Pioneering personalized medicine in epigenetics

ORYZON

CORPORATE PRESENTATION

2Q-2021

ORY:SM / ORY.MC

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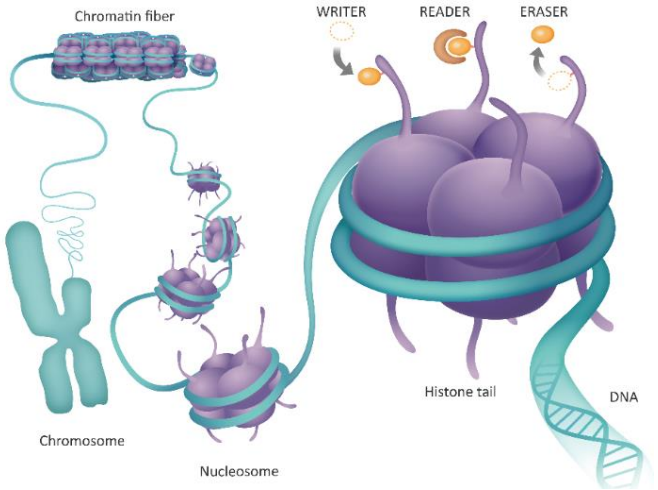
An epigenetic champion determined to bring new therapies to the patients



- Epigenetics expertise applied to oncology and CNS indications
- Two molecules with positive clinical data in humans
  Programs in Phase II
- A leading & growing epigenetic platform with an expanding pipeline
- One of the most liquid biotech stocks in Europe
- Cash & cash equivalents of ~$50m by Dec 31st 2020[1]
  Cash runway till 2023

(1) https://www.oryzon.com/en/news-events/news/oryzon-reports-results-and-corporate-update-4th-quarter-and-year-ended-december-31

Multiple shots on goal to address significant unmet medical needs

Iadademstat (ORY-1001)
LSD1 inhibitor

ONCOLOGY
Differentiation
Anti-cancer stemness

- AML / SCLC / Solid Tumors
- 4 Phase I/II clinical trials: ≈100 patients treated
- Safe & well tolerated
- Phase II in AML ongoing (+80% ORRs on evaluable pts)
- Phase II w ICIs in prep

AML: Acute Myeloid Leukemia
SCLC: Small Cell Lung Cancer

Vafidemstat (ORY-2001)
LSD1 inhibitor

CNS & COVID-19
Prosynaptic
Anti-neuroinflammatory

- BPD / SCZ / PMS / AD
- 6 Phase I/II clinical trials: +300 subjects treated
- Safe & well tolerated
- Efficacious in Phase IIa in aggression
- Phase IIb in BPD (ongoing) and SCZ (in prep)
- Deploying a precision medicine approach

BPD: Borderline Personality Disorder
SCZ: Schizophrenia
PMS: Phelan McDermid
AD: Alzheimer's Disease

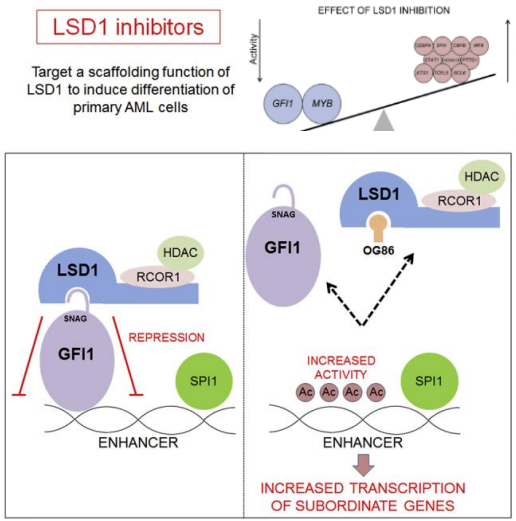
Growing pipeline

HDAC-6 inhibitor
Other epigenetic targets

- HDAC6i ready for nomination
- Additional leads against a variety of new targets

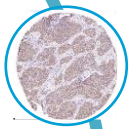
IADADEMSTAT
A Phase II Clinical Stage Agent in Oncology

Iadademstat (ORY-1001): The most potent LSD1 inhibitor



Modified from Maiques-Diaz et al. 2018, Cell Reports 22, 3641–3659

LSD1 is involved in different cancers and in cancer stemness



High levels of LSD1 often correlate with more aggressive forms of cancer and/or bad prognosis

Iadademstat is a highly potent and selective, oral LSD1i. First-in-class & best-in-class

Safe and well tolerated in Phase I and various Phase II studies (~100 subjects dosed)

Journal of Clinical Oncology

Produced strong differentiation and showed antileukemic activity in a FiM Phase I/Ib trial in R/R-AML

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Iadademstat produces differentiation and has antileukemic activity in R/R AML patients

original reports

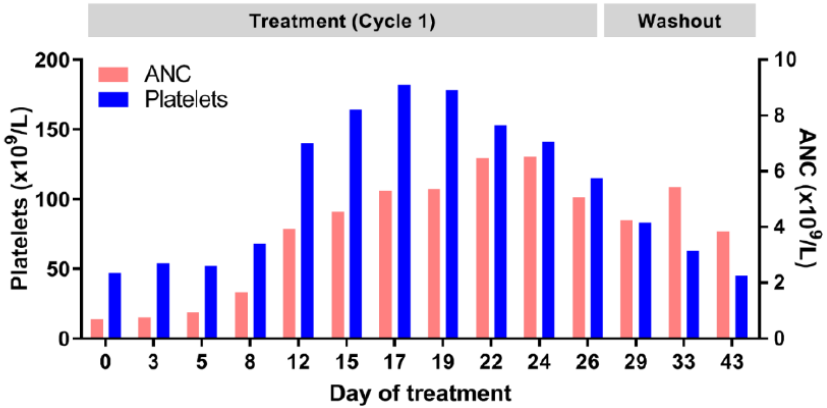
First-in-Human Phase I Study of Iadademstat (ORY-1001): A First-in-Class Lysine-Specific Histone Demethylase 1A Inhibitor, in Relapsed or Refractory Acute Myeloid Leukemia

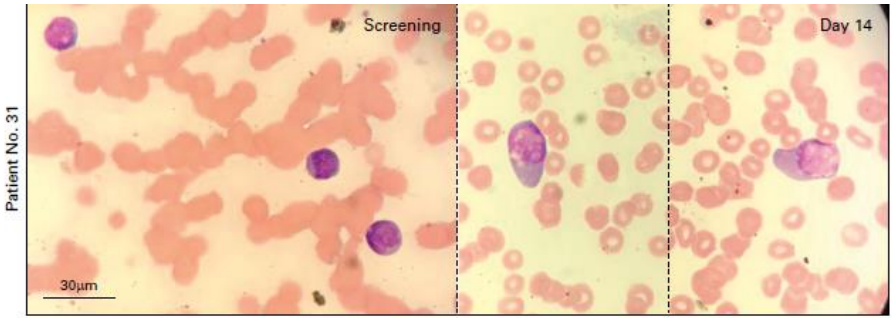
Olga Salamero, MD[1]; Pau Montesinos, MD[2,3]; Christophe Willekens, MD[4]; José Antonio Pérez-Simón, MD, PhD[5,6]; Arnaud Pigneux, MD, PhD[7]; Christian Récher, MD, PhD[8]; Rakesh Popat, MB, BS, PhD[9]; Cecilia Carpio, MD[1]; César Molinero, MD, PhD[10]; Cristina Mascaró, PhD[10]; Joaquim Vila[10]; M. Isabel Arévalo, PhD[10]; Tamara Maes, PhD[10]; Carlos Buesa, PhD[10]; Francesc Bosch, MD, PhD[1]; and Tim C. P. Somervaille, MBBS, PhD[11,12]

https://ascopubs.org/doi/full/10.1200/JCO.19.03250

41 R/R AML patients → **Good safety profile, Good pharmacology** → **Strong differentiation, Antileukemic activity**

Journal of Clinical Oncology®





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ALICE: A Phase II trial in AML with LSD1i in Combination with azacitidine in the Elderly or unfit

- Multicenter, single arm & open label study
- Up to 36 patients to be enrolled
- Primary endpoint: Safety and tolerability of the combo with hypomethylating agent azacitidine
- Secondary endpoints: Response; time to response; duration of response; overall survival

- Accrual status as per Dec 31, 2020:
  21 patients enrolled, of which:
  - 20 patients enrolled as per protocol
  - 14 evaluable patients (bone marrow aspirate available after C1)
  - 5 patients not evaluable (no available bone marrow aspirate)
  - 1 patient still in C1

