A GLOBAL LEADER IN EPIGENETICS

INVESTOR PRESENTATION
MADX: ORY
APRIL 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. This presentation is not an offer of securities for sale in the United States. The Company's securities may not be offered or sold in the United States absent registration or an exemption from registration. Any public offering of the Company's securities to be made in the United States will be made by means of a prospectus that may be obtained from the Company or the selling security holder, as applicable, that will contain detailed information about the Company and management, as well as financial statements.
**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** 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 up to $500M(*)
- IP portfolio with technology developed in-house (+20 patent families)
- Additional **18.2M€** raised from blue chip investors in the US and Europe in March 2017
- **Cash runway** expected till 2H2019

(*) Aggregate contingent milestone payments.
CARLOS BUESA: CEO
PhD in Biochemistry and Molecular Biology. Author of more than thirty papers and patents internationally. In 2000, he founded Oryzon Genomics, and since 2001 he has served as Chief Executive Officer and Chairman of the Board of Directors. He has taken several advanced programs on finance, business development, negotiation skills and human resources. He is also PADE at the IESE Business School. He is Board Member of the VC Fund Inveready and Deputy President of the Spanish BioIndustry Association.

NEUS VIRGILI: Intellectual Property Director
B.Sc. in Organic Chemistry from the University of Barcelona
Qualified European Patent Attorney
She has over 20 years experience in pharmaceutical IP
From 2011 IP Officer at Oryzon

ENRIC RELLO: Chief Financial Officer
B.Sc. in Business, University of Barcelona
HBS Finance Excellence Program. Harvard Business School (Executive Education) USA
1993-1997 Biochemie SA (Novartis) Financial Controller / Controller Manager
1997- 2007 Sandoz Industrial Products S.A. (Novartis), CFO Spanish Affiliate
From May 2011 CFO at Oryzon

CESAR MOLINERO: Medical and Clinical Operations Director
PhD in Medicine from the University of Barcelona & AMP at ESADE Business School and Babson
In 1992 he joined the Medical Department of KabiPharmacia
In 1994, he joined the Department of Clinical Research at Laboratorios Esteve where, in 1998, he assumed responsibilities as Medical Adviser
In 2002 he joined Madaus S.A. (Barcelona) as Medical and Regulatory Affairs Director, and later with responsibility as Group VP for Medical, R&D and Regulatory Affairs
Joined Oryzon in January 2014

EMILI TORRELL: Director of Business Development
B.Sc. in Sciences, Autonomous University of Barcelona
MBA at ESADE and PDG at IESE Business School
In the business development area from 1990 in the most relevant Spanish companies Prodesfarma, Almirall and Laboratorios Esteve
From 2007 BD Director at Oryzon

TAMARA MAES: Founder and Chief Scientific Officer
PhD in Biotechnology from the University of Ghent, Belgium. She has produced over twenty scientific papers and patents internationally and has developed innovative HTS methods for functional genomics
She is SAB member on several public institutions as CSIC and private companies. Since 2016 Scientific Advisor of the ADDF

One of the most experienced and respected managerial teams in the Biopharmaceutical industry in Spain
Team members have a track record in product discovery & in advancing successfully through product development phases
Demonstrated ability to close world class deals and to lead, and participate in international consortia
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>MOLECULE</th>
<th>TARGET</th>
<th>INDICATION</th>
<th>DISCOVERY</th>
<th>H2L</th>
<th>LEAD OPTIMIZATION</th>
<th>PRECLINICAL</th>
<th>PHASE I</th>
<th>PHASE IIA</th>
<th>PHASE IIIB</th>
<th>PHASE III</th>
<th>PARTNER</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORY-1001 (*)</td>
<td>LSD1</td>
<td>Leukemia(**)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Roche</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Small Cell Lung Cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Roche</td>
</tr>
<tr>
<td>ORY-2001</td>
<td>LSD1-MAOB</td>
<td>Alzheimer’s Disease Parkinson’s Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other Dementias</td>
<td></td>
<td></td>
<td></td>
<td>Roche</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Multiple Sclerosis Other CNS Autoimmune</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Huntington’s Disease Other Orphan Diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORY-3001</td>
<td>LSD1</td>
<td>Undisclosed Indication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Assets</td>
<td>Other KDMs</td>
<td>Cancer Other indications</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other Epigenetic Targets</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(*) ORY-1001 is also known under Roche’s ID codes RG6016 and ROY051790

(**) Phase I/II A in Acute Leukemia has been done in the same trial
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 is 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

A big market potential

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
PHASE I/IIA HIGHLIGHTS: ORY-1001 IN ACUTE LEUKEMIA

✓ Preliminary data presented at ASH 2016.

