ORYZON reports results and corporate update for 4th quarter and year ended December 31, 2020

MADRID, SPAIN and CAMBRIDGE, MA, UNITED STATES, February 22nd, 2021 – Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with strong unmet medical need, today reported financial results for the fourth quarter of 2020 and provided an update on recent developments.

Dr Carlos Buesa, Oryzon's Chief Executive Officer, said: "Oryzon made strong progress in 2020, achieving a number of important clinical milestones that further our pioneering work in personalized medicine in epigenetics. New clinical data in acute myeloid leukemia corroborate the strong clinical activity of iadademstat and signals a clear path ahead for the development of the molecule in oncology. In CNS, the regulatory green light to start our first Phase IIb study in borderline personality disorder and the collaboration in precision medicine with Columbia University to start an observational study in *Setd1a*-deficient schizophrenia patients are significant steps forward in our epigenetic approach to CNS. We finished the year with a reinforced cash position of $48.6 million, which provides funding for the further developing of our exciting pipeline until 1Q 2023."

Fourth Quarter and Recent Highlights

Iadademstat in oncology:

- Additional positive efficacy data from the ongoing Phase II trial ALICE, investigating iadademstat in combination with azacitidine in acute myeloid leukemia (AML), was presented at the ASH-2020 conference in December 2020:
  - Robust signals of clinical efficacy, with reported objective responses in 11 out of 13 evaluable patients (85% ORR): of these, 64% were complete remissions (7CR/CRi).
  - Encouraging duration of responses, with 86% of the CR/CRi lasting more than 6 months.
  - Longest remission was 690 days, still ongoing.
  - Several patients had also improved or overcome their dependency on blood transfusions.
  - Iadademstat and azacitidine combination shows a good safety profile.
- FDA Orphan Drug Designation granted to iadademstat for the treatment of AML. The drug now has orphan designation in both U.S. and EU.

Vafidemstat in neurological and inflammatory disease:

- Received approval from the Spanish Drug Agency (AEMPS) for its Clinical Trial Application (CTA) to conduct a Phase IIb clinical trial with vafidemstat in patients with Borderline Personality Disorder (BPD). The study, named PORTICO, is a multicenter, double-blind, randomized, placebo-controlled Phase IIb to evaluate the efficacy and safety of vafidemstat in BPD patients. The trial has two primary objectives: reduction of aggression/agitation and overall BPD improvement. The study will

include 156 patients, with 78 patients in each arm, and has a pre-defined interim analysis to adjust the sample size in case of excessive variability around the endpoints or an unexpectedly high placebo rate. Sites in the U.S., Spain and at least two other European countries will participate in the trial, with two Spanish hospitals activated in the first stage.

- Entered pioneering precision medicine collaboration in schizophrenia with researchers from Columbia University in New York. The goal is to perform an exhaustive functional psychometric characterization of individuals carrying mutations in the *Setd1a* gene to build a foundation for a subsequent precision psychiatry clinical trial with vafidemstat for SETD1A-associated psychiatric disorders. SETD1A is a histone methyltransferase that is a key schizophrenia susceptibility gene. The collaboration also includes fundamental research in preclinical *Setd1a* models.
- The precision medicine collaboration with the Institute of Medical and Molecular Genetics (INGEMM) of the La Paz University Hospital in Madrid in patients with Phelan-McDermid Syndrome (PMS) is advancing. The first patients have been monitored for functional impairment using a set of diverse validated scales in the field. These activities will continue with more genetically characterized PMS patients and are expected to be concluded by 1Q 2021. The aim is that this cognitive, behavioral and functional baseline assessment of PMS patients will inform a future clinical study with vafidemstat.
- Continued preparations for a new Phase IIb clinical trial (EVOLUTION) to evaluate vafidemstat's efficacy on negative symptoms and cognition in schizophrenia patients. This project is partly funded by public funds from the Spanish Ministry of Science and Innovation and will be performed in collaboration with the Research Institute of Vall d'Hebrón (VHIR) in Barcelona.
- The ongoing study in severe Covid-19 patients, named ESCAPE, continues recruitment. This is an open-label, randomized, double arm Phase II trial to assess the efficacy and tolerability of vafidemstat in combination with standard of care, to prevent progression to Acute Respiratory Distress Syndrome (ARDS). The study is initially designed to recruit 40 patients but may be upsized if necessary. Recruitment has proceeded vigorously during 4Q 2020.

Financial Update: Fourth Quarter 2020 Financial Results

Research and development (R&D) expenses were $3.4 and $13.6 million, respectively, for the quarter and 12 months ended December 31, 2020, compared to $3.6 and $12.7 million, respectively, for the quarter and 12 months ended December 31, 2019. The $0.9 million increase was driven primarily by expenses associated with advancing the company's clinical trials.

General and administrative expenses were $0.8 and $3.5 million, respectively, for the quarter and 12 months ended December 31, 2020, compared to $0.5 and $3.2 million, for the quarter and 12 months ended December 2019.

Net losses were $1.2 and $5.3 million, respectively, for the quarter and 12 months ended December 31, 2020, compared to net losses of $0.8 and $4.3 million, respectively, for quarter and 12 months ended December 2019.

Negative net result of $4.2 million (-$0.08 per share) for the 12 months ended December 31, 2020, compared to a negative net result of $4.1 million for the 12 months ended December 31, 2019.

Cash, cash equivalents and marketable securities totaled $48.6 million as of December 31, 2020, compared to $39.6 million as of December 31, 2019.