Last report presented at

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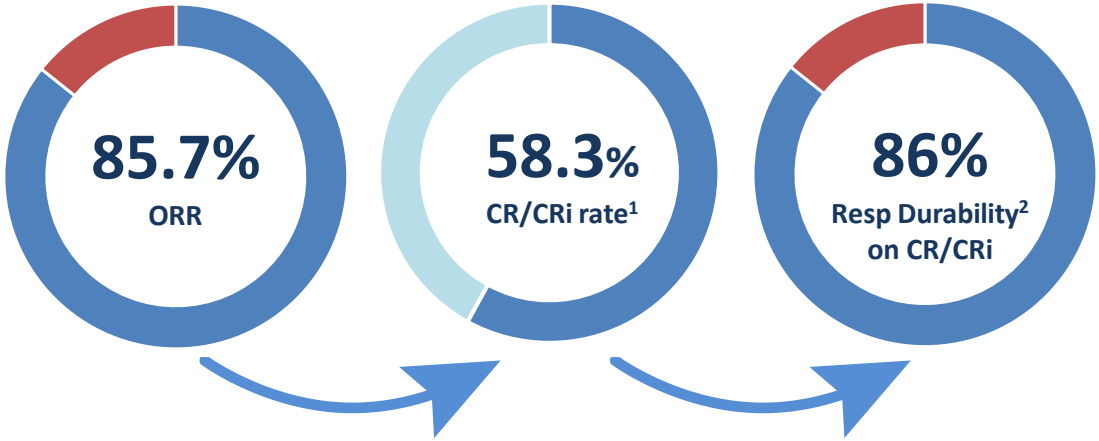
Phase II ALICE: High ORR rates, rapid onset of action, and clinically meaningful durability



- Long responses maturing: 4 Patients already >1year, longest EFS response (ongoing) >2 years
- 40% transfusion independent patients from those with >120d on treatment

Data from ASH2020 updated as per Dec 31 and corresponding to 14 evaluable patients
(1) % over the ORR population (2) Durability >6 months

- The combo appears as **safe and well tolerated**
- From the 41 SAEs, only 2 have been considered to be probably related to iadademstat (1 ICH and 1 DS)
- No QTc prolongation; no neuronal, hepatic, renal or any other organ toxicity

https://www.oryzon.com/sites/default/files/events/20201207_ASH2020_poster.pdf

Next clinical update: June 9-17 2021

EHA EUROPEAN HEMATOLOGY ASSOCIATION

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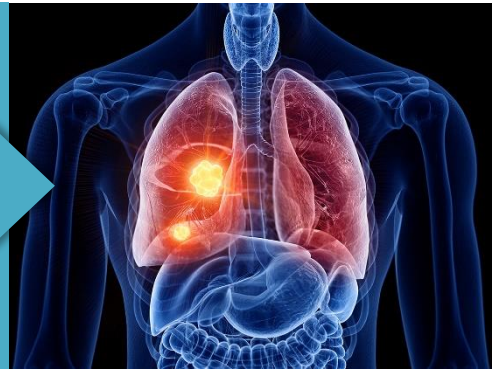
Iadademstat a therapeutic approach for SCLC with a well-defined MoA

SCLC is very aggressive and represents 10% to 15% of all lung cancers

LSD1 is a **well characterized target in SCLC**

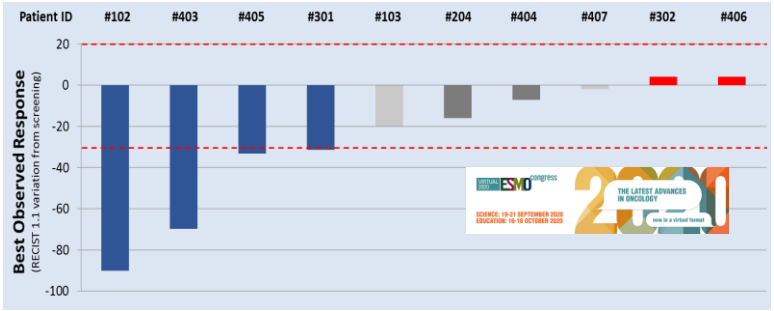


- Two clinical studies done with iadademstat in SCLC:
  - Phase I study (NCT02913443) (18 patients) → RP2D in mono
  - Phase IIa (CLEPSIDRA) (14 patients) → Safety in mono & Signs of clinical efficacy

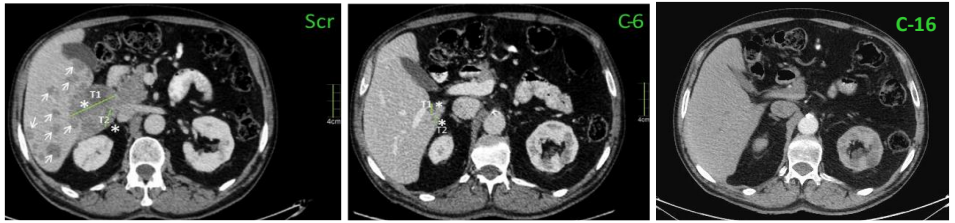
- Iadademstat produces **complete and durable tumor regression** in different **chemoresistant SCLC PDX models**
- Iadademstat is **efficacious in combos with platinum/etoposide and other agents as ICIs**
- Identified and patented **biomarkers** that differentiate SCLC tumors by sensitivity to LSD1i

Iadademstat: SCLC Phase II CLEPSIDRA - encouraging efficacy signals

- Open label, multicenter, Phase IIa study
- Biomarker selected, sensitive platinum 2L ED-SCLC patients
- iada in combination with 4-6 cycles carboplatin/etoposide (21 d/cycle). After chemo, iada could be administered alone
- 14 patients enrolled. Study finalized



- Platinum/etoposide in combo with iadademstat showed hematotoxicity
- Iada alone was safe and well tolerated. Toxicity disappeared when treated with iada alone
- Despite suboptimal dosing, efficacy signals were encouraging with **40% OR** and **mean DoR of 4.5 months**
- **60 % clinical benefit rate** (6/10 evaluable patients): 4PRs + 2 long-term SD
- One patient had 15 cycles in monotherapy, with a total tumor size reduction of 90% and a relative tumor size reduction during iadademstat monotherapy of 53%

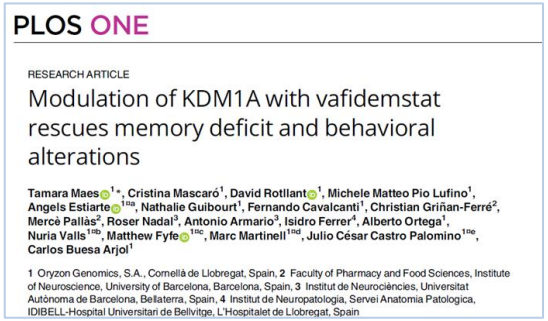


ODD granted for AML

- Potential for fast market regulatory path in AML. To be announced in 2H2021
- New trials in combo in preparation in solid and rare tumors. To be announced in 2H2021
- Strong clinical activity gravitating towards US in 2021-2023. Favoring a broad utilization through combinations and investigator-initiated trials
- A clear registrational strategy

VAFIDEMSTAT
A Phase II compound for CNS diseases

Vafidemstat (ORY-2001): a “Neuron-fixer” drug in Phase IIb



PLOS ONE

RESEARCH ARTICLE

Modulation of KDM1A with vafidemstat rescues memory deficit and behavioral alterations

Tamara Maes[1]*, Cristina Mascaró[1], David Rotllant[1], Michele Matteo Pio Lufino[1], Angels Estiarte[1ne], Nathalie Guibourt[1], Fernando Cavalcanti[1], Christian Griñan-Ferré[2], Mercè Pallàs[2], Roser Nadal[3], Antonio Armario[3], Isidro Ferrer[4], Alberto Ortega[1], Nuria Valls[1ne], Matthew Fyfe[1ne], Marc Martinell[1ned], Julio César Castro Palomino[1ne], Carlos Buesa Arjol[1]

1 Oryzon Genomics, S.A., Cornellà de Llobregat, Spain, 2 Faculty of Pharmacy and Food Sciences, Institute of Neuroscience, University of Barcelona, Barcelona, Spain, 3 Institut de Neurociències, Universitat Autònoma de Barcelona, Bellaterra, Spain, 4 Institut de Neuropatologia, Servei Anatomia Patologica, IDIBELL-Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain

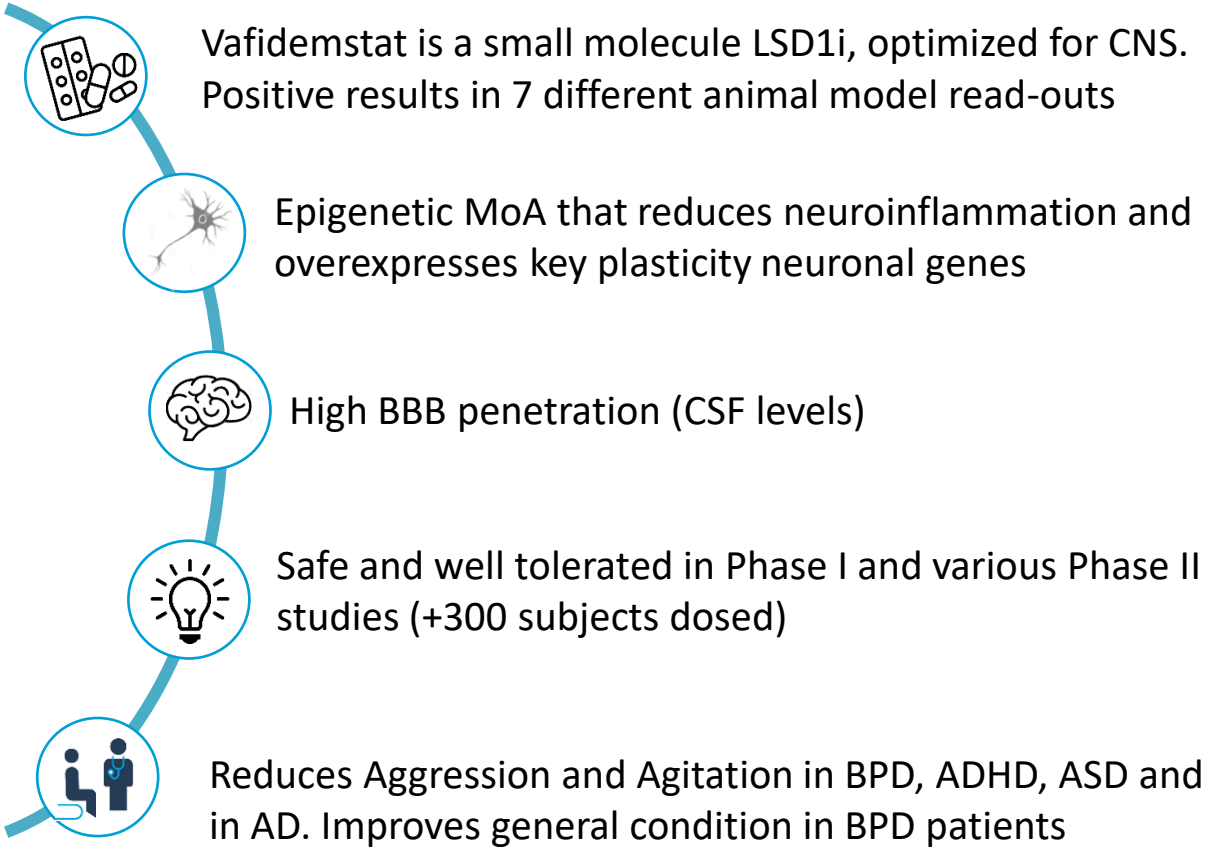
CNS Drugs
https://doi.org/10.1007/s40263-021-00797-x

ORIGINAL RESEARCH ARTICLE

First-in-Human Randomized Trial to Assess Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of the KDM1A Inhibitor Vafidemstat

Rosa María Antonijoan[1,2] · Juan Manuel Ferrero-Cafiero[1] · Jimena Coimbra[1] · Montse Puntes[1] · Joan Martínez-Colomer[1] · María Isabel Arévalo[3] · Cristina Mascaró[3] · Cesar Molinero[3] · Carlos Buesa[3] · Tamara Maes[3]

Accepted: 12 February 2021



Vafidemstat is a small molecule LSD1i, optimized for CNS. Positive results in 7 different animal model read-outs

Epigenetic MoA that reduces neuroinflammation and overexpresses key plasticity neuronal genes

High BBB penetration (CSF levels)

Safe and well tolerated in Phase I and various Phase II studies (+300 subjects dosed)

Reduces Aggression and Agitation in BPD, ADHD, ASD and in AD. Improves general condition in BPD patients

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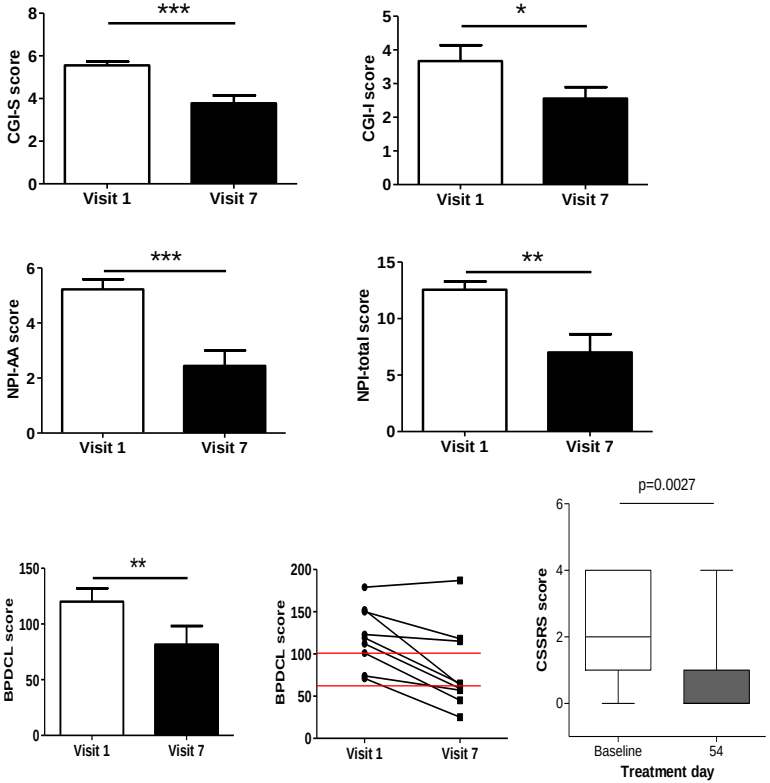
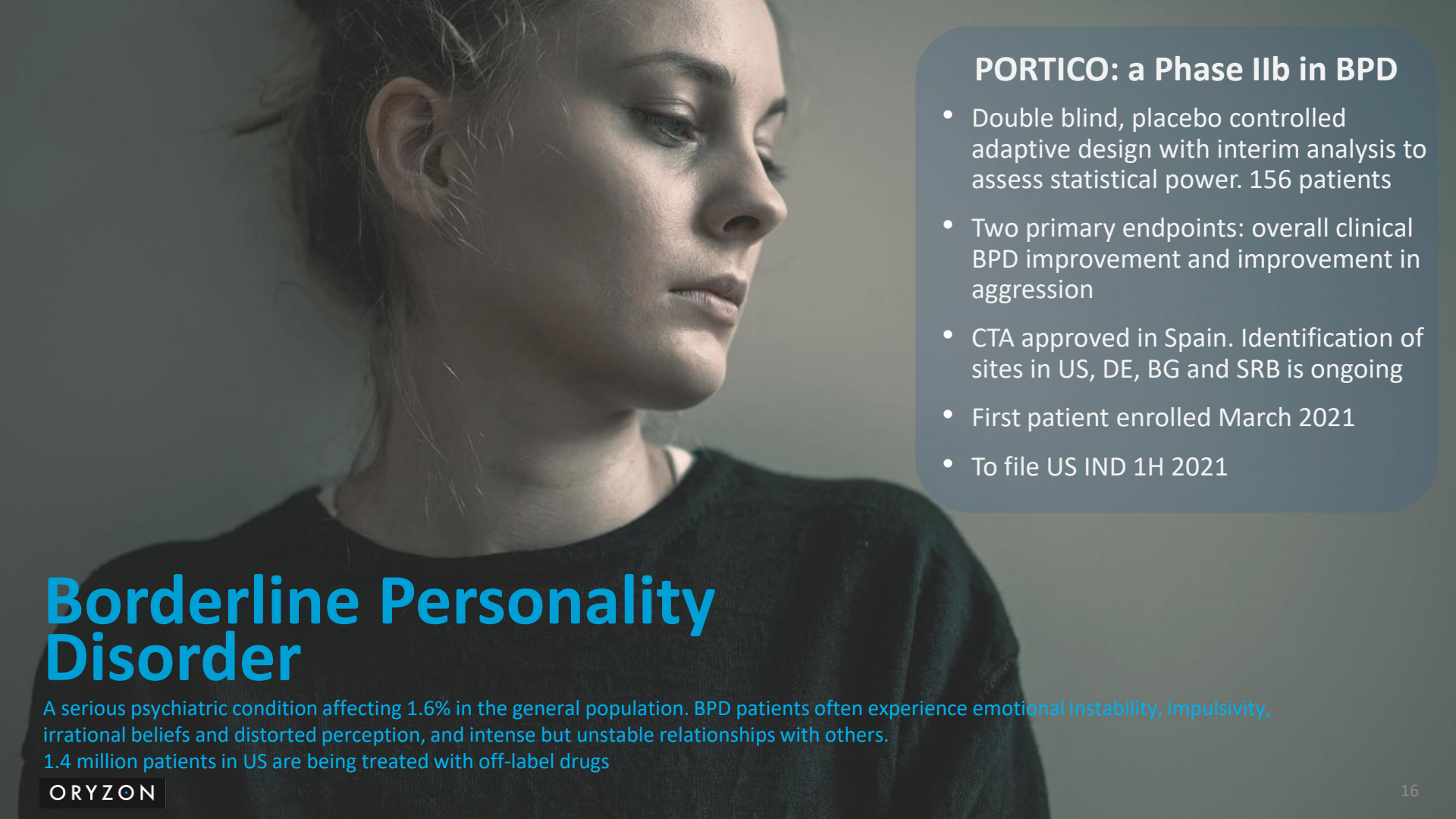
Vafidemstat reduces agitation and aggression: REIMAGINE, a Phase IIa basket trial in psychiatry

