

Company Overview

October 2019



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Investor Highlights: Salarius Pharmaceuticals is an Epigenetic Focused Clinical-stage Oncology Biotech Company

1 Salarius has a differentiated LSD1 inhibitor with expected human data in 2020

- Multi-company interest and clinical data validates LSD1 as a therapeutic target

2 Development strategy focused on Speed to Market and Market Expansion

- Speed to Market: Ewing sarcoma trial → Rare Pediatric Disease and Orphan Status Designation
- Market Expansion: Advanced Solid Tumor trial → Hormonal cancers, sarcomas (\$1B+ markets)

3 Seasoned management team leading Salarius

- Experienced in product, clinical and early stage development

4 Lead clinical program funded by extensive non-dilutive capital

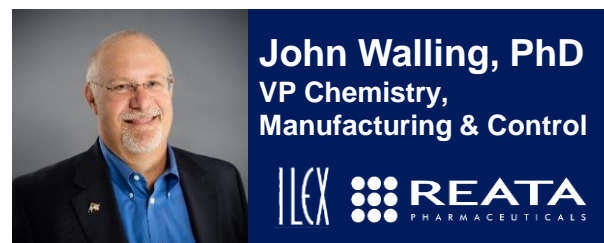
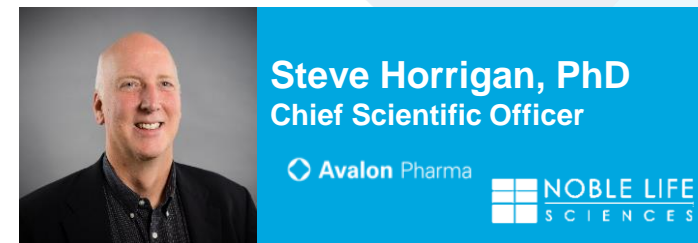
- \$18.7M CPRIT award and support from the National Pediatric Cancer Foundation

5 Opportune time to capitalize on growth potential

- Potential to expand into other indications of high value (including immunotherapy)
- Relatively short timeline to pivotal inflection points



Seasoned Leadership Team



Board of Directors

**David Arthur,
MBA**

Salarius
Pharmaceuticals

**Jonathan Northrup,
MBA**

Stingray
Therapeutics

Eli Lilly

**Tess Burleson,
CPA**

Translational
Genomics Research
Institute

**Paul Lammers,
MD MSc**

Triumvira
Immunologics

Merck-Sorono

**Bruce McCreedy,
PhD**

Precision
BioSciences

Triangle
Pharmaceuticals

**William McVicar,
PhD**

Flex Pharma

Inotek
Pharmaceuticals

**Arnold Hanish,
CPA**

Omeros Corporation

Eli Lilly



Salarius Development Pipeline

	Indication	Preclinical	Clinical*	Status
Seclidemstat	Ewing Sarcoma	Dose Escalation and Expansion Refractory and Relapsed Ewing		<ul style="list-style-type: none"> Phase 1/2 enrolling up to 50 patients Dose escalation in cohort 4 Safety and efficacy data in 2020
	Advanced Solid Tumors	Dose Escalation and Expansion Enriching for mutations and prostate ¹		<ul style="list-style-type: none"> Phase 1 enrolling up to 50 patients Dose escalation in cohort 4 Safety and efficacy data in 2020
	Glioblastoma	In vivo studies ongoing		<ul style="list-style-type: none"> Partnership with The Ivy Brain Tumor Center/ NeuroTrials LLC Preparing for Phase 0 study

¹ Advanced Solid Tumor Study is open to all non-Ewing solid tumor patients except for primary CNS tumors

* Expanded Phase 2 in Ewing sarcoma could potentially be a registration study following discussions with the FDA regarding improvements in response, duration of response compared to SOC



Salarius is Poised to Add to the Growing Epigenetic Wave

The epigenetic space has been increasing in activity since 2018

Preclinical



~\$1B deal (\$40M upfront) to advance a preclinical asset (lead optimization)

Clinical



Phase 1: LSD1; Ewing's and Solid Tumors



Phase 1: EZH2 and BET inhibitors; solid/heme



Phase 2: LSD1; AML and SCLC



Phase 2b: Raised \$40M to advance LSD1 program

Drug registration



Submitted an NDA for Epithelioid Sarcoma (1H2019) and has plans to submit another for Follicular Lymphoma (2H2019)

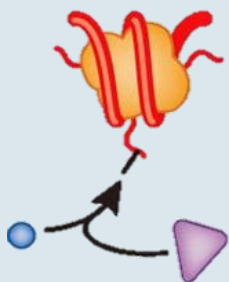


Salarius is an Epigenetic Focused Oncology Biotech Company

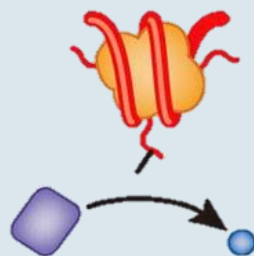
Epigenetics addresses how cells regulate gene expression through various chemical modifications

Epigenetic enzymes can be grouped into:

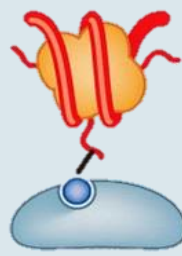
Writers



Erasers



Readers



Tarakhovsky Nat Immunol 2010

Examples:

DNMT1

DNA
methyltransferase 1

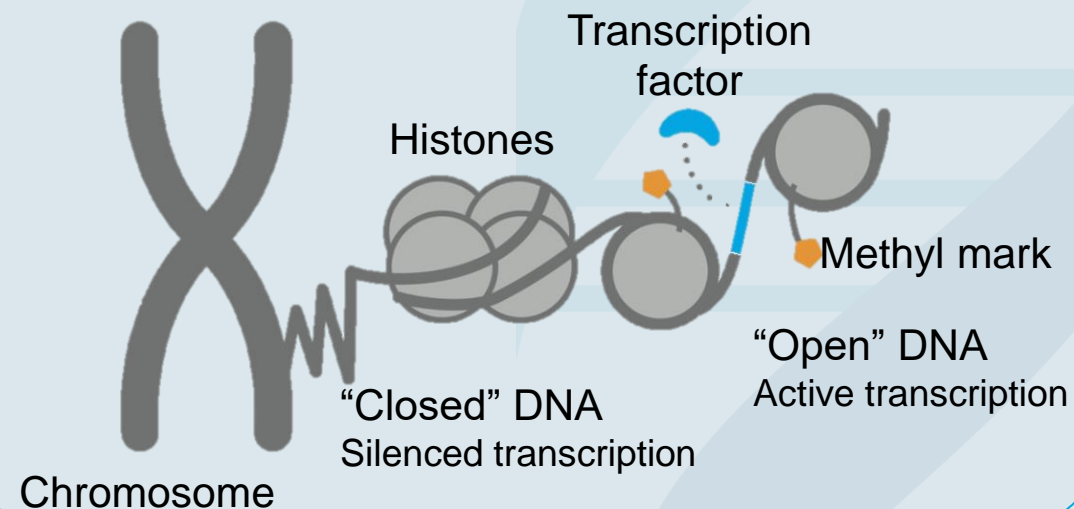
LSD1

Lysine specific
Demethylase 1 (LSD1)

BRD

Bromodomain
proteins

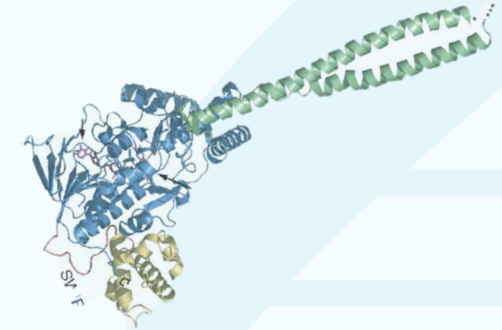
Salarius' lead compound inhibits LSD1, a methyl mark eraser that influences “closing” and “opening” of DNA to alter gene transcription



LSD1 Is An Attractive Target For Cancer Therapy

- **Lysine Specific Demethylase 1 (LSD1)** is an epigenetic “eraser” that is a target of interest for solid tumors and hematological cancers

- LSD1 overexpression is often correlated with poor prognosis via regulation of pathways involved in:
 - Cell differentiation
 - Cell motility
 - Stem-like phenotype
 - Cell cycle
- LSD1 associates with over 60 gene regulatory proteins¹



LSD1 affects gene expression via enzymatic and scaffolding properties

Lead compound, **Secclidemstat** (SP-2577), comprehensively inhibits **LSD1**



LSD1 is a target of interest given its role in cancer progression



Review

Expanding the Role of the Histone Lysine-Specific Demethylase LSD1 in Cancer

Lysine-specific demethylase 1 (LSD1/KDM1A/AOF2/BHC110) is expressed and is an epigenetic drug target in chondrosarcoma, Ewing's sarcoma, osteosarcoma, and rhabdomyosarcoma☆☆☆

Cell

LSD1 Is a Subunit of the NuRD Complex and Targets the Metastasis Programs in Breast Cancer

OPEN ACCESS Freely available online



Over-Expression of LSD1 Promotes Proliferation, Migration and Invasion in Non-Small Cell Lung Cancer

Recent works demonstrate LSD1's demethylation independent activity



ARTICLES

<https://doi.org/10.1038/s41589-019-0263-0>

CRISPR-suppressor scanning reveals a nonenzymatic role of LSD1 in AML

2019

DOI: 10.1002/psc.27888

RESEARCH ARTICLE

2019

Pediatric Blood & Cancer



aspho
The American Society of
Pediatric Hematology/Oncology

WILEY

Catalytic inhibition of KDM1A in Ewing sarcoma is insufficient as a therapeutic strategy

Cell Reports

2018

Enhancer Activation by Pharmacologic Displacement of LSD1 from GFI1 Induces Differentiation in Acute Myeloid Leukemia

ARTICLES

<https://doi.org/10.1038/s41590-018-0273-1>



2019

Histone demethylase LSD1 is required for germinal center formation and BCL6-driven lymphomagenesis



