

## **Safe Harbor Statement**

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Any statement in this presentation that is not a historical fact is a forward-looking statement. Forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially and reported results should not be considered as an indication of future performance. Examples of such statements include, but are not limited to: statements relating to the overall ability of epigenetic regulator drugs to correct gene changes in disease, including how modulation of LSD1 may increase responsiveness to checkpoint inhibition; the commercial or market opportunity and expansion for each therapeutic option, including the availability and value of a pediatric priority review voucher for in-clinic treatments and potential for accelerated approval; the adequacy of our capital to support our future operations and our ability to successfully initiate and complete clinical trials and regulatory submissions; Seclidemstat's impact in Ewing sarcoma and as a potential new and less-toxic treatment; expected dose escalation and dose expansion; expected cohort readouts; expected therapeutic options for SP-2577 and related effects and projected efficacy, including SP-2577's ability to inhibit LSD1; the potential for SP-2577 to differentiate itself from competing LSD1-inhibitors; timing of development and future milestones, including for each of SP-2577's indications; the nature, strategy and focus of Salarius; and the development, expected timeline and commercial potential of any of our product candidates or our competitors. We may not actually achieve the plans, carry out the intentions or meet the expectations, objectives or projections disclosed in the forward-looking statements and you should not place undue reliance on these forward-looking statements. Such statements are based on management's current expectations and involve risks and uncertainties. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors, including, without limitation: risks and uncertainties associated with the availability of sufficient resources to meet our business objectives and operational requirements, including amounts remaining available under the CPRIT grant; the risk that we may not obtain or maintain sufficient levels of reimbursement for our clinical trials and product development, including from CPRIT; the ability to project future cash utilization and reserves needed for contingent future liabilities and business operations; the fact that the results of earlier studies and trials may not be predictive of future clinical trial results; our quarter-end closing procedures and finalization of our quarterly financial results; the sufficiency of our intellectual property protections; risks related to the drug development and the regulatory approval process; other legal and regulatory uncertainties; the market price of our common stock and our ability to maintain the listing of our common stock on Nasdaq; the impact of the ongoing COVID-19 pandemic and the success of any measures we have taken or may take in response thereto; and the impact of competitive products and technological changes. We disclaim any intent or obligation to update these forward-looking statements to reflect events or circumstances that exist after the date on which they were made. You should review additional disclosures we make in our filings with the Securities and Exchange Commission, including our Quarterly Reports on Form 10-Q, Annual Reports on Form 10-K, and Current Reports on Form 8-K. You may access these documents for no charge at http://www.sec.gov. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy, nor shall there be any sale of these securities in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or other jurisdiction.



### **Mission Statement**



Developing treatments for patients that need them the most

## **Corporate Overview**

Salarius's mission is to develop treatments for patients who need them most



Drugs that regulate gene expression ("epigenetics") have shown clinical efficacy plus immunooncology potential



Lead candidate, seclidemstat is a novel, oral, reversible LSD1 inhibitor that regulates gene expression and is currently in Phase 1/2 Ewing and Ewing-related sarcoma and Phase 1/2 solid tumor clinical trials



Seclidemstat FDA designations for Ewing sarcoma:

(1) Rare Pediatric Disease Designation, (2) Orphan Drug Designation, and (3) Fast Track Approval



Strong cash position with \$36.6M as of March 31, 2021. In addition, non-dilutive funding leads to low monthly burn rate

Original \$18.7M¹ award from Cancer Prevention Research Institute of Texas (CPRIT) with \$4.8M remaining



Market expansion in targeted cancers with LSD1 sensitive mutations and immunotherapy (checkpoint inhibitor combos) and hematologic cancers

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# Recent and Anticipated Milestones