✓ 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 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

✓ 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

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

✓ 2 of these exhibited a differentiation syndrome

✓ 23% of Bone Marrow responses (3/13)

Before treatment During treatment (patient 0206)
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.

ORY-1001 might be a potential combinatorial therapeutic option in the treatment of several types of acute myeloid leukemia. Pharmacodynamic biomarkers identified for M4-M5 leukemias.

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.

In Small Cell Lung Cancer (SCLC; Milleti et al., 2016, AACR: “Neuroendocrine gene transcript expression is associated with efficacy to lysine-specific demethylase-1 inhibitor RO7051790 in small cell lung cancer-derived cell lines”). High levels of neuroendocrine markers ASCL1, DDC, and GRP; a gene signature based on these markers predicts response to RO7051790 in SCLC cell lines (p-value 0.0055). ~50% of SCLC patients express high levels of ASCL1, DDC, and GRP, suggesting that this subpopulation may benefit from an RO7051790 based therapy.

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 expected in 2H 2019.
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

Luca Lovrečić, et al., 2013 The Role of Epigenetics in Neurodegenerative Diseases
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 pluripotent or multipotent cells. The LSD1-REST/NRSF complex has been described as a master regulator of neuronal gene expression.

- Neurospecific LSD1 (nLSD1) isoforms LSD1-8a and LSD1-2a/LSD1-8a exist and are highly expressed in the nervous system in order to promote neurite morphogenesis (Zibetti et al., 2010). They may act as a dominant negative (Rusconi et al. 2016).

- 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 possible role in protein quality control (Periz et al., 2015).
ORY-2001 – A COMPOUND FOR CNS expected to be ready for Phase II in 2H2017

**Pharmacological Properties**
- A selective dual LSD1-MAO-B inhibitor
- Optimal ADMET and PK profiles
- Crosses efficiently the BBB
- Once daily oral bioavailable
- 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
The senescence accelerated mouse (SAMP8) as a model for oxidative stress and Alzheimer's disease

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

The senescence accelerated mouse (SAMP8) is a spontaneous animal model of reproduction of amyloid precursor protein (APP) and oxidative damage. It develops early memory and changes in the brain, which result in decreased efficiency of amyloid β protein (APP) accumulation over time. APP accumulates in the brain in aged SAMP8 mice. This leads to the formation of amyloid plaques in the brain, which are linked to the development of Alzheimer's disease. The senescence accelerated mouse model is used to study the role of oxidative stress and APP accumulation in the development of Alzheimer's disease.

Review Article
Senescence-Accelerated Mice P8: A Tool to Study Brain Aging and Alzheimer’s Disease in a Mouse Model

Mercè Pallàs

The senescence accelerated mouse (SAMP8) is a spontaneous animal model of reproduction of amyloid precursor protein (APP) and oxidative damage. It develops early memory and changes in the brain, which result in decreased efficiency of amyloid β protein (APP) accumulation over time. APP accumulates in the brain in aged SAMP8 mice. This leads to the formation of amyloid plaques in the brain, which are linked to the development of Alzheimer's disease. The senescence accelerated mouse model is used to study the role of oxidative stress and APP accumulation in the development of Alzheimer's disease.

Table 1
Comparison of Alzheimer's disease, SAMP8 mouse, and transgenic mouse 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>Marked</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
- 10 studies in the last 5 years, +350 animals tested
- Other +readouts in animal models of MS, HD, PD and other human CNS disorders

ORY-2001 restores the discrimination index in SAMP8 mice

Meta-analysis of cognitive deficit of untreated SAMP8 mice (historical data)
ORY-2001: A possible disease modifier drug

- Cross over Experiment

<table>
<thead>
<tr>
<th>Month</th>
<th>Treatment</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>SAMR1 Vehicle</td>
<td>0+0</td>
</tr>
<tr>
<td>7</td>
<td>SAMP8 Vehicle</td>
<td>0+0</td>
</tr>
<tr>
<td>6</td>
<td>SAMP8 ORY-2001 Vehicle</td>
<td>1+0</td>
</tr>
<tr>
<td>7</td>
<td>SAMP8 ORY-2001 Vehicle</td>
<td>1+0</td>
</tr>
<tr>
<td>6</td>
<td>SAMP8 Vehicle ORY-2001</td>
<td>0+1</td>
</tr>
</tbody>
</table>

