A GLOBAL LEADER IN EPIGENETICS

INVESTOR PRESENTATION
MADX: ORY
JUNE 2017
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COMPANY HIGHLIGHTS

✓ MADX: ORY  A **publicly traded** company on the Spanish Stock Exchange. Aprox. $115-120m Market Cap

✓ 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 fully developed in-house (+20 patent families)

✓ **Raised €32M** (in 2015-2016).

✓ 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.

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

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:
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

• 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
Oryzon announces appointment of new Chief Medical Officer and expansion of its Medical Department

Marketwire  May. 16, 2017, 08:00 AM
BARCELONA, SPAIN and CAMBRIDGE, MA

Dr. Roger A. Bullock, a world KOL in the field, graduated in Physiological Sciences at Keble College in Oxford University and got his MB.BS at London University. He specialized in Old Age medicine and in neurodegenerative and neuropsychiatric disorders.

He has extensive experience as clinical researcher, having participated in more than 70 clinical trials in Alzheimer's disease and other CNS conditions. Over his 30-year research career, he has authored and co-authored more than 100 peer-reviewed publications and book chapters in this domain and presented at numerous conferences. Recently he has been working as a consultant for companies active in the CNS space, including Lilly and Merck.
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

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**EPIGENETICS: THE CRITICAL ROLE OF HISTONE CODING**
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 IIB</th>
<th>PHASE III</th>
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<tr>
<td>ORY-1001 (*)</td>
<td>LSD1</td>
<td>Leukemia (**)</td>
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<td>ORY-2001</td>
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(*) ORY-1001 is also known under Roche's ID codes RG6016 and RO7051790

(**) 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 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

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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

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A big market potential
**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)

![Graph showing patient 0701's response](image-url)
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.

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.

ROCHE has already started a Phase I with ORY-1001 (RG6016) in Small Cell Lung Cancer (data expected in 2H 2019).
HDACi improves HD symptoms in animal models
HDAC2 inhibition recovers memory on the AD bi-tg CK-p25 Tg mouse model
HDAC inhibition improves FTD
HDAC inhibition improves MS in EAE models

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 is an epigenetic modulator that regulates gene expression

- The first characterized histone demethylase: demethylates mono- and dimethyl-H3K4 in association with transcription repressors

- Also reported to demethylate mono- and dimethyl-H3K9, E2F1, p53, DNMT1

- LSD1 plays an important role in the development of CNS

- **LSD1 is a key component of different CNS transcriptional complexes** interacting with different transcription factors and very often with HDAC1 and HDAC2
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

✓ 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 → finishing
  Phase I
  ✓ Alzheimer’s Disease is lead indication → Phase IIA Planned
  ✓ Additional indications: MS and HD → Phase IIA Planned

✓ Biomarkers identified
✓ Exclusively owned by Oryzon
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

Xiaoci Li, Chao Li, Xiu-fang Cui, Yue Zhang, Gui-rong Zhang, Peng Li, Huang Huang, Yue-ying Zhao, Xiao-chen Bo, Sheng-qi Wang, Wen-xia Zhou and Yong-xiang Zhang

1 Department of Neuroimmunopharmacology, Beijing Institute of Pharmacology and Toxicology, Beijing, China
2 Department of Neuroimmunopharmacology, Beijing Institute of Pharmacology and Toxicology, Beijing, China

Edited by: Guohua Song, The City University of New York, USA

Received by: Josef M. Depestele, Garcia, University Pablo de Olavidea, Seville, Spain

Received by: Jose M. Depestele Garcia, University Pablo de Olavidea, Seville, Spain

Correspondence: Xiaoci Li and Yong-xiang Zhang, Department of Neuroimmunopharmacology, Beijing Institute of Pharmacology and Toxicology, 27 Xingfu Road, Haidian District, Beijing, 100193, China.

E-mail: chaozhi@126.com, chaoz@pku.edu.cn

These authors have contributed equally to this work.

Harboring the behavioral and histopathological signatures 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 RAFT1, MAPT, PTGS2, CDKN2A, CAMK2A, NTRK2, AGER, ADRB1K, MCMAP and STUS1, which may have implicated the dysfunction of biological processes in the brains of SAMP8 mice. Specifically, we found microRNAs, including miR-1, miR-124, miR-134, miR-145, miR-155, miR-18a, miR-22, miR-26a, miR-101, miR-106b, and miR-125b, that might regulate the expression of genes 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, synthetic core network, apoptosis

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>
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<tr>
<td>Amyloid plaques</td>
<td>Yes</td>
<td>Late&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Yes</td>
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<tr>
<td>Phosphorylated tau</td>
<td>Increased</td>
<td>Increased</td>
<td>In some models</td>
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<tr>
<td>Cerebral amyloid angiopathy</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Neuron loss</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<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>
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<tr>
<td>Glossis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<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>
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<tr>
<td>Circadian rhythm disturbances</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Oxidative damage</td>
<td>Yes</td>
<td>Yes</td>
<td>4 months to 8 months</td>
</tr>
</tbody>
</table>

<sup>a</sup> 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>
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<tr>
<td>6</td>
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<td>Vehicle</td>
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<td>7</td>
<td>SAMP8 Vehicle</td>
<td>Vehicle</td>
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<td>SAMP8 ORY-2001</td>
<td>ORY-2001</td>
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<td>SAMP8 ORY-2001</td>
<td>Vehicle</td>
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<tr>
<td></td>
<td>SAMP8 Vehicle</td>
<td>ORY-2001</td>
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✓ 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
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