	Development Milestones	Timing
<b>②</b>	Rare Pediatric Disease, Orphan Status Designation, and Fast Track Designation	2017-2019
<b>②</b>	Phase 1 Ewing data (pediatric subcommittee Oncologic Drug Advisory Committee)	1H 2020
	CPRIT Distribution	2H 2020
<b>②</b>	Additional Phase 1 Ewing data - RP2D Established (Press release 02/17/21)	1Q2021
<b>②</b>	Initiate Ewing sarcoma and Ewing-related sarcoma expansion (Press release 02/24/21)	1Q 2021
	Phase 1 Ewing early safety and efficacy data readouts (complete dose escalation ASCO21)	1H 2021
<b>②</b>	Phase 1 AST early safety and efficacy data readouts (dose escalation ASCO21)	1H 2021
<b>②</b>	Initiate potential hematologic trial	1H2021
	Initiate potential immunotherapy combo trial	2H2021
	Clinical updates from ongoing trials to be presented at scientific conferences	2H 2021
	Potential early readouts from the Ewing and Ewing-related sarcoma Expansion Phase	1H 2022
	Full data readouts from completed Ewing and Ewing-related sarcoma Expansion Phase	2H 2022
	Early readouts from immunotherapy combo and hematologic trials	2022



## **Development Pipeline**

	Indication	Preclinical	Phase 1	Phase 2 <sup>1</sup>	Status
Seclidemstat	Ewing and Ewing-related Sarcomas	Dose Expansion a	at RP2D		<ul> <li>Phase 1/Phase 2 enrolling up to 80 patients</li> <li>Recommended Phase 2 Dose (PR2D) established</li> </ul>
	Advanced Solid Tumors	Dose Escalation a Expansion <sup>2</sup>	and		Phase 1/Phase 2 enrolling up to 50 patients
	Immunotherapy	In vitro and In vivo studies ongoing			Identifying combinations and indications for clinical trials
	Hematologic cancers	In vitro and In vivo studies ongoing			Identifying combinations and indication for clinical trials

<sup>2.</sup> Open to all non-Ewing sarcoma solid tumor patients except for primary CNS tumors, potential to enrich for patients with sensitive mutations and prostate cancer that can be monitored with prostate specific antigen



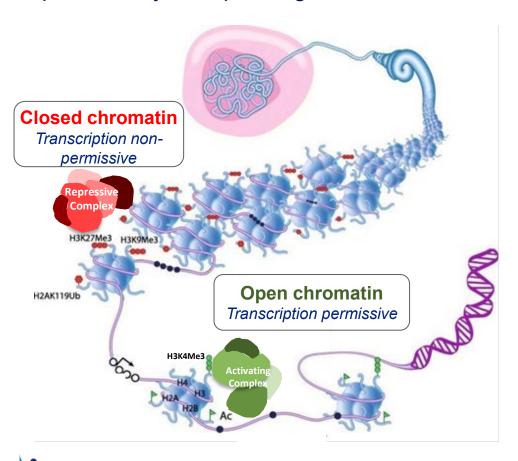
<sup>1.</sup> Expanded Phase 2 in Ewing sarcoma could potentially be a registration study with improvements in response or duration of response compared to the existing standard of care and FDA's agreement



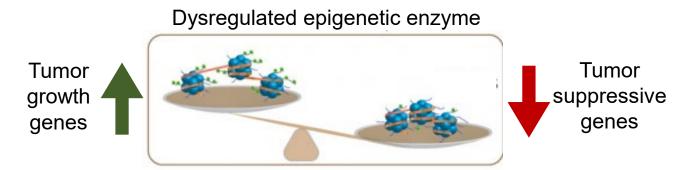
Seclidemstat Overview

## Epigenetic enzymes are attractive targets for cancer therapy

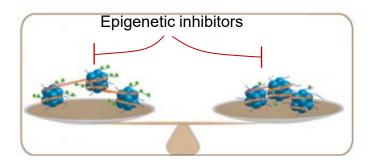
Epigenetic modifying enzymes affect gene expression by manipulating the chromatin structure

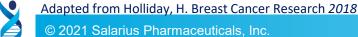


Dysregulated epigenetic enzymes can disrupt the transcriptional balance and lead to cancer development



Drugs that correct dysregulated epigenetic enzymes can help treat cancer by restoring to a balanced transcriptional state





Adapted from Marcin et al. Biomed Intel 2018.