- The drug restored memory function after the deficit had developed
- The delayed start cohort (0+1) experienced the full benefit
- The early start (1+0) cohort continued to show significant benefit 1 month after treatment interruption

→ Disease modifying potential
PoC studies in SAMP8 mice

✓ The effect is driven by LSD1 but there is an additive / synergistic effect provided by the MAOB component

✓ ORY-2001 provides a dose dependent protective effect in the medium-term memory of mice, compared to age-matched SAMP8 mice
LSD1 function in the brain: LSD1-8a KO mice

Embryonic Development: Regular LSD1 expressed in the brain

Birth: A specific Neuro-spliced form of LSD1 is expressed in the brain

- Neurogenesis
- Neuronal differentiation
- Neurite extension

LSD1-8a KO mice (Zibetti et al, Wang et al)

- Neuronal differentiation ↓, Neurite extension ↓
- Long Term Memory ↓
- Induction of Egr ↓, Fos ↓, Npas4 ↓, Arc ↓
**Hippocampal gene expression changes induced by ORY-2001**

- **ORY-2001 up-regulated genes associated with improved cognitive function, neuroplasticity and memory, including:** Egr, Fos, Nr4a1, Npas4, Arc... i.e. the pharmacological intervention mimicks the stimulation of LSD1-8a, supports the observation of improved memory.

- **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.**
Hippocampal gene expression changes induced by ORY-2001

- ORY-2001 up-regulated genes associated with improved cognitive function, neuroplasticity and memory, including: Egr, Fos, Nr4a1, Npas4, Arc... i.e. the pharmacological intervention mimicks the stimulation of LSD1-8a, supports the observation of improved memory.

- 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.
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)

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

APP/PS1 mice
mutant APPswe
PSEN1dE9

APP/PS1 mice
mutant APPswe
PSEN1dE9

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

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

S100a9 upregulated in hippocampus, memory impairment, amyloid pathology
(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)
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 in Experimental Autoimmune Encephalomyelitis (EAE)

- Model for multiple sclerosis
  - C57BL/6 mice immunized s.c. with 100 μg of MOG35–55

- Treatment after onset of EAE symptoms (d11) during 2 weeks with:

ORY-2001 clearly reduced the Mean Clinical Score, ORY-LSD1 was less effective, Rasagiline appeared to marginally delay onset but effects were not significant.

- Increased cellularity in lymph nodes, spleen indicate reduced egress of lymphocytes
- Lower doses of ORY-2001 were also effective (0.5mpk and 0.05 mpk)
ORY-2001 greatly reduces infiltration of inflammatory cells and demyelination in the spinal cord of EAE mice.

Spinal cords were isolated at the end of treatment (26 days after immunization) and processed for histopathological analysis. Transverse cervical and lumbar sections selected at the peak of clinical disease were stained with Kluver-Barrera. Arrows point to areas of demyelination and inflammatory cell infiltration. The mean number of demyelination plaques in the lumbar and cervical regions is shown, demonstrating absent or greatly reduced demyelination in the cervical and lumbar sections of ORY-2001 treated animals.
LSD1 plays a role in expression of neuronal genes thru demethylation of H3K4 and H3K9
ORY-2001 Phase I Clinical Trial - SAFETY

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

- **Multiple Ascending Dose (MAD):** five dose levels x 5 days were initially tested in young volunteers, no relevant/significant side effects observed: to test possible hematological effects an additional cohort was added

- The Phase I study has provided detailed information that allows us to model the dose response in human vs preclinical species and to establish a safe administration scheme for long term efficacy studies of ORY-2001 in Phase II trials in neurodegeneration and neuroinflammation.
ORY-2001 DEVELOPMENT TIMELINE

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

<table>
<thead>
<tr>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3Q2015</td>
<td>4Q2015</td>
<td>1Q2016</td>
</tr>
</tbody>
</table>

CMC / 4W Reg Tox  IB / IMPD  CTA  Phase I  (SAD)  Phase I  (MAD)  9M Reg Tox

Additional Preclinical Work to Broaden CDP

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 an emerging field with high interest from Pharma (select acquisitions: Roche/Tensha; Celgene/Acetylon; Merck/OncoEthix) and from Specialized Investors (Imago, Constellation)
✓ High quality science and a broad patent portfolio on LSD1, one of the hottest targets in this area (GSK, Celgene, Incyte, Takeda). Competitive Patent portfolio with +20 patent families, many already granted in USA
✓ ORYZON is a pioneer in epigenetics