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.
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**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)

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

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

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

- 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)

**APP/PS1 mice**
mutant APPswe
PSEN1dE9

- 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 in Experimental Autoimmune Encephalomyelitis (EAE)

- Experimental autoimmune encephalomyelitis (EAE) is the most commonly used experimental model for human MS
- Dose response effect of ORY-2001 on chronic active EAE at 3-0.05 mg/kg, p.o. (therapeutic setting):

ORY-2001 shows effect on clinical score at dose levels down to 0.05 mg/kg p.o.
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.
Oryzon plans to pursue Multiple Sclerosis alongside Alzheimer’s disease for ORY-2001
ORY-2001 Phase I Study

A Phase I study with 106 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
Orally administered ORY-2001 was well tolerated

No clinically significant changes were found in the laboratory tests, vital signs, ECGs, physical findings, or adverse events incidence. No SAEs have been reported in SAD or MAD. Tolerance in elderly similar to young volunteers.
TOXICOLOGICAL DATA, THERAPEUTIC WINDOW AND PKs

HUMAN PK in Multiple Ascending Dose

<table>
<thead>
<tr>
<th>MAD dose Mean (CV%)</th>
<th>$T_{max}$ ss (h)*</th>
<th>$C_{max}$ ss (pg/mL)</th>
<th>$AUC_{0-t}$ (h·pg/mL) (D1)</th>
<th>$AUC_{0-t}$ ss (h·pg/mL) (D5)</th>
<th>$T_{1/2}$ (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2 mg</td>
<td>5.1 (1.7%)</td>
<td>2317 (17%)</td>
<td>18733 (21%)</td>
<td>37686 (18%)</td>
<td>22 (25%)</td>
</tr>
<tr>
<td>0.6 mg</td>
<td>2.25 (1.4%)</td>
<td>7654 (39%)</td>
<td>50567 (28%)</td>
<td>113676 (49%)</td>
<td>22 (33%)</td>
</tr>
<tr>
<td>1.0 mg</td>
<td>1.83 (1.7%)</td>
<td>14108 (43%)</td>
<td>95081 (35%)</td>
<td>198736 (38%)</td>
<td>23 (14%)</td>
</tr>
<tr>
<td>1.5 mg</td>
<td>1.17 (0.4%)</td>
<td>23607 (18%)</td>
<td>137960 (17%)</td>
<td>298693 (17%)</td>
<td>22 (11%)</td>
</tr>
<tr>
<td>2.5 mg</td>
<td>2.17 (1.7%)</td>
<td>49921 (59%)</td>
<td>292248 (45%)</td>
<td>634208 (65%)</td>
<td>22 (11%)</td>
</tr>
</tbody>
</table>
CL01-ORY-2001: TE in human PBMCs confirmed in the MAD cohorts

The graph shows mean ± SD LSD1 TE per cohort in PBMC samples obtained from human healthy volunteers at 12, 108, and 192 h after the first dose of 5-daily ORY-2001 repeated oral doses in the MAD cohorts (dose levels of 0.2 to 4.0 mg).

The MAD analysis of accepted samples demonstrated:

- Overall **dose-dependent response**
- A tendency for **saturation** in the TE effect

LSD1 TE at **Multiple Ascending Dose (MAD)** (levels 0.2 to 4.0 mg) of ORY-2001
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

ORY-2001 CDP

<table>
<thead>
<tr>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>3Q2015</td>
<td>4Q2015</td>
<td>1Q2016</td>
</tr>
<tr>
<td></td>
<td>2Q2016</td>
<td>3Q2016</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4Q2016</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1H2017</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2H2017</td>
</tr>
</tbody>
</table>

- CTA
- Phase I (SAD)
- Phase I (MAD)
- 9M Reg Tox
- Additional Preclinical Work to Broaden CDP
- Phase II Dossier

PLANNED ORY-2001 CDP

- Phase II-A 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)

✓ ORY-2001 finishing Phase I and with additional PoC in in several human disease animal models

✓ Three Phase II clinical trials expected to start in 4Q 2017 – 1Q 2018

✓ ORY-3001, a third LSD1 inhibitor, 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.
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

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

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

ORY-1001: LEAD CANCER ASSET
- FPI in Phase I SCLC by Roche 1Q
  - Phase I-IIIA study expected to formally close 2Q

ORY-2001: LEAD CNS ASSET
- Top Line Phase I (ADPD-2017 Conference) 1Q
  - Phase I Final Data (AAIC-2017 London) 2Q
  - Anticipated filing CTA / IND for Phase II-A in AD (CTAD-2017 Boston) 4Q
  - Additional Preclinical Data of ORY-2001 in animal models of other human CNS disorders (SFN-2017 Washington DC) 4Q
  - Additional Preclinical Data of ORY-2001 in MS (ECTRIMS-2017 Paris) 4Q
  - Anticipated filing CTA / IND for Phase II-A in MS 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
THANK YOU VERY MUCH!

CARLOS BUESA
C.E.O. & President
cbuesa@oryzon.com

EMILY TORRELL
BDO
etorrell@oryzon.com

ANNA K. BARAN
IR Director
abarann@oryzon.com
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.

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
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 (lقاء 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 VicePresident 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).