# **Epigenetic Space Is Gaining Momentum And Epigenetic Focused Biotechs Are Increasing In Valuation**

## **Epigenetic Space**



#### **EZH2** inhibitor (tazemetostat)

Approved in epithelioid sarcoma – monotherapy Approved for R/R follicular lymphoma – monotherapy **Market Cap:** ~\$780M<sup>1</sup>



(NASDAQ: CNST)

#### **BET inhibitor (CPI-0610)**

Positive Phase 2 data in combination with existing standard of care in myelofibrosis **LSD1 (CPI-482)** program recently announced **Market Cap:** ~\$1.6B<sup>1</sup>

Announced acquisition by MorphoSys In June 2021

### **LSD1 Inhibitor Space**



#### **Reversible LSD1 inhibitor**

- Single agent has shown preliminary (dose escalation) antitumor activity
- No significant hematologic toxicity to date



#### **Reversible LSD1 inhibitor**

- Single agent shows anti-tumor activity
- Initiating trial in combination with checkpoint inhibitors



#### **Irreversible LSD1 inhibitor**

- Shown success in AML in combo with 5-aza
- Hematological toxicity can be a limitation



#### **Irreversible LSD1 inhibitor**

- Showing success in myeloproliferative diseases
- Raised \$80M Series C
- IPO announced June 2021

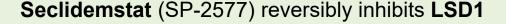
1. July 6, 2021



## LSD1 - A Validated Target For Cancer Therapy

Lysine Specific Demethylase 1 (LSD1) affects gene expression through enzymatic activity and scaffolding properties (protein-protein interactions), making it an attractive target for solid tumors and hematological cancers.

LSD1 in Normal Cells and Cancer Cells <sup>1</sup>			
Normal Cells	LSD1 is necessary for stem cell maintenance and cell development processes (e.g., blood cells)		
Cancer Cells	<ul> <li>LSD1 is over expressed</li> <li>LSD1 acts incorrectly to silence or activate genes leading to disease progression</li> <li>Validated target: LSD1 CRISPR deletion often detrimental to cancer cells</li> </ul>		



- Reverses incorrect gene expression, killing or preventing the growth of cancer cells
- Inhibits both the enzymatic and scaffolding activity



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# More Comprehensive Inhibition of LSD1 Positively Impacts **Therapeutic Activity**

#### Degree of LSD1 inhibition



### **Enzymatic activity – Demethylation**

Impact: Moderately alter gene expression



Partial scaffolding\* inhibition of LSD1 – protein interaction

Impact: Alter gene expression in cancers (AML, SCLC) driven by SNAG domain proteins (e.g. GFI1B)



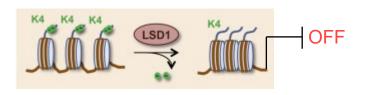




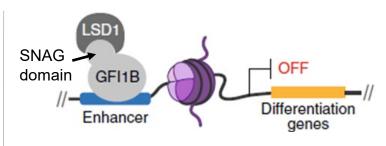
### **Broader scaffolding inhibition** of LSD1 – protein interaction

Impact: Potential efficacy in broader range of cancer types, destabilize LSD1 and complexes

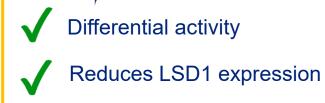
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## Ewing Sarcoma - Unmet Need Represents a Meaningful **Product Opportunity**

### **Diagnosis**

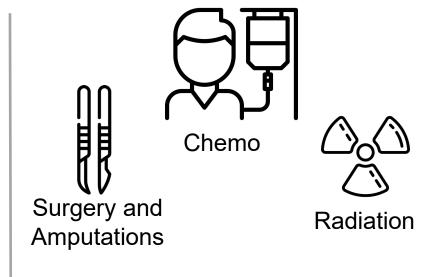


~500 patients diagnosed each year Median age of diagnosis ~15 years

- 75% localized<sup>1</sup>
- 25% with metastasis<sup>1</sup>

<sup>1</sup> Pishas, K. et al. (2016)

### **Standard of Care**



- About 40% of patients are refractory or relapse<sup>2</sup>
- 70-90% 5-year mortality rate<sup>2</sup>
- No standardized 2<sup>nd</sup> line treatment

# Salarius' Vision

An effective, non-toxic, oral treatment option:

- Accelerated US approval
- Rapid market uptake
- \$200M+ Global Sales<sup>3</sup> (est.)
- Possible Priority Review Voucher of \$80M - \$150M



Fast Track Designation



**Orphan Drug Designation** 

<sup>3</sup> Represents longer term vision and does not represent estimate of future performance, financial or otherwise. There is no assurance that

we will achieve our longer-term vision.