- Single center, single arm, open label study
- 30 patients, PPAS: n=23: 9 BPD, 6 ASD, 8 ADHD
- Primary endpoint: Safety & tolerability
- Secondary endpoints: Reduction of aggression / Other disease related outcomes
- Study finalized. Data presented at EPA-2020

Vafidemstat was safe and well tolerated, reduced agitation-aggression and improved overall status in BPD patients

BPD patients





PORTICO: a Phase IIb in BPD

- Double blind, placebo controlled adaptive design with interim analysis to assess statistical power. 156 patients
- Two primary endpoints: overall clinical BPD improvement and improvement in aggression
- CTA approved in Spain. Identification of sites in US, DE, BG and SRB is ongoing
- First patient enrolled March 2021
- To file US IND 1H 2021

Borderline Personality Disorder

A serious psychiatric condition affecting 1.6% in the general population. BPD patients often experience emotional instability, impulsivity, irrational beliefs and distorted perception, and intense but unstable relationships with others.
1.4 million patients in US are being treated with off-label drugs

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Schizophrenia

Prevalence of schizophrenia (SCZ) and related psychotic disorders in the US range between 0.25% and 0.64%.
No current approved treatments for the Negative Symptoms

EVOLUTION: a Phase IIb in SCZ

- Double blind, placebo controlled adaptive design with interim analysis to assess statistical power. 80 patients (40 vafi : 40 placebo)
- 2 arms, vafi as add-on to SoC. 6 months of treatment
- Primary endpoint: efficacy to address SCZ Negative and Cognitive Symptoms
- 6-10 sites
- Spanish government funded
- CTA submitted & FPI expected 1H 2021

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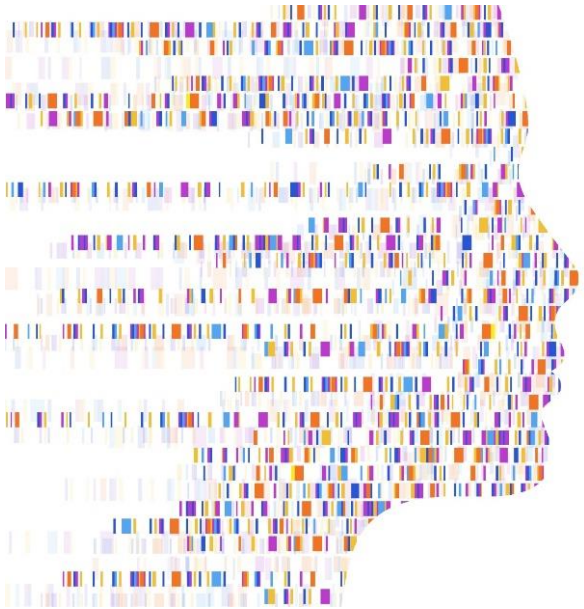
LSD1 and Precision Medicine in CNS



- LSD1 is mainly expressed in the CNS and plays a critical role in neurogenesis and the regulation of cortical development
- After birth, LSD1 contributes to neurite morphogenesis in the mammalian cortex
- LSD1 is the most abundant histone demethylase in the PFC
- LSD1 localizes in-vivo to enhancers and promoters of confirmed CNS disease risk genes
- LSD1 has been involved in neurodevelopmental diseases

Methylation is involved in SCZ and ASD; LSD1 inhibition rescues phenotypes in genetic models

- Mutations of *SETD1A* have been implicated in schizophrenia, developmental disorders like autism spectrum disorder (ASD) and other rare syndromes
- Mice with the mutated *Setd1a* gene recapitulate human schizophrenia symptoms
- Oryzon-LSD1 inhibitors reverse these deficiencies

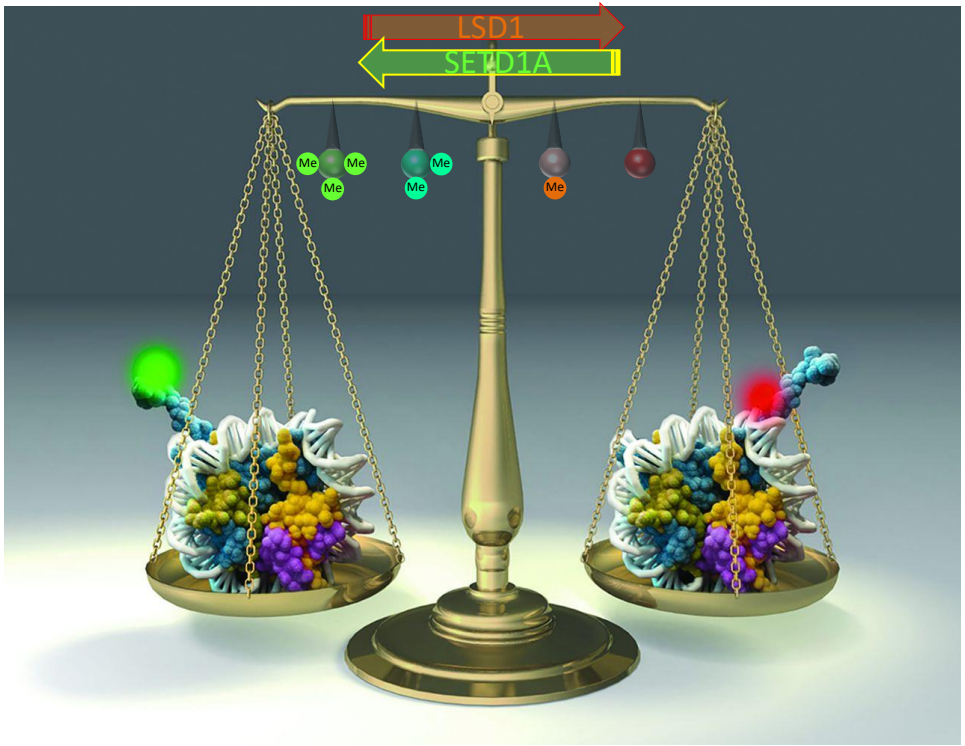

Neuron

ARTICLE | ONLINE NOW

Recapitulation and Reversal of Schizophrenia-Related Phenotypes in *Setd1a*-Deficient Mice

Jun Mukai [7, 8] • Enrico Cannavò [7] • Gregg W. Crabtree • ... Atsushi Takata • Bin Xu • Joseph A. Gogos [10] • Show all authors • Show footnotes

Published: October 09, 2019 • DOI: https://doi.org/10.1016/j.neuron.2019.09.014



Modified from Andrea Piunti and Ali Shilatifard, Science 2016;352:aad9780

SETD1A is a histone methyltransferase that belongs to the COMPASS family: six H3K4 methyltransferases that also contains KMT2A (or MLL1), KMT2B (or MLL2), KMT2C (or MLL3) and KMT2G (or SET1B).

