record in the industry
- Top Governance according to Public Company standards
2017 CATALYSTS

2014
- Transformational deal with Roche ($21M) on ORY-1001

2015-16
- CONSOLIDATION PERIOD
- Public in Europe ($36M raised)
- ORY-1001: Clinical Data Presented at ASH-2016
- Second Asset (ORY-2001 in clinic development)

2017
- ORY-1001: LEAD CANCER ASSET
  - Phase I-IIA study formally closed
  - FPI in Phase I SCLC by Roche
- ORY-2001: LEAD CNS ASSET
  - Complete Phase I finalized
  - Human Target Engagement demonstrated
  - CTA / IND for Phase II-A approved for MS
  - CTA / IND for Phase II-B approved for AD
  - CTA / IND for Phase II-A approved for HD
  - FPI in a Phase II-A study on MS
- ORY-3001:
  - CTA / IND approved for a Phase I study on an orphan indication yet to be disclosed
- CORPORATE
  - Prepare to Dual List on the NASDAQ in the near future

2018
- ORY-2001: LEAD CNS ASSET
  - FPI in a Phase II-A study on AD
  - FPI in a Phase II-A study on HD
THANK YOU VERY MUCH!
CARLOS BUESA
C.E.O. & President
cbuesa@oryzon.com

EMILI TORRELL
BDO
etorreall@oryzon.com

ANNA K. BARAN
IR Director
abaran@oryzon.com