Rare Pediatric Drug Designation

13

<sup>&</sup>lt;sup>2</sup> Van Mater, et al. Oncotargets (2019)

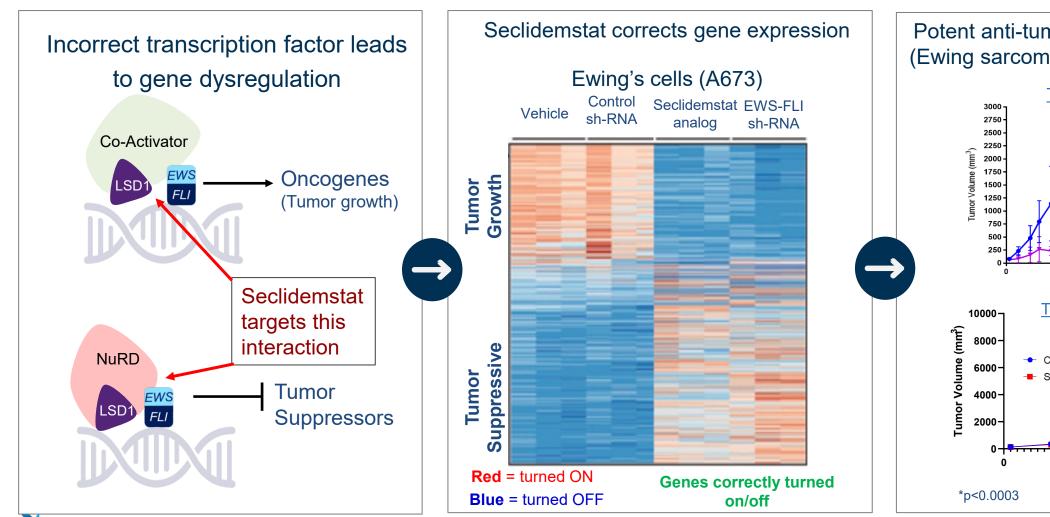


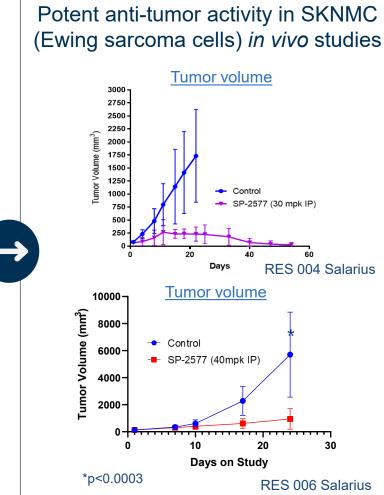


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# Targeting The Root Cause Of Ewing Sarcoma Via LSD1 Inhibition

Ewing sarcoma is driven by an easily diagnosed chromosomal translocation, i.e., EWS-FLI





## Seclidemstat's mechanism of action results in anti-proliferative activity in Ewing-related (FET-rearranged) sarcomas

- Salarius's ongoing Ewing sarcoma trial amended to include FET-rearranged sarcomas at the RP2D supported by preclinical and clinical data
  - Clinical data: FET-rearranged sarcoma patients<sup>1</sup> treated at doses below the RP2D have a median time to progression above a commonly used benchmark for assessing single agent activity in soft tissue sarcomas