Platform + Broad Product Pipeline: aim for 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 (RG6016)
✓ A dual LSD1-MAOB inhibitor finishing Phase I and with PoC in in several human disease animal models
✓ Three Phase IIA-IIB clinical trials expected to start in 2H 2017
✓ A third LSD1 inhibitor being developed for an orphan disease and Phase I expected in 2017
✓ Other epigenetic programs in development

Financials and Governance

✓ Cash runway expected until 2H-2019, but wanting to invest more to capture the upside of our Phase IIs in ORY-2001 and other clinical programs
✓ A dynamic and capital efficient company with excellent know-how (40 people)
✓ An experienced public company board with thorough understanding of the industry
✓ Top governance according to public company standards
$28M in cash and cash equivalents at the end of the year (Dec 31st, audited accounts by Grant Thornton)

Oryzon Raised EUR 18.2M through a Private Placement with US and European Investors (March 31st)

- The offering included institutional investors specialized in healthcare and life sciences from the US, Spain and rest of Europe.
- The majority of the funds were raised from international investors, reinforcing and diversifying the Company's shareholder base.
- The Company intends to use the net proceeds from the capital increase to finance its research and development of clinical pipeline candidates and for working capital and general corporate purposes.

<table>
<thead>
<tr>
<th>ORYZON GENOMICS SA</th>
</tr>
</thead>
<tbody>
<tr>
<td>BALANCE SHEET DATA (AUDITED)</td>
</tr>
<tr>
<td>(US $, amounts in thousands)</td>
</tr>
<tr>
<td>December 31, 2016</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
</tr>
<tr>
<td>Marquetable securities</td>
</tr>
<tr>
<td>Total Assets</td>
</tr>
<tr>
<td>Deferred revenue</td>
</tr>
<tr>
<td>Total Stockholders' equity</td>
</tr>
</tbody>
</table>
On April 7th 2017, Oryzon Genomics had 1,514 shareholders.

- The 45.46% of the shares are owned by the reference shareholders.

All the Company shares are common shares, without any additional options or warrants.
## ANTICIPATED ORYZON CATALYSTS

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

### 2015-16
- **CONSOLIDATION PERIOD**
  - ORY-1001: Clinical Data Presented at ASH-2016
  - Second Asset (ORY-2001 in clinic development)

### 2017
- ORY-1001: LEAD CANCER ASSET
  - FPI in Phase I SCLC by Roche 1Q
  - Phase I-IIA study expected to formally close 2Q
- ORY-2001: LEAD CNS ASSET
  - Top Line Phase I (ADPD-2017 Conference) 1Q
  - Anticipated demonstration of human target engagement 2Q
  - Anticipated Phase I Completion 2Q
  - Anticipated filing CTA / IND for Phase II-A in MS 2H
  - Anticipated filing CTA / IND for Phase II-B in AD 2H
  - Anticipated filing CTA / IND for Phase II-A in HD 2H
  - Anticipated FPI in a Phase II-A study in MS 2H
- ORY-3001:
  - Anticipated filing CTA / IND for Phase I study on an orphan indication yet to be disclosed 2H

### 2018
- ORY-2001: LEAD CNS ASSET
  - Anticipated FPI in a Phase II-B study in AD 1Q
  - Anticipated FPI in a Phase II-A study in HD 1Q
THANK YOU VERY MUCH!
CARLOS BUESA
C.E.O. & President
cbuesa@oryzon.com

EMILI TORRELL
BDO
etorre@oryzon.com

ANNA K. BARAN
IR Director
abaran@oryzon.com
APPENDIX
CARLOS BUESA: Chairman of the Board & Founder
PhD in Biochemistry and Molecular Biology. Author of more than thirty papers and patents internationally. In 2000, he founded Oryzon Genomics, and since 2001 he has served as Chief Executive Officer and Chairman of the Board of Directors. He has taken several advanced programs on finance, business development, negotiation skills and human resources. He is also PADE at the IESE Business School. He is a Board Member of the VC Fund Inveready and Deputy President of the Spanish BioIndustry Association.