Competitive Landscape and Differentiation

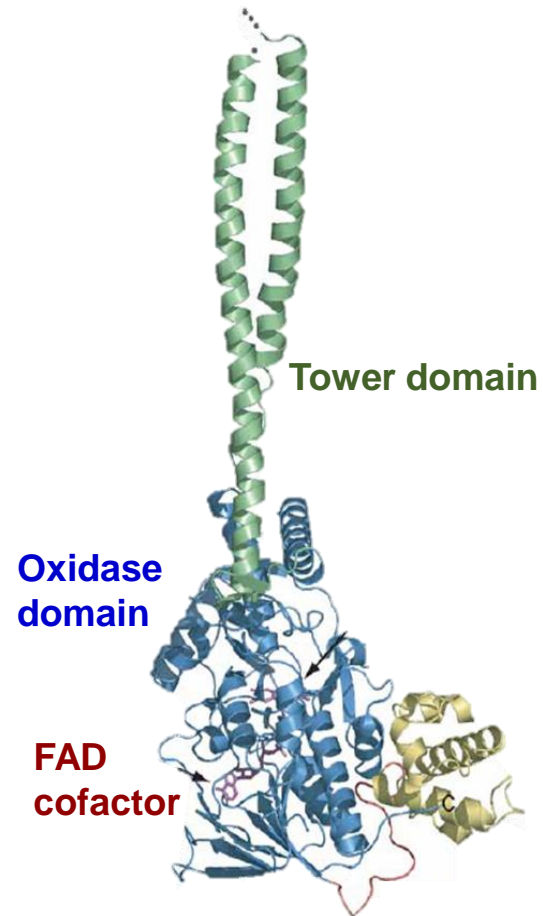










Seclidemstat is a Differentiated Inhibitor Addressing Areas of High Unmet Need Supported by Strong IP

- Secclidemstat (SP-2577) is a small molecule oral therapeutic differentiated by:
 - (1) Mechanism – reversible vs. irreversible
 - (2) Binding location – comprehensive inhibition of enzymatic and scaffolding properties
- Strategically positioned in indications of high unmet need w/ strong mechanistic rationale:
 - Ewing Sarcoma – Aggressive childhood bone cancer, no approved targeted treatments
 - Other Sarcomas – Share a similar biology to Ewing sarcoma
 - Late Stage Prostate/Breast/Ovarian and other cancers are upside
- Composition of matter patents allowed globally
 - US patent expires in 2032 exclusive of possible extensions



LSD1 Competitive Landscape Demonstrates Seclidemstat's Differentiation



	Company	Drug Name	MoA	Indications and Phase
In clinic		SP-2577	Reversible	Ewing sarcoma (Ph1), Advanced Solid Tumors (Ph1)
		INCB59872	Irreversible	Advanced malignancies (AML, SCLC) (Ph1/2), Ewing sarcoma (Ph1b)
		ORY-1001 (RG6016)	Irreversible	AML (Ph2b), SCLC (Ph2a)
		CC-90011	Reversible	Non-Hodgkin's lymphoma and AST (Ph1), SCLC (Ph1)
		IMG-7289	Irreversible	AML and myelodysplastic syndrome (Ph1/2a completed), myelofibrosis (Ph2b)
Preclinic ¹		BEA-17	Reversible	Glioblastoma
		RASP-201	Reversible	AML
		HM9XXX series	Reversible	AML and SCLC

¹Not an exhaustive list of companies in preclinical stage



Degree of LSD1 Inhibition Impacts Therapeutic Activity

Amount of LSD1 function inhibited

Enzymatic activity – Demethylation

Impact: Moderately alter gene expression

LSD1-- SNAG domain association

Impact: Alter gene expression – cancers driven by SNAG domain proteins (AML, SCLC)

Broader LSD1 – cofactor associations

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



- ✓ Differential activity
- ✓ Toxicology Profile

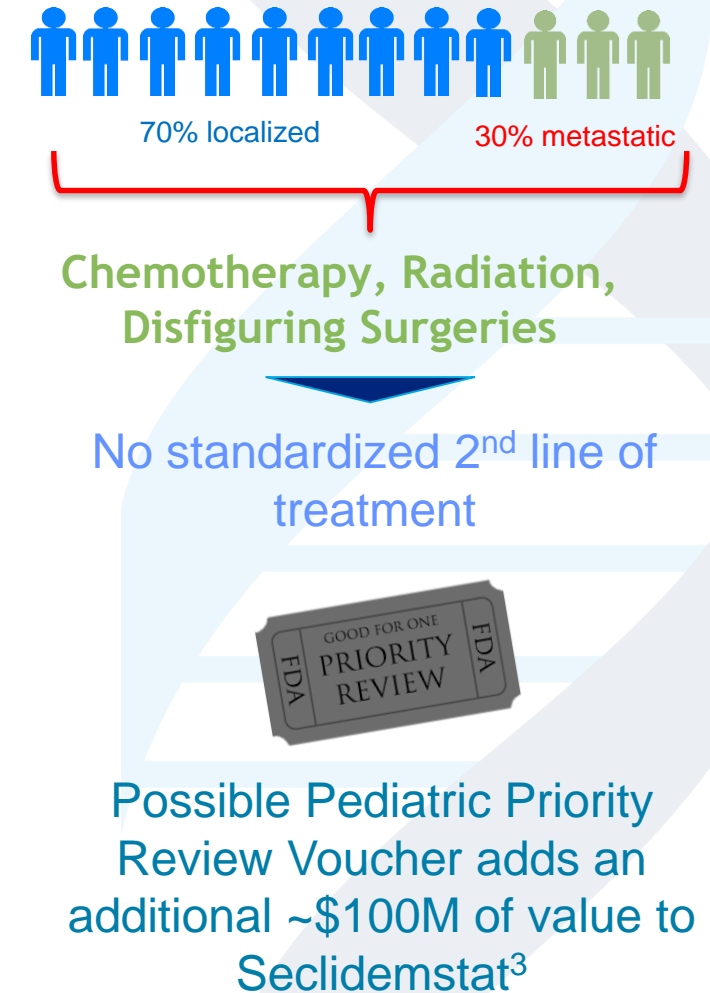


**Speed to Market:
Seclidemstat in Ewing
sarcoma**



Ewing Sarcoma – High Unmet Need in a Critical Population

- Devastating, painful disease that mostly affects children and adolescents
 - ~500 cases diagnosed annually in the US; median age of diagnosis is 15 years old¹
 - Current treatment causes debilitating short and long-term side effects
 - **70% of patients with relapsed/metastatic disease will succumb to the disease²**
- Salarius is developing an **effective and less-toxic treatment option**
 - Strong mechanistic rationale to target LSD1 -- cures in animal models
 - Potential FDA designations allow for accelerated approval opportunities
 - Orphan Status and Rare Pediatric Disease Designation granted
 - \$200M+ global market*