## **EWS** Ewing sarcoma

**Ewing-related** sarcomas:

Myxoid liposarcoma

**EWS** 

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**FUS** 

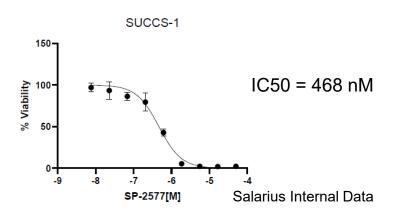
Desmoplastic Small Round cell tumor



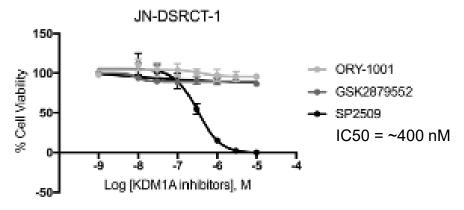
Clear cell sarcoma



#### Clear cell sarcoma



#### Desmoplastic Small Round Cell Tumor



Romo-Morales A et al. Pediatr Blood Cancer. 2019.

## Ewing Sarcoma and FET-rearranged Sarcomas Phase 1/2 Trial

# Open-label dose escalation / dose expansion trial design

#### **Dose escalation** (completed 1Q2021)

- Seclidemstat has a manageable safety profile
- RP2D established

# **Dose expansion** amended to reach more sarcoma patients (initiating 1Q2021)

- Arm 1: Up to 30 Ewing sarcoma patients treated in combination with Topotecan/Cyclophosphamide
- Arm 2: Up to 30 FET-rearranged sarcoma patients (including 15 myxoid liposarcoma) treated with single agent seclidemstat

Primary objective: Safety, Tolerability

Secondary objectives: Anti-tumor assessment

Exploratory: Hemoglobin F, cfDNA, CTCs







Signs of anti-tumor activity in patients at or below the RP2D



Presenting full dose escalation findings and dose expansion design at ASCO 2021



# Phase 1a Ewing Safety Data And Preliminary Drug Activity Observed In Patient's Target Lesions As Assessed By Investigator

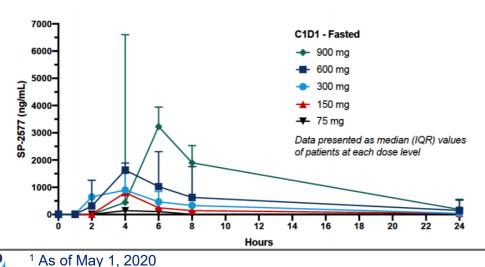
#### Early dose escalation results

#### Patients enrolled<sup>1</sup>: 21 patients

- No treatment related deaths or study discontinuations due to treatment-related adverse events
- Dose-limiting toxicities have not prevented dose escalation

#### **Pharmacokinetics**:

- At dose levels 900 mg BID and above cohorts achieving drug levels of preclinical efficacious concentrations
- 5-8 hour half-life supports BID dosing



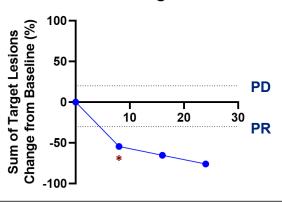
# Preliminary drug activity in target lesions of refractory Ewing's patient

- Feb 2016: 30 year-old male diagnosed and treated with standard VDC/IE chemotherapy
- July 2017: Presented with bone lesion and treated with standard I/T chemotherapy
- Feb 2019: External beam radiation treatment
- Sep 2019: Enrolled in SP-2577 study at 600 mg BID dose cohort.

Prospectively defined target lesions decreased 76% in size after 6 months of treatment

- Partial Response (PR) of target lesions
- At cycle 2 non-target lesions increased resulting in overall assessment of Progressive Disease (PD) per RECIST 1.1.
- Patient continued treatment for additional 4 cycles (total of 6 cycles) due to response in target lesions and clinical benefit as determined by Investigator.