Methylation is involved in Kabuki syndrome; LSD1 inhibition rescues phenotypes in genetic models

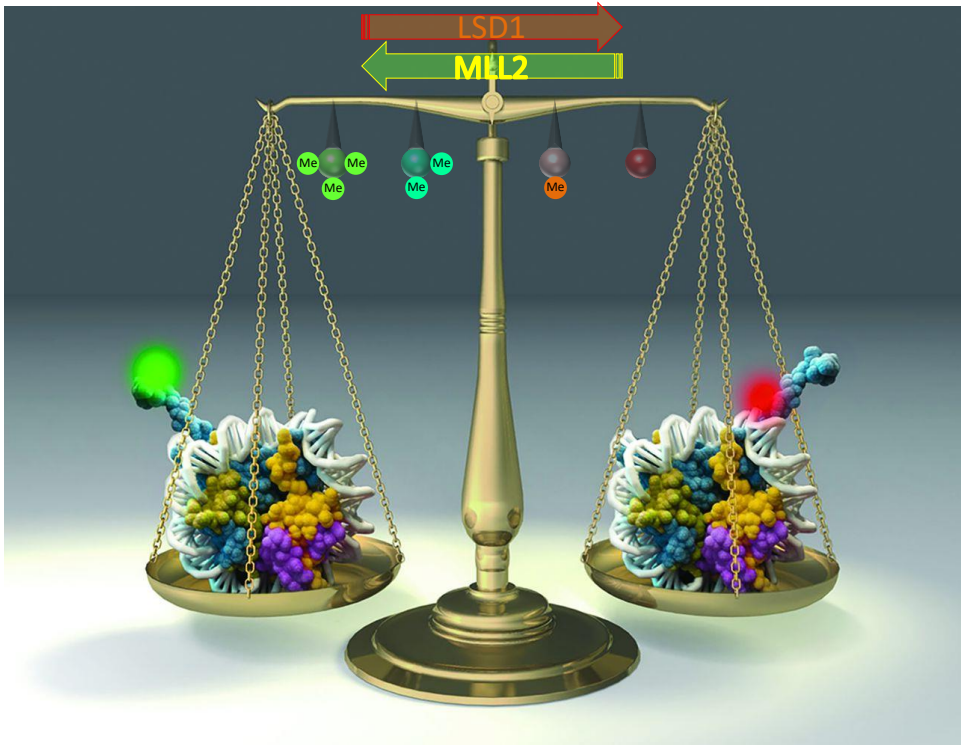
- Mutations of *MLL2 (KMT2D)* have been implicated in Kabuki syndrome
- Mice with the mutated *MLL2* gene recapitulate Kabuki patient symptoms like cranio-facial abnormalities, growth retardation, and immune dysregulation
- LSD1 inhibitors reverse these deficiencies

Molecular Therapy
Methods & Clinical Development
Volume 20, 12 March 2021, Pages 779-791

Original Article

Inhibition of KDM1A activity restores adult neurogenesis and improves hippocampal memory in a mouse model of Kabuki syndrome

Li Zhang [1], Genay Pilarowski [1, 7], Emilio Merlo Pich [2], Atsushi Nakatani [2], John Dunlop [3], Rina Baba [2], Satoru Matsuda [2], Masaki Daini [2], Yasushi Hattori [2], Shigemitsu Matsumoto [2], Mitsuhiro Ito [2], Haruhide Kimura [2], Hans Tomas Bjornsson [1, 4, 5, 6]

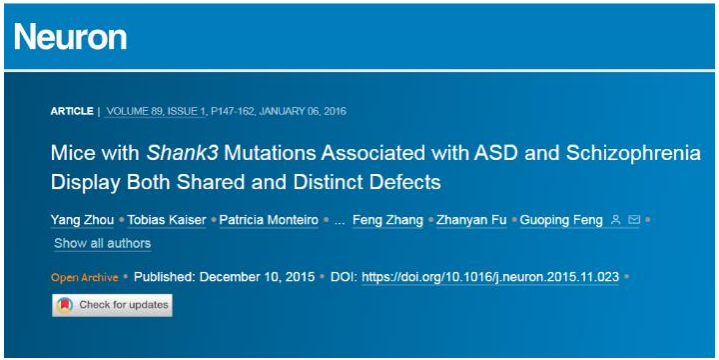


Modified from Andrea Piunti and Ali Shilatifard, Science 2016;352:aad9780

MLL2 is a histone methyltransferase that belongs to the COMPASS family: six H3K4 methyltransferases that also contains KMT2A (or MLL1), KMT2C (or MLL3), KMT2F (or SETD1A), and KMT2G (or SET1B)

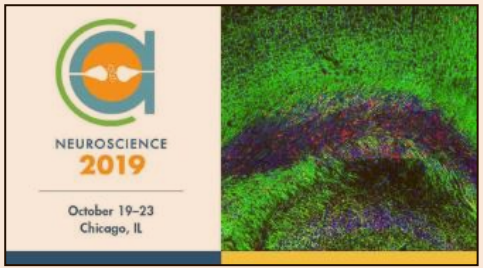
Shank3 mutations cause ASD, Phelan-McDermid syndrome and SCZ

- *SHANK3* encodes a protein that is essential for proper functioning of the synapse, the junction between neurons
- The majority of people lacking a functional copy of the *Shank3* gene have both autism and severe intellectual disability
- Mice with the mutated *Shank3* gene recapitulate human PMS-ASD symptoms
- Oryzon-LSD1 inhibitors reverse these deficiencies alone or in combination with HDAC2 inhibitors



LSD1 inhib. restores Prefrontal Cortex electrophysiological dysfunctions in *Shank3* mutant mice

Zhen Yan *Oral Comm* SFN-2019



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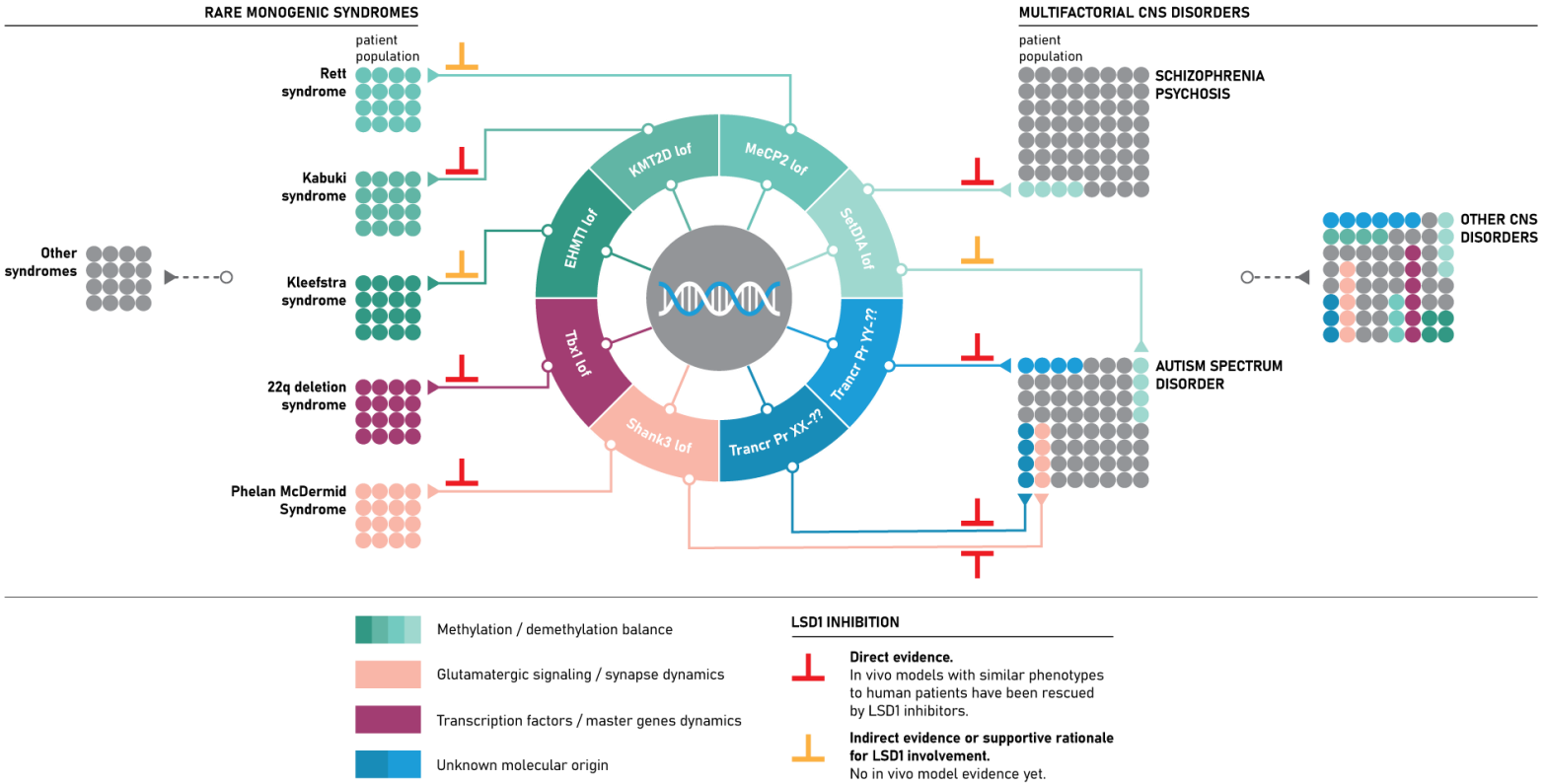
LSD1 inhibition, a key target for personalized therapy in CNS