¹ Sarcoma Foundation: Ewing's Sarcoma from www.curesarcoma.org/patient-resources/sarcoma-subtypes/Ewings-sarcoma/

² Pishas, Kathleen I and Stephen L Lessnick. "Recent advances in targeted therapy for Ewing sarcoma" *F1000Research* vol. 5 F1000 Faculty Rev-2077. 25 Aug. 2016

* Based on market and estimated price of Seclidemstat

³ Based on average selling price, see Appendix A



Therapeutic Opportunities In Ewing Sarcoma: EWS-FLI Inhibition Via LSD1 Targeting

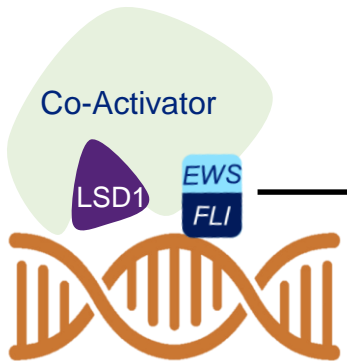
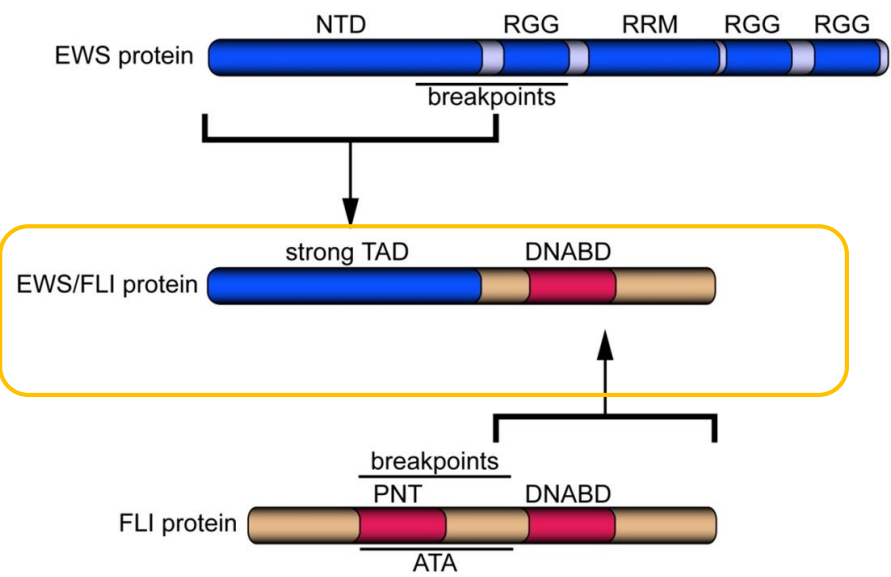
Ewing sarcoma is driven by a chromosomal translocation



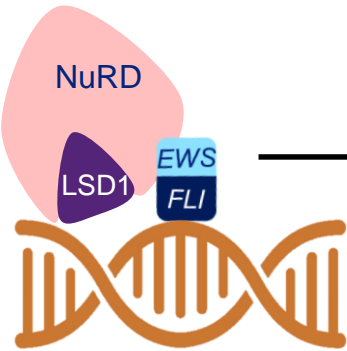
Aberrant transcription factor - gene dysregulation



Oncophenotype
Ewing cells (A673)

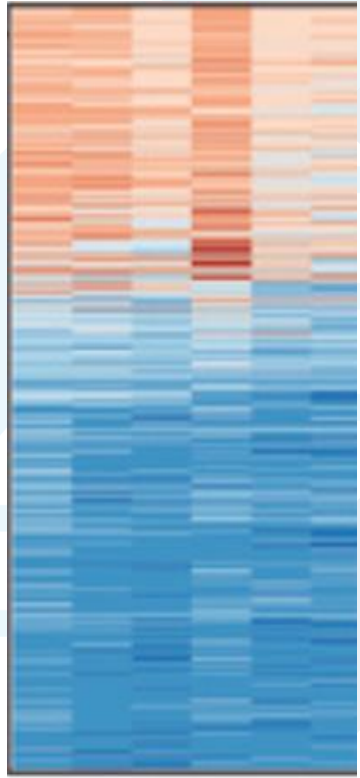


Oncogenes
(Tumor growth)