#### **Decrease in Target Lesion Size**



<sup>\*</sup> PD in non-target lesions at 8 weeks, patient continued therapy

AS OI Way 1, 2020

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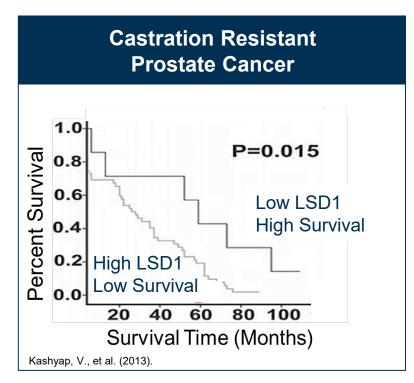


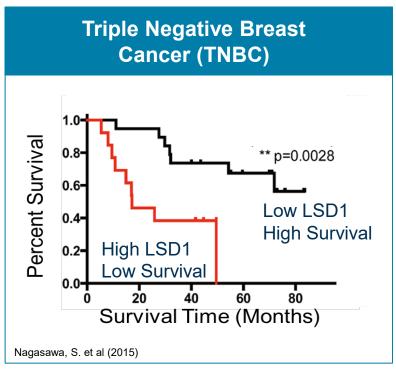
# LSD1 Overexpression Increases With Disease Progression And Correlates With Poor Patient Prognosis – Seclidemstat Reduces LSD1 Activity



# Increased LSD1 expression correlates with solid tumor progression

- High LSD1 expression in ~30% of primary prostate tumors, but >90% of advanced castration resistant prostate cancer<sup>1</sup>
- LSD1 expression associated with shorter survival in Triple Negative Breast cancer





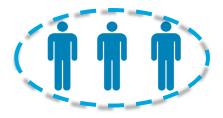
Ongoing Phase 1 Advanced Solid Tumor Study sites: Honor Health, Phoenix AZ and Sarcoma Oncology Center, Santa Monica CA



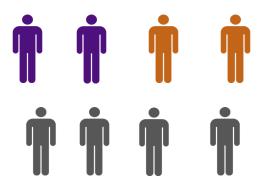
<sup>1</sup> Sehrawat, A. et. al., 2018

# Seclidemstat Expansion Strategy Built Upon Patient Targeting, Increasing Immuno-oncology Response & Hematological Cancers

### **Patient Targeting**



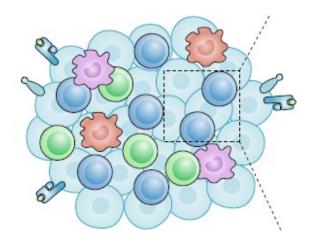
Potential enrollment to target patients with an increased chance of response to seclidemstat



Represents patient with potential sensitizing mutations identified by Salarius

# **Increase Response to Checkpoint Inhibitors**

LSD1 inhibition can turn **cold** tumors to **hot** tumors

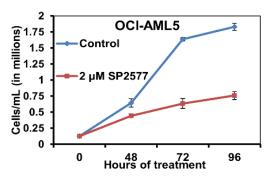


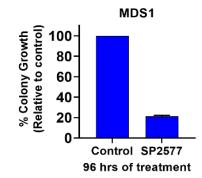
May help increase patient response to IO therapies

Topper, M.J., et al. Nature Reviews (2019)

### **Hematologic Cancers**

Seclidemstat (SP-2577) inhibits Acute Myeloid Leukemia (AML) and Myelodysplastic Syndrome (MDS) cell growth





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# Combination of Possibilities Presents Significant Market Opportunity for Seclidemstat

#### **SPEED TO MARKET**

Ewing and Ewing related sarcomas 500 to 2000 patients diagnosed/year



Potential for accelerated approval, priority review

# \$80M-\$150M

Possible Pediatric Priority Review Voucher (est.)

\$400M+
Global Sales per year (est)<sup>1</sup>

#### **EXPANDING INTO LARGER MARKETS**

#### POTENTIAL TO IDENTIFY SELECT PATIENT

Ongoing work to identify genetic backgrounds that may increase patient response to LSD1 inhibition



Market Potential in Solid Tumors <sup>2,3,4,5,6</sup>

\$1B+

#### POTENTIAL TO ENTER INTO IMMUNOTHERAPY

Sensitizing resistant cancers to checkpoint Inhibitors

#### POTENTIAL TO ENTER INTO HEMATOLOGIC CANCERS

Hematologic cancers with clinical evidence for LSD1i



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21

## Salarius Investment Opportunity: Clinical Stage Biotech With Several Value-driving Inflection Points Occurring In 2021