- LSD1 acts as a downstream molecular hub where a variety of neuronal signaling pathways converge
- LSD1 inhibition can correct distinct independent deficiencies occurring upstream



LSD1 inhibition paves the way for personalized medicine in psychiatry

Collaborations ongoing with major clinical institutions to inform and prepare personalized medicine clinical studies

SETD1A-related SCZ

- Patients carrying these mutations identified in the Amish community in US
- Study to characterize psychometrically up to 60 subjects
- Results expected in 3Q21

SHANK3-related ASD

- +200 patients carrying these mutations identified in Spain
- Study to characterize psychometrically up to 40 subjects
- Results expected in 3Q21

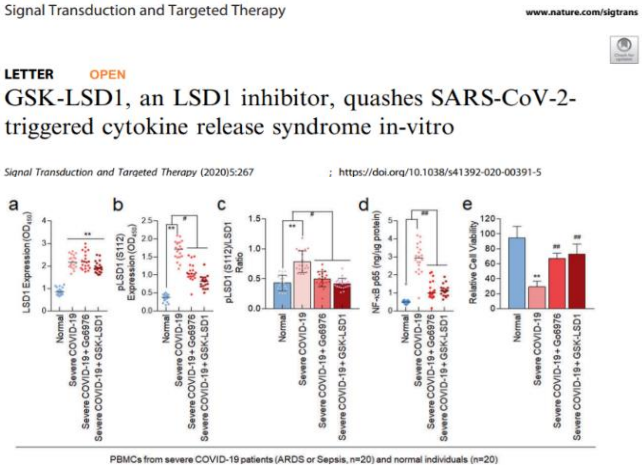
ESCAPE: Phase II trial with vafidemstat to prevent ARDS in severe COVID-19 patients

ESCAPE RATIONAL:

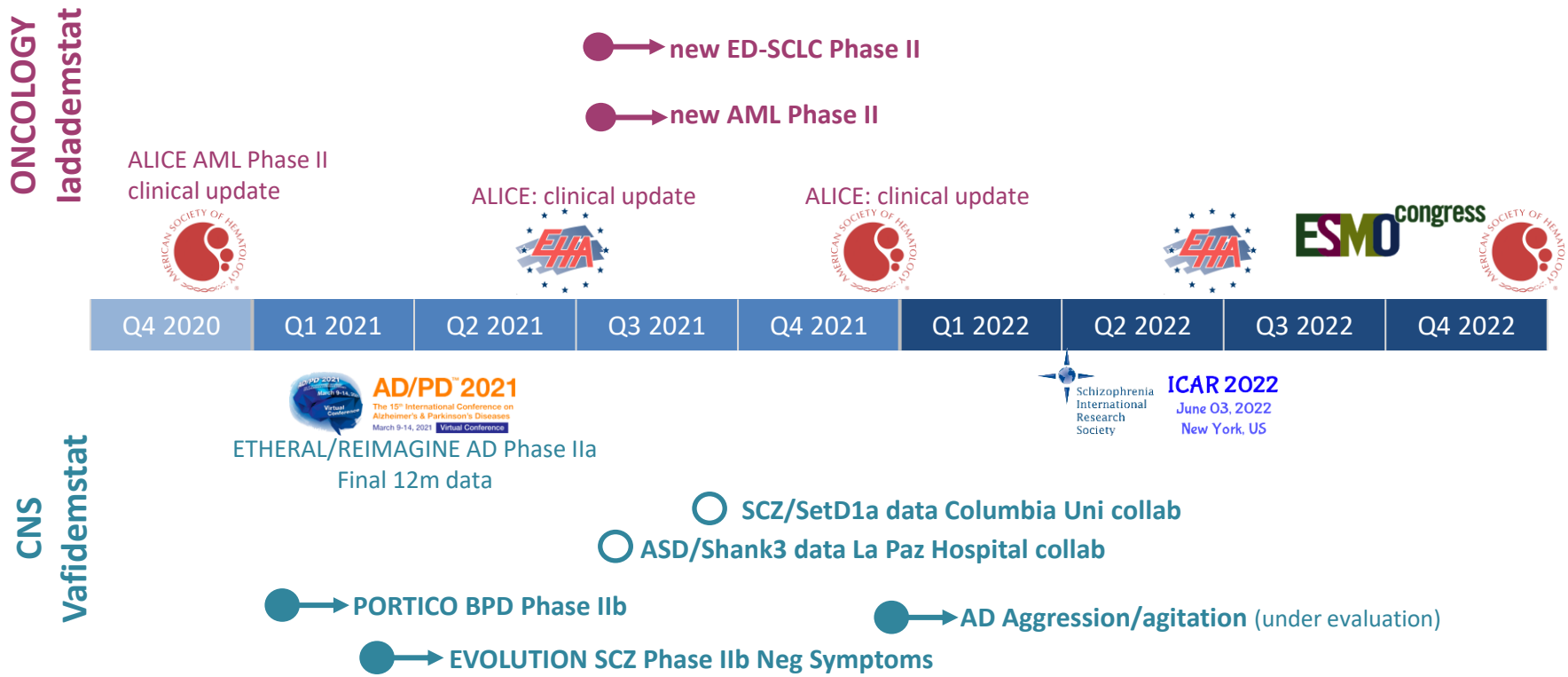
- Vafidemstat is safe in the elderly
- Vafidemstat reduces inflammation
- LSD1 inhibitors reduce cytokine release syndrome *ex-vivo* in Covid-19

Multi-center, open label, two arms, randomized study in combination with best supportive care (1:1)

- N= 40+20. Six centers in Madrid and Barcelona metropolitan areas.
- Primary endpoint: efficacy of vafidemstat in preventing Acute Respiratory Distress Syndrome (ARDS) in adult severely ill patients with COVID-19
- Secondary endpoints: Reduction of systemic and pulmonary inflammatory biomarkers
- Recruitment finalized
- Analysis ongoing (preliminary results expected in 1H 2021)



A rich flow of clinical catalysts ahead



ONCOLOGY

Iadademstat

- First-in-class & best-in-class LSD1i in Oncology
- Safe: ~100 patients dosed
- Robust and durable responses in AML (85% ORRs)
- FDA & EMA ODD in AML
- A SCLC trial with ICI in preparation
- A dual registrational strategy

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A unique dual EPIGENETIC proposition in CNS and ONCOLOGY

- A personalized medicine approach with multiple shots on goal
- 2 Phase II programs. Safety proven in +400 subjects dosed
- Well funded to 2023
- Value-inflection updates in 2021-22

CNS

Vafidemstat

- First-in-class LSD1i in CNS
- Safe: +300 subjects in several trials
- Reduces agitation and aggression in psychiatric disorders (BPD, ADHD, ASD) and in AD
- Two new Phase IIb studies in 2021 in BPD and SCZ
- Trials in genetically-defined patient subpopulations in SCZ and ASD under study

Thank you

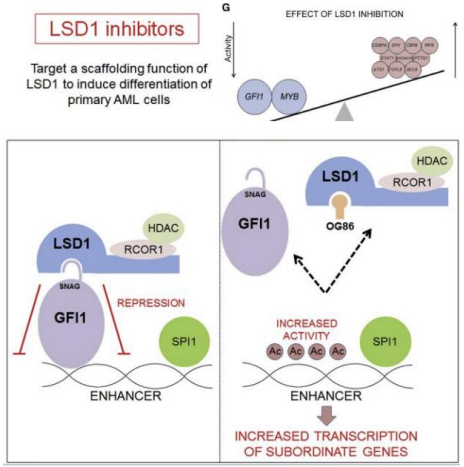
Backup Slides

Iadademstat: A potent and selective LSD1 inhibitor with similar MoA in AML and SCLC

LSD1 (aka KDM1A) is known to form a complex (CoREST) with corepressor proteins including RCOR and HDAC proteins, to augment its gene repressor activity

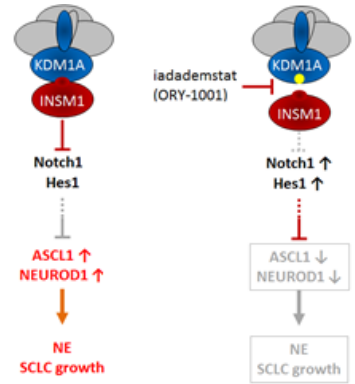
- In hematopoietic cells, LSD1 also physically interacts with growth factor – independent 1 (GFI1) or growth factor – independent 1B (GFI1B), which are transcriptional repressors and critical regulators of hematopoietic cell lineage development and differentiation.

- **Iadademstat** inhibits the recruitment of LSD1 by SNAG domain transcription factors like GFI1, key in the differentiation block in AML.