Tumor Suppressors

Tumor Growth
Tumor Suppression



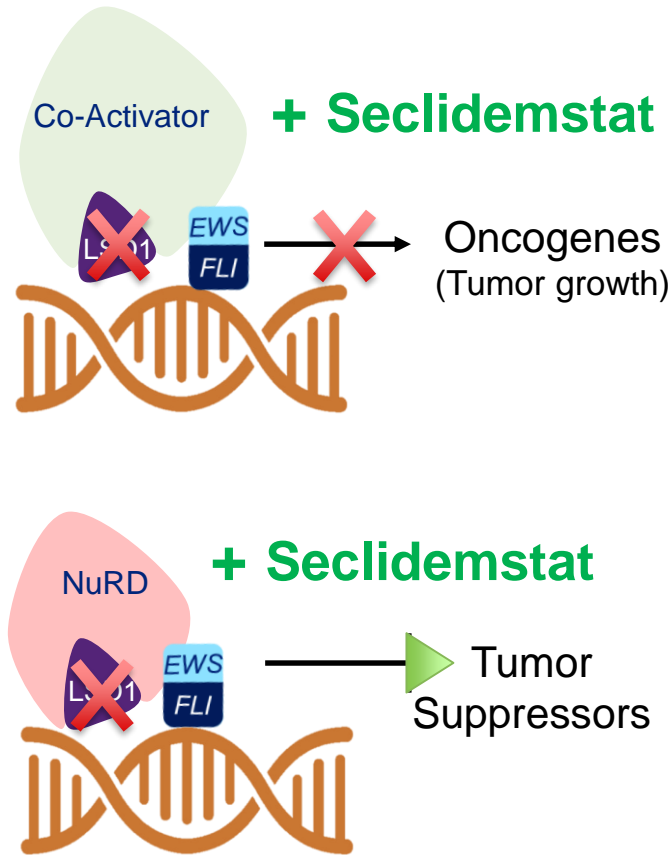
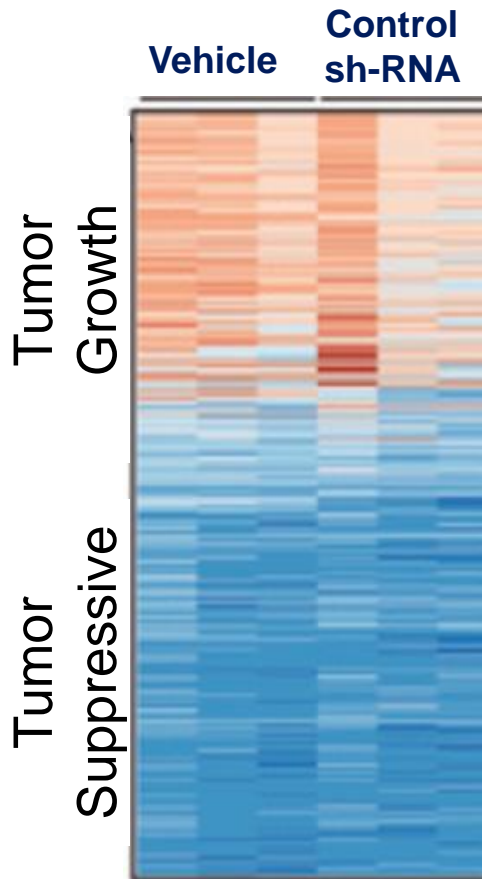
Red = Incorrectly turned ON
Blue = Incorrectly turned OFF

Sankar et al. *Clinical cancer research* 20.17 (2014)



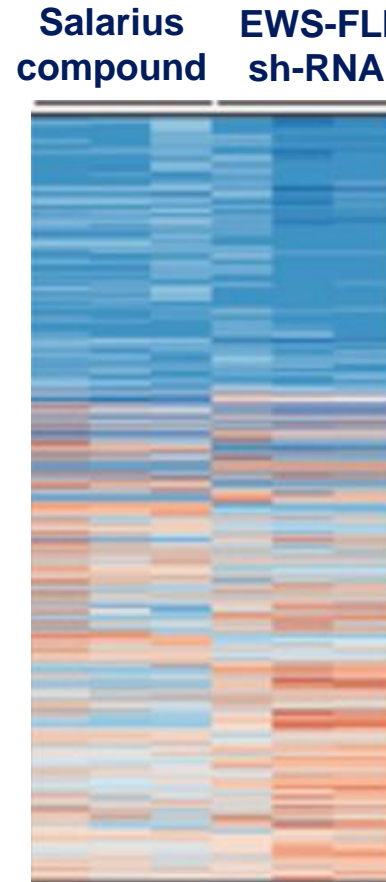
Secclidemstat Reverses Ewing Sarcoma Gene Expression

Ewing's cells (A673)

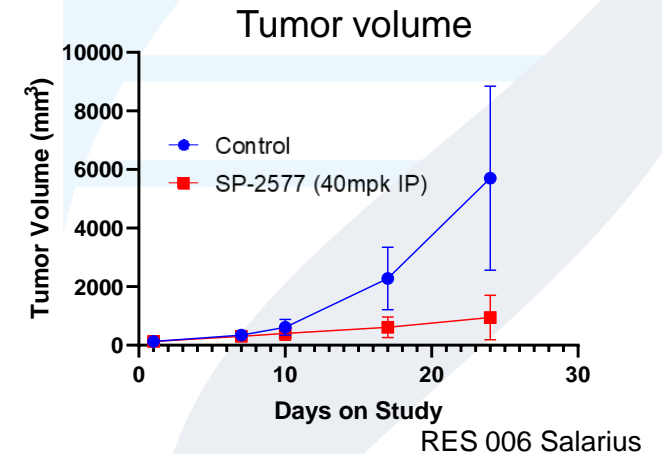
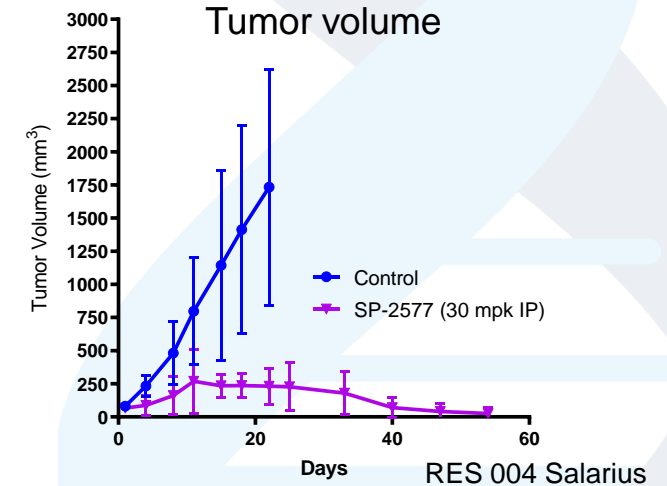