Lead compound, seclidemstat, is in the growing epigenetic therapy space

Clinical data suggests seclidemstat has a manageable safety profile and has demonstrated anti-tumor activity in patients with advanced disease



Extensive non-dilutive funding coupled with low quarterly burn rate. Strong cash position

- Original \$18.7M<sup>1</sup> Award from CPRIT
- Received financial support from NPCF \$36.6M as of March 31, 2021



Recipient of FDA designations that facilitates rapid product development

- Orphan Drug Designation
- Rare Pediatric Disease Designation
- Fast Track Designation

## Salarius anticipates several value-inflection announcements in the upcoming months:



Clinical safety and efficacy data to be presented at scientific conferences



Announcement of additional seclidemstat clinical trials in attractive indications



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# LSD1 Competitive Landscape Highlights Seclidemstat's Differentiation

	Company	Drug Name	Binding Mechanism	Indications and Phase
In clinic <sup>1</sup>	Salarius PHARMACEUTICALS	SP-2577 (Seclidemstat)	Reversible	Ewing sarcoma (Ph1/2), Advanced Solid Tumors (Ph1/2)
	ORYZON	ORY-1001 (RG6016)	Irreversible	AML combo (Ph2b), SCLC combo (Ph2a )
	(Celgene (BMS)	CC-90011	Reversible	Non-Hodgkin's lymphoma and AST (Ph1), SCLC combo (Ph1b), IO combo (Ph 2), Prostate (Ph1), AML (Ph1/2)
	Imago 🔭	IMG-7289	Irreversible	Myelofibrosis (Ph2b), essential thrombocythemia (Ph2a), Polycythemia vera (Phase 2a)

Seclidemstat's
differentiated binding
mechanism (reversibility)
and binding location
shows potential
increased therapeutic
activity and safety\*

	BE/(CTICA"	BEA-17	Reversible	Glioblastoma, IO
Preclinic <sup>2</sup>	RASNA THERAPEUTICS	RASP-201	Reversible	AML
Prec	Hanmi	HM9XXX series	Reversible	AML and SCLC
	Constellation PHARMACEUTICALS	CPI-482	Irreversible	Myeloproliferative neoplasms

Preclinical research is shifting to develop reversible LSD1 inhibitors

<sup>2</sup>Not an exhaustive list of companies in preclinical stage



### **Appendix A: Additional Sources**

#### Combination of Possibilities Presents Significant Market Opportunity for Seclidemstat

<sup>1</sup>Represents longer term vision and does not represent estimate of future performance, financial or otherwise. There is no assurance that we will achieve our longer term vision.

<sup>2</sup> Cancer of the Ovary – Cancer Stat Facts, The National Cancer Institute: Surveillance, Epidemiology and End Results Program <a href="https://seer.cancer.gov/statfacts/html/ovary.html">https://seer.cancer.gov/statfacts/html/ovary.html</a>.

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<sup>&</sup>lt;sup>3</sup> GlobalData: Prostate Cancer: Global Drug Forecast and Market Analysis to 2028

<sup>&</sup>lt;sup>4</sup> GlobalData and Epidemiology Market Size Database, TNBC

<sup>&</sup>lt;sup>5</sup> GlobalData: Opportunity Analyzer: Ovarian Cancer - Opportunity Analysis and Forecast to 2025

<sup>&</sup>lt;sup>6</sup> Morel, D., et al. Ann of Oncology 2017

<sup>&</sup>lt;sup>7</sup> https://www.forbes.com/sites/greatspeculations/2019/03/12/how-much-can-mercks-share-price-grow-if-keytruda-gets-10-share-of-oncology-drug-market/#77edba677e18

<sup>&</sup>lt;sup>8</sup> Hematological Malignancies. Apr 2020. Brand Essence Market Research.

## **Appendix B: US Intellectual Property Portfolio**

- Composition of matter: #8,987,335
- Composition of matter: #9,266,838
- Methods of Use: #9,642,857
- Methods of Use: #9,555,024