- Insulinoma-associated protein 1 (INSM1) is a zinc-finger transcription factor that plays an important role in the development of neuroendocrine tissues. INSM1 interacts with LSD1 via its SNAG domain and the resulting complex controls neuroendocrine differentiation.

- **Iadademstat** inhibits recruitment of LSD1 by INSM1 resulting in reactivation of the NOTCH signaling, reduced expression of the transcription factor ASCL1 and tumor growth inhibition in SCLC models.

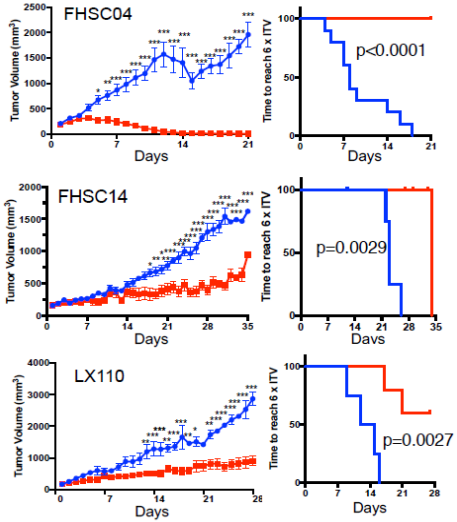


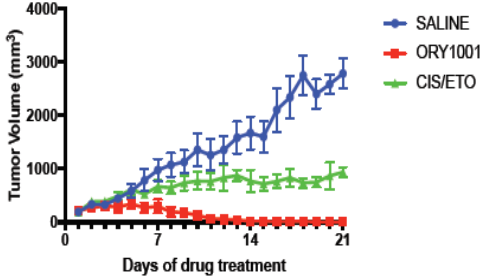
ORYZON

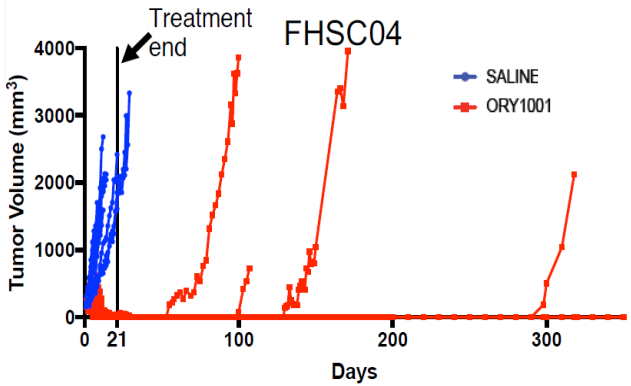
Iadademstat is efficacious in monotherapy in some PDX-SCLC xenografts

Response to iadademstat in PDX models of SCLC is remarkably strong and durable in some cases

- FHSC04 model: derived from a SCLC patient who relapsed after first line therapy
- **6/10 FHSC04 mice treated with iadademstat did not show relapse after 300 days**
- Biomarkers for LSD1 responsiveness identified and used to stratify patients in CLEPSIDRA





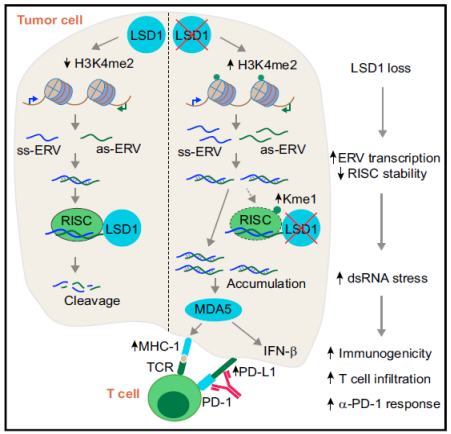


Sci Signal. 2019 Feb 5;12(567)

FRED HUTCHINSON CANCER RESEARCH CENTER
A LIFE OF SCIENCE

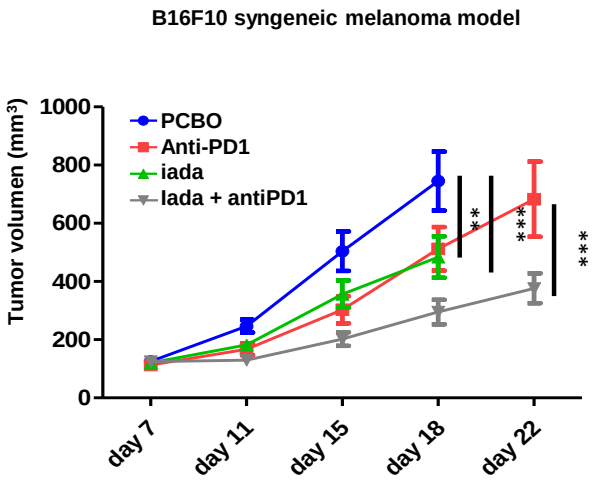
ORYZON

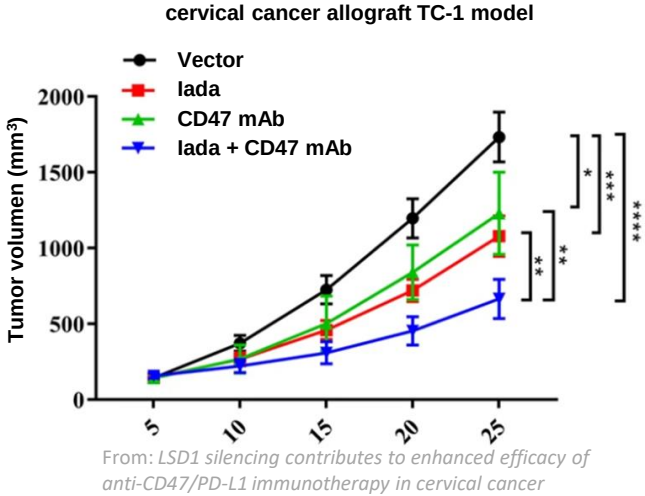
LSD1 and I-O: Emerging relevant literature supporting synergy in immune cold-tumors



Cell

LSD1 Ablation Stimulates Anti-tumor Immunity and Enables Checkpoint Blockade





From: *LSD1 silencing contributes to enhanced efficacy of anti-CD47/PD-L1 immunotherapy in cervical cancer*

Oncogene

Explore our content ▾ Journal information ▾

nature > oncogene > articles > article

Article | Published 15 August 2018

Inhibition of histone lysine-specific demethylase 1 elicits breast tumor immunity and enhances antitumor efficacy of immune checkpoint blockade

Ye Qin, Shauna N. Vasilatos, Lin Chen, Hao Wu, Zhishen Cao, Yumei Fu, Min Huang, Anda M. Vlad, Binfeng Lu, Steffi Oesterreich, Nancy E. Davidson & Yi Huang

Antitumoral activity of iadademstat in combination with immunotherapy in different in-vivo models of melanoma and other tumors support exploring this combination in the clinic

Journal of Clinical Oncology. 2019;37:e14248 and Company unpublished data

https://www.nature.com/articles/s41419-021-03556-4

Cell. 2018 Jul 26; 174(3): 549–563.e19

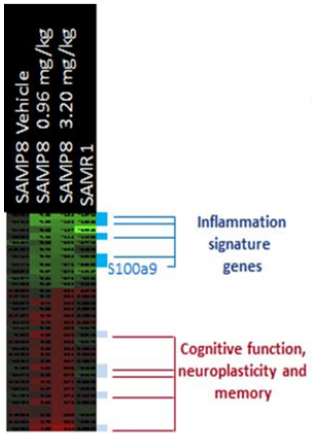
ORYZON

Vafidemstat: Upstream epigenetic mechanism produces an anti-inflammatory and prosynaptic response

LSD1 localizes *in-vivo* to enhancers and promoters of confirmed CNS disease risk genes

LSD1 binds to TFs that control IEG expression and stress in the PFC-amygdala axis, including SRF

- Vafidemstat **up-regulates** genes associated with **Neuroplasticity & Cognition**
- Vafidemstat **reduces** the expression of **inflammatory** genes as S100A9 and others in SAMP8 AD model and IL-6, IL-1B and many others in MS models



Vafidemstat potently **down-regulated** the expression of a subset of genes related to immune reaction and **inflammation** as **S100A9** involved in OPC defective remyelination

Antiinflammatory

Genes **up-regulated** in SAMP8 mice by vafidemstat included:

Baiap3: involved in retrograde trafficking

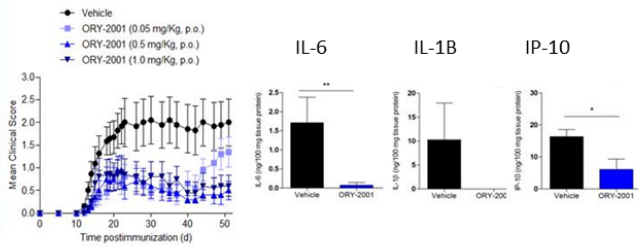
Prph: mutated in Amyotrophic Lateral Sclerosis (ALS)