Red = Incorrectly turned ON
Blue = Incorrectly turned OFF

Ewing's cells (A673)



SKNMC in vivo studies



Sankar et al. *Clinical cancer research* 2017 (2014)



Ewing Sarcoma Phase 1/2 Targeting Safety And Efficacy Data Readouts In 2020

**CURRENTLY ENROLLING AT
8 CLINICAL SITES**



Open-label dose escalation / dose expansion study design

Dose escalation

- Dose escalation in cohort 4
- ~20 patients → On track to establish Maximum Tolerated Dose by 1H2020
- Targeting AACR or ASCO for data release

Dose expansion

- ~20 patients at MTD → Safety and efficacy data in 2H2020/1H2021

Early data shows PK is dose proportional

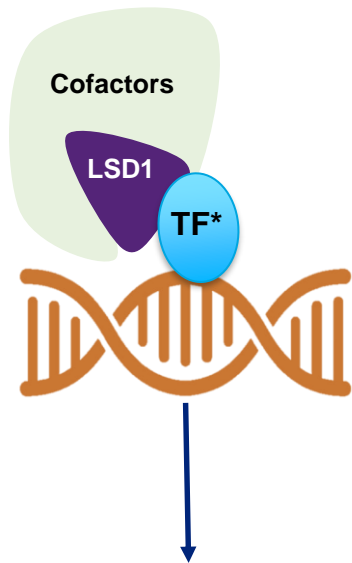


Market Expansion: Secclidemstat in Advanced Solid Tumors



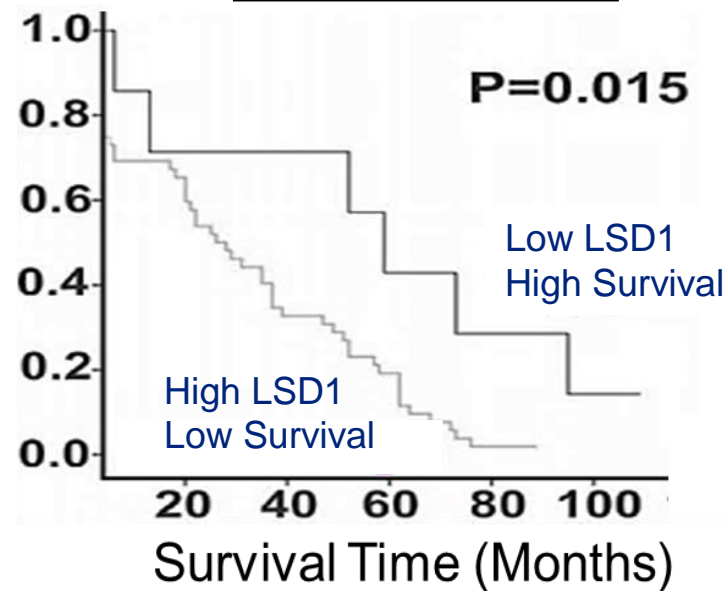
LSD1 Expression Levels are Correlated with Poor Patient Prognosis Across Several Cancer Types

LSD1 associates with different cofactors to drive disease progression across various indications



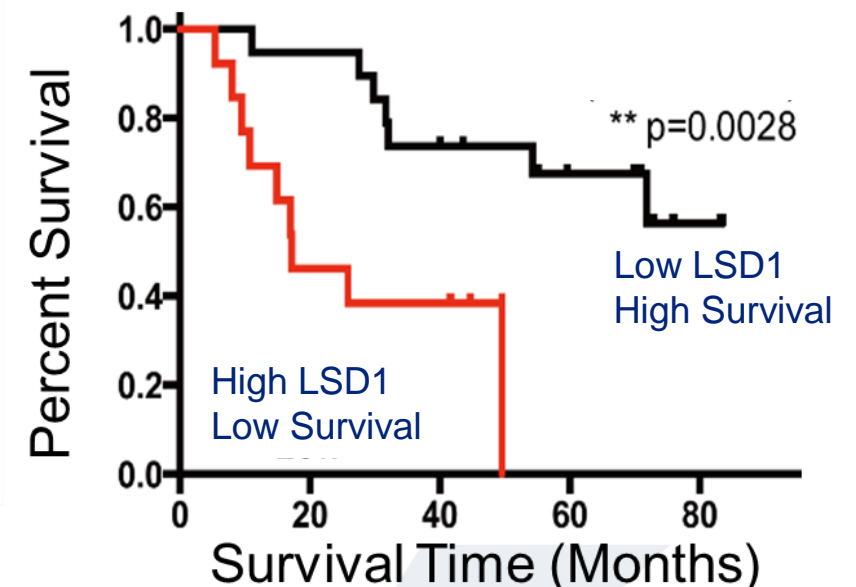
Pro-Tumor Signaling

Castration Resistant Prostate Cancer



Kashyap, V., et al. (2013).