ORYZON GENOMICS, S.A.
BALANCE SHEET DATA (AUDITED)[1]
(Amounts in thousands US $)

	December 31st, 2020	December 31st, 2019
Cash and cash equivalents	48.599	39.430
Marketable securities	0	159
Total Assets	115.478	89.946
Deferred revenue	0	0
Total Stockholders' equity	93.175	68.648

ORYZON GENOMICS, S.A.
STATEMENTS OF OPERATIONS (AUDITED)1
(US $, amounts in thousands except per share data)

	Three Months Ended December 31st		Twelve Months Ended December 31st	
	2020	2019	2020	2019
Collaboration Revenue	0	0	0	0
Operating expenses:				
Research and Development	3.376	3.553	13.591	12.715
General and administrative	776	516	3.484	3.185
Total operating expenses	4.152	4.069	17.075	15.900
Loss from Operations	-4.152	-4.069	-17.075	-15.900
Other income, net	2.904	3.301	11.805	11.589
Net Loss	-1.248	-768	-5.270	-4.312
Net Financial & Tax	-143	-296	1.098	174
Net Result	-1.391	-1.064	-4.172	-4.138
Loss per share allocable to common stockholders:				
Basic	-0,03	-0,02	-0,08	-0,10
Diluted	-0,03	-0,02	-0,08	-0,10
Weighted average Shares outstanding				
Basic	52.761.554	45.488.554	49.234.647	41.589.158
Diluted	52.761.554	45.488.554	49.234.647	41.589.158

[1] Spanish GAAP

* Exchange Euro/Dollar (1.227 for 2020 and 1.123 in 2019)

About Oryzon

Founded in 2000 in Barcelona, Spain, Oryzon (ISIN Code: ES0167733015) is a clinical stage biopharmaceutical company considered as the European champion in Epigenetics. Oryzon has one of the strongest portfolios in the field. Oryzon's LSD1 program has rendered two compounds, vafidemstat and iadademstat, in Phase II clinical trials. In addition, Oryzon has ongoing programs for developing inhibitors against other epigenetic targets. Oryzon has a strong technological platform for biomarker identification and performs biomarker and target validation for a variety of malignant and neurological diseases. Oryzon has offices in Spain and the United States. Oryzon is one of the most liquid biotech stocks in Europe with +90 M shares negotiated in 2020 (ORY:SM / ORY.MC / ORYZF US OTC mkt). The company had a +25% stock performance in 2020 and its cash runway is expected to extend till 1Q2023. For more information, visit www.oryzon.com

About Iadademstat

Iadademstat (ORY-1001) is a small oral molecule, which acts as a highly selective inhibitor of the epigenetic enzyme LSD1 and has a powerful differentiating effect in hematologic cancers (See Maes et al., Cancer Cell 2018 Mar 12; 33 (3): 495-511.e12.doi: 10.1016 / j.ccell.2018.02.002.). A first Phase I/IIa clinical trial with iadademstat in refractory and relapsed acute leukemia patients demonstrated the safety and good tolerability of the drug and preliminary signs of antileukemic activity, including a CRi. Beyond hematological cancers, the inhibition of LSD1 has been proposed as a valid therapeutic approach in some solid tumors such as small cell lung cancer (SCLC), neuroendocrine tumors, medulloblastoma and others. Iadademstat has been tested in four clinical trials (two in monotherapy in SCLC and AML, and two in combination, in SCLC and AML) in more than 100 patients. In the combination studies, ALICE (ongoing), a Phase IIa trial in combination with azacitidine in elderly or unfit AML patients, and CLEPSIDRA (finalized), a Phase IIa trial in combination with platinum/etoposide in second line ED-SCLC patients, preliminary efficacy results have been reported.

About Vafidemstat

Vafidemstat (ORY-2001) is an oral, CNS optimized LSD1 inhibitor. The molecule acts on several levels: it reduces cognitive impairment, including memory loss and neuroinflammation, and at the same time has neuroprotective effects. In animal studies vafidemstat not only restores memory but reduces the exacerbated aggressiveness of SAMP8 mice, a model for accelerated aging and Alzheimer's disease (AD), to normal levels and also reduces social avoidance and enhances sociability in murine models. In addition, vafidemstat exhibits fast, strong and durable efficacy in several preclinical models of multiple sclerosis (MS). Oryzon has performed two Phase IIa clinical trials in aggressiveness in patients with different psychiatric disorders (REIMAGINE) and in aggressive/agitated patients with moderate or severe AD (REIMAGINE-AD), with positive preliminary clinical results reported in both. Additional finalized Phase IIa clinical trials with vafidemstat include the ETHERAL trial in patients with Mild to Moderate AD, where a significant reduction of the inflammatory biomarker YKL40 has been observed after 6 months of treatment, and the pilot, small scale SATEEN trial in Relapse-Remitting and Secondary Progressive MS. A Phase IIb trial in borderline personality disorder (PORTICO) has been recently authorized and the company is preparing a Phase IIb trial in schizophrenia patients (EVOLUTION). Vafidemstat is also being explored in a Phase II in severe Covid-19 patients (ESCAPE) assessing the capability of the drug to prevent ARDS, one of the most severe complications of the viral infection.

FORWARD-LOOKING STATEMENTS

This communication contains, or may contain, forward-looking information and statements about Oryzon, 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 believes that the expectations reflected in such forward-looking statements are reasonable, investors and holders of Oryzon 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 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 to the Spanish Comisión Nacional del Mercado de Valores (CNMV), which are accessible to the public. Forward-looking statements are not guarantees of future performance and have not been reviewed by the auditors of Oryzon. 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 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 on the date hereof. Except as required

by applicable law, Oryzon 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 press release is not an offer of securities for sale in the United States or any other jurisdiction. Oryzon's securities may not be offered or sold in the United States absent registration or an exemption from registration. Any public offering of Oryzon's securities to be made in the United States will be made by means of a prospectus that may be obtained from Oryzon or the selling security holder, as applicable, that will contain detailed information about Oryzon and management, as well as financial statements.

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