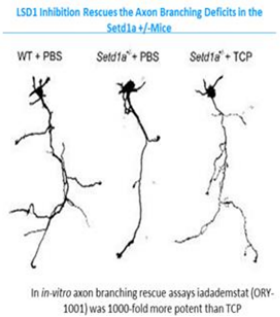
Fabp7: upregulation in drosophila favors long term memory consolidation

Doc2a: activity-dependent modulator of excitatory synaptic transmission, relevant to memory formation

Kremen2 and Rspo1: regulators of the WNT pathway

Prosynaptic

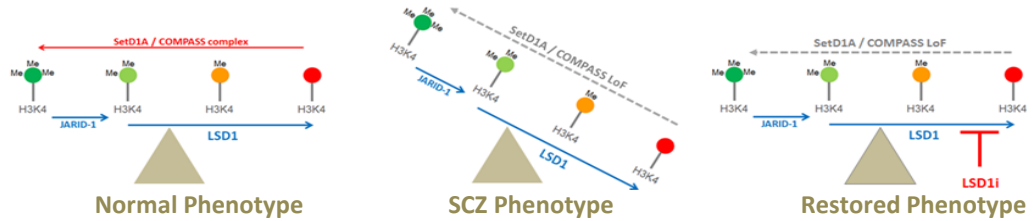




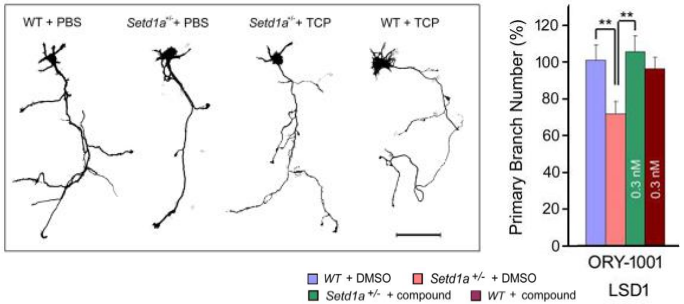
***Mukai** J, et al. **Neuron**. 2019 Oct 1. pii: S0896-6273(19)30787-1.*

Methylation is involved in SCZ and ASD and LSD1 inhibition rescues phenotypes in genetic models

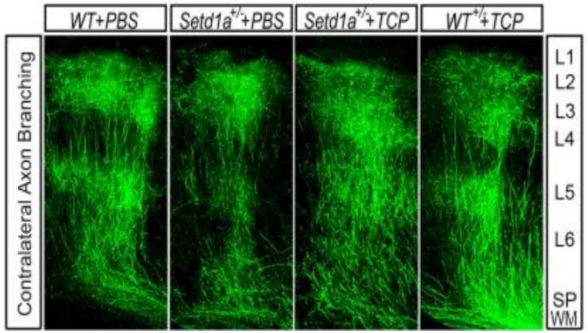
- **A clear molecular mechanism of action**



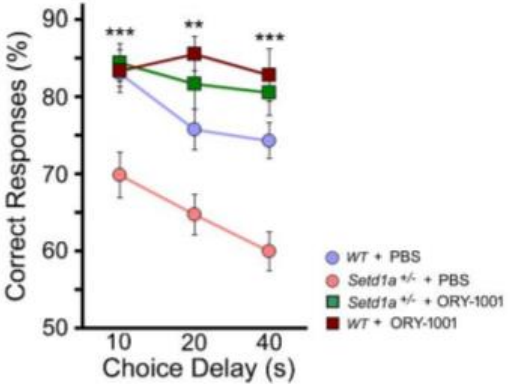
Ex-vivo ORY-1001 rescues anatomical neuronal branching deficits in prefrontal cortex neurons of Setd1a $^{+/-}$mice



LSD1 inhibition rescues the contralateral axon branching and navigation deficits in-vivo in Setd1a $^{+/-}$mice



Rescue of WM performance in Setd1a+/- mice treated with ORY-1001

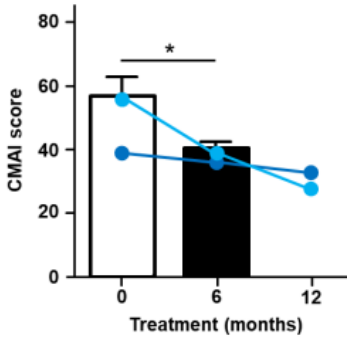


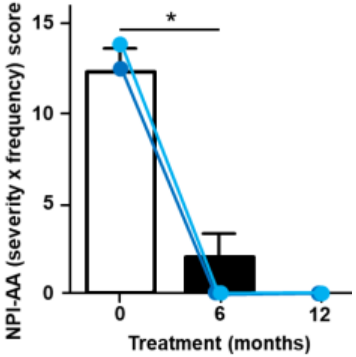
Alzheimer’s disease & Aggression-agitation in AD

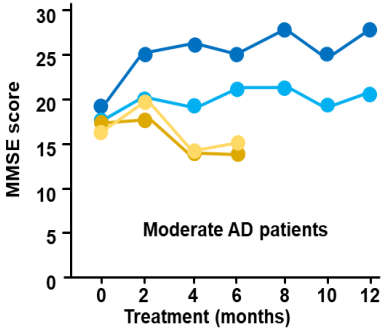
Vafidemstat reduces agitation and aggression in moderate and severe AD patients

REIMAGINE-AD

- Single center, single arm, open label Phase IIa study
- N = 12 patients
- Primary endpoint: Reduction of aggression as measured by validated scales
- Secondary endpoints: Safety and tolerability; QoL plus other disease related outcomes
- A protocol amendment was granted to extend the treatment up to 12 months for those patients with signals of cognitive improvement after initial 6 months of treatment (N=2, 2 out of 4 moderate AD patients)







- **Safe and well tolerated**
- **Significant reduction of agitation/aggression after 6 and 12 months of treatment**
- **Anecdotal sustained benefit in cognition after 12 months in a subset of AD patients**

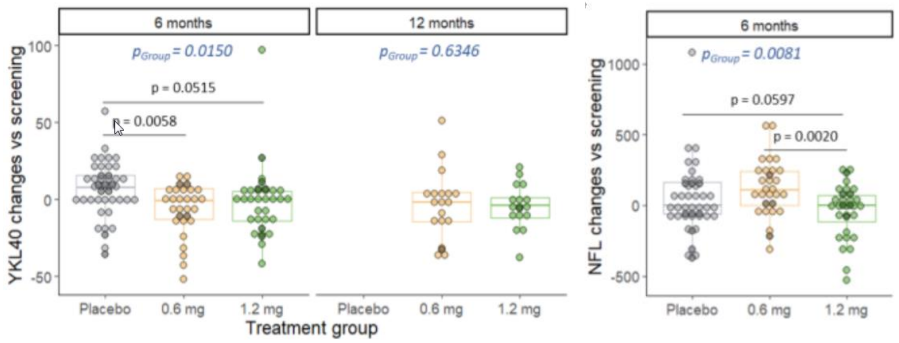
Vafidemstat is safe and reduces CSF levels of an inflammatory biomarker in AD patients

ETHERAL: A double-blind Phase IIa study to inform and design future studies

- Multicenter, 6 +6 months randomized. Placebo +2 intervention arms. 140 patients enrolled. EU+US study
- **Primary endpoint:** Safety and tolerability
- **Secondary endpoints:**
  - Cognition/Agitation/Apathy/ Depression/QoL
  - Volumetric MRI
  - CSF BIOMARKERS

ETHERAL-EU and US trial AEs (N=140) Number of patients (%) event count	Placebo-controlled period			Non placebo-controlled period	
	Placebo (N=56)	Vafidemstat 0.6 mg (N=42)	Vafidemstat 1.2 mg (N=42)	Vafidemstat 0.6 mg (N=51)	Vafidemstat 1.2 mg (N=51)
Dropout patients	9 (16%)	8 (19%)	7 (17%)	15 (29%)	15 (29%)
Total AEs	40 (71%) 140	39 (93%) 146	37 (88%) 168	35 (69%) 95	44 (86%) 139
Drug-related AEs	17 (30%) 30	16 (43%) 34	17 (50%) 38	11 (22%) 15	14 (27%) 23
Total SAEs	4 (9%) 4	3 (8%) 3	4 (12%) 8	4 (8%) 5	3 (6%) 4
Drug-related SAEs	1 (2%) 2	-	1 (3%) 1	1 (2%) 1	-

- **Safe and well tolerated at both doses after 12-month treatment**
- **Good PK and Target engagement**
- **Vafidemstat treatment reduces CSF levels of the inflammatory biomarker YKL-40 at 6 months in AD patients**



Thank you