TAMARA MAES: ViceChairman of the Board & Founder
PhD in Biotechnology from the University of Ghent, Belgium. She has produced over twenty scientific papers and patents internationally and has developed innovative HTS methods for functional genomics. She founded Oryzon and since 2001 she has been the CSO. She has created the Epigenetic Program of the Company. She is SAB member on several public institutions as CSIC and private companies. Since 2016, she has been appointed Scientific Advisor of the ADDF

Josep Ma Echarri Torres
Bachelor degree both in Economics and Actuarial science, and a master in finance from ESADE Business School. He is a founding partner and Chief Executive Officer of Inveready, a venture fund specialized in seed capital investments with investments in more than 20 Biotech companies with c. of EUR100 million under management. He sits in the board of a number of biotechnology companies like PaloBiofarma, Ability Pharmaceuticals and others. Previously, he was Chief Financial Officer of Oryzon from 2003 to 2007. He is also a Board member of other public companies like FERSA, Independent Board Mmember and president of the Audit Committee (FRS.MC), AGILE (MAB.AGIL) or ATRYS Health (MAB.ATR). He also serves as Senior VicePresident and board member of the public telecommunication company MasMovil, the fourth largest telco company in Spain, where he was leading a financing round of +1B Euro.
Antonio Fornieles Melero (Independent)
Lead Director
He brings to Oryzon over 30 years of audit experience. Mr. Fornieles was a partner at KPMG since 1994 to the end of 2014. He was responsible for the audit function at KPMG Spain and then Global Chief Operating Officer for the audit function at KPMG. On March 1st, 2016, he was appointed as President of ABENGOA, a listed company of the infrastructure sector, to lead its financial restructuring process and prepare a new viability plan of the company. He resigned on November 22nd, 2016 after a restructuring agreement was entered into with new investors and bank creditors to allow the financial viability of the company. He was a lecturer in the faculty of economics and business studies at the University of Cádiz. He received a B.S in Economics and Business Studies from the Complutense University of Madrid and a Diploma in Business Management from the San Telmo Business School.

Ramón Adell Ramón (Independent)
President of the Audit and Compliance Committee.
He is Full Professor of Financial Economics and Accounting at the University of Barcelona. Mr. Adell has been an Independent Director of Gas Natural SDG SA since 2010, chairman of its Audit Committee since 2012, and a member of its Strategic Committee since 2015. He was also a key member of the team that developed and implemented the financial derivatives market in the Spanish Stock Exchange. Mr. Adell has published a number of books and articles and is a regular speaker at conferences on business management. He holds a Ph.D in Economics and Business Administration and a B.A. in Law. Mr. Adell is also a Certified Public Accountant and Financial Analyst.

Isabel Aguilera Navarro (Independent)
President of the Remunerations and Nominations Committee.
She is currently a Non-Executive Director and adviser to various companies, such as Indra, Banco BMN, AEGON-Spain and EGASA. Her professional career has mostly been related to the field of information technology. In the past, she has held executive positions in multinational companies such as Airtel, Olivetti and NH Hoteles. She has been CEO for DELL in South Europe, CEO for Google Inc. in Spain and Portugal and President for General Electric in Spain and Portugal. She holds a degree in Architecture and Urban Planning and an MBA from the IE Business School.
Najeti Capital, S.A., represented by Thibaud Durand
Graduated from the Ecole Superieure de Commerce de Reims (France) held a European Management Program (Icade E4 - European Management) from the Universidad Pontificia Comillas (Madrid, Spain) and an MBA, International in IE (Instituto de Empresa, Madrid, Spain). He has been a member of the Board of Directors of several companies and organizations such as ARC International (France), The Genetics Company (Switzerland), EuropaBio (Spain), ASCRI (Spain). Currently he is a member of the Board of SAS Najeti, and is Executive Vice President of Capital Najeti SAU, and member of the Board of Palau Pharma and EcoSolution.

Najeti, S.A.S., represented by Ignacio Manzanares Secades
PhD in Organic Chemistry from the Autonomous University of Madrid (1991). In 2003 he studied top management (PDG) at IESE Business School, University of Navarra. He has held various positions in the biotechnology company PharmaMar for 14 years, the last 6 as Vice President of Research & Development.
He was Director General at the Catalan Institute of Chemical Research (2003-2007), Scientific Director at Najeti CAPITAL SA (2007-2011) and Director at the TECNALIA Health Division (2011-2015). He was a member of scientific councils and has served as Scientific Consultant to multiple biotechnology companies. He is currently Scientific and Advisor Strategic at Najeti CAPITAL SA and other technology companies.

Najeti, S.L., represented by Roberto del Navío Alonso
Bachelor of Law and International, MBA (Instituto de Empresa). Since 1999, currently CEO and Managing Director in Spain of French investment company Najeti Capital SA dedicated to investing in innovative technology companies in Spain and the U.S. (Silicon Valley) in strategic sectors (biotechnology, telecommunications, security, renewable energy). He has been director in more than ten Boards of Directors and various committees. Residing in Colorado (USA) he is now the CEO of UVAX Concepts USA Inc. He is also Knowledge Manager of the Innovation and Technology at the EOI (School of Industrial Organization of Madrid).