Triple Negative Breast Cancer (TNBC)



Nagasawa, S. et al (2015)

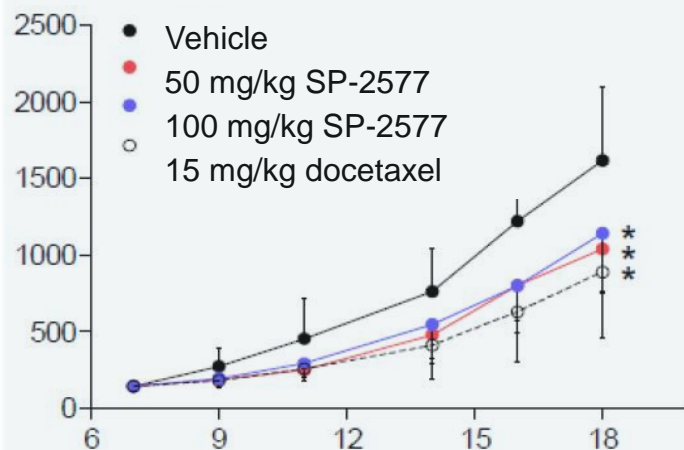
*transcription factors vary based on cancer type



Internal and External Data Demonstrate Single Agent Activity in Hard to Treat Cancers

Prostate Cancer

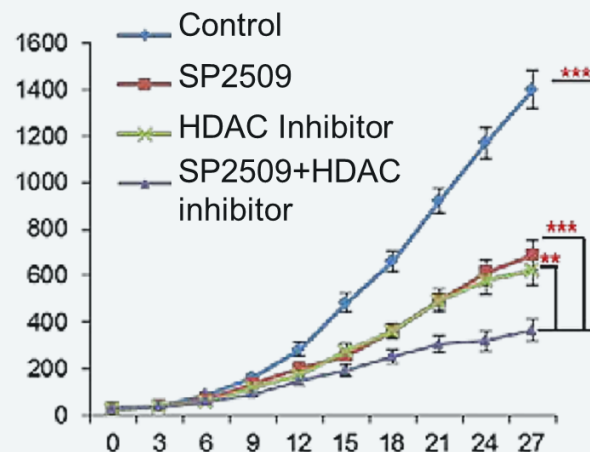
Seclidemstat slows tumor growth in difficult to treat 22RV1 androgen variant animal model



RES 007 Salarius

Triple Negative Breast Cancer

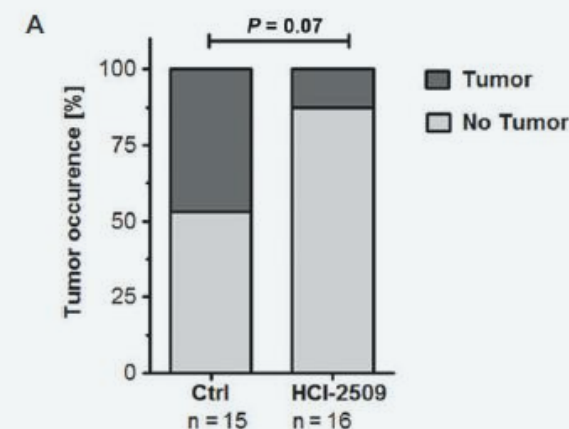
Seclidemstat analog showed ~50% single agent activity, and synergy with an HDAC inhibitor



Cao, Chunyu, et al. *International journal of cancer* (2018)

Non-Small Cell Lung Cancer

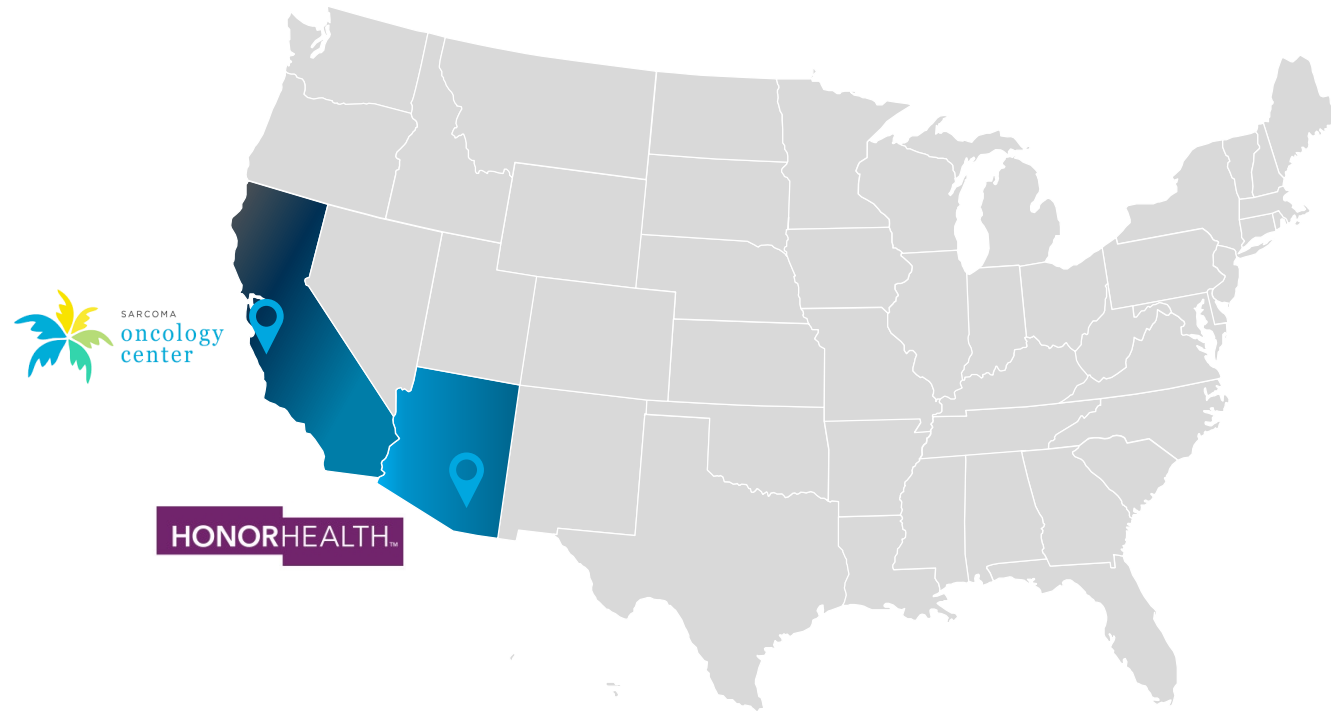
Seclidemstat analog decreased tumor occurrence in tumors driven by EGFR or KRAS mutations



Macheleidt, Iris F., et al. *Molecular Oncology* (2018)



Advanced Solid Tumor Clinical Trial Overview



Open-label dose escalation / dose expansion study design

- Enrolling advanced malignancies and enriching for indications Seclidemstat has shown preclinical efficacy
 - Dose level 4
 - Prostate, breast, related sarcomas, patients with specific genetic backgrounds
- Potential for early signs of therapeutic activity via biomarker readout
- Cohort readouts in 2020



Future Opportunities



Therapeutic Options for Seclidemstat

1

Monotherapy

Currently in clinical proof-of-concept. Preclinically, Seclidemstat has anti-tumor activity across range of cancer types

2

Synergy with chemotherapy

Preclinically, LSD1i shows ability to re-sensitize cells to standard of care agents

3

Synergy with targeted agents

Seclidemstat and its analog shows synergy with other agents such as PARP, EGFR, HDAC, DNMT1 inhibitors

4

In combination with checkpoint inhibitors

Seclidemstat may increase tumor immunogenicity influencing T cell infiltration, antigen presentation

Salarius' ongoing clinical and preclinical work will further clarify the best options for different patients.



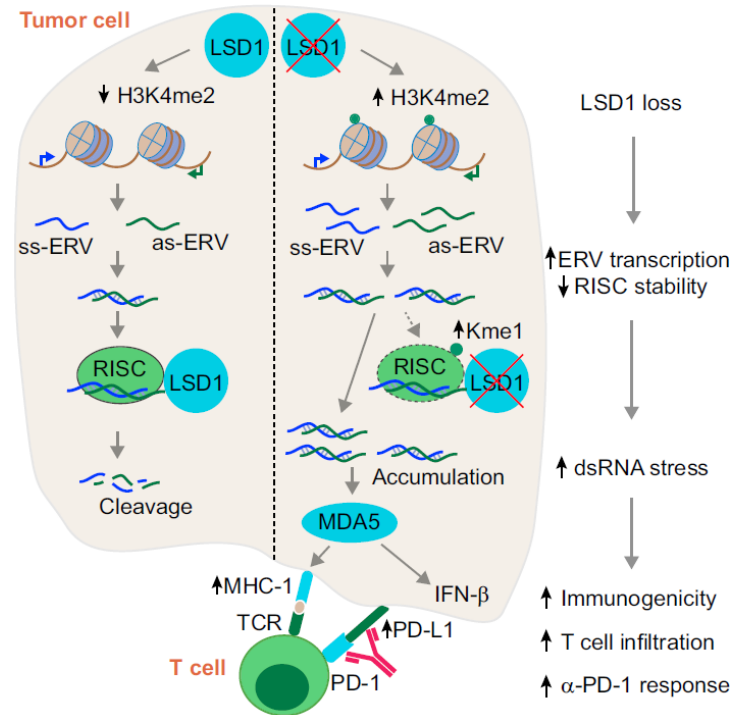
LSD1 Ablation Improves Immunotherapy Efficacy

Cell

Article

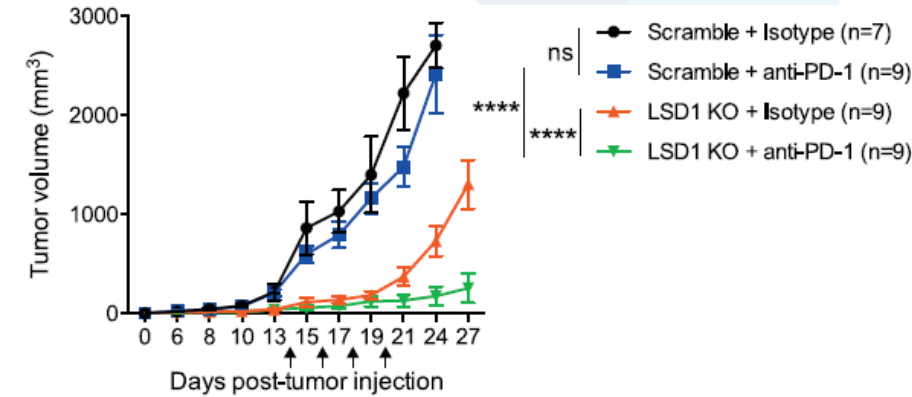
LSD1 Ablation Stimulates Anti-tumor Immunity and Enables Checkpoint Blockade

- LSD1 ablation leads to activation of the IFN pathway and **increases a tumor's immunogenicity**
- Provides a potential therapeutic options for immune-refractory patients



"Cold" tumors turn "hot"

In vivo tumor model



LSD1 KO +PD-1 treatment leads to significant tumor volume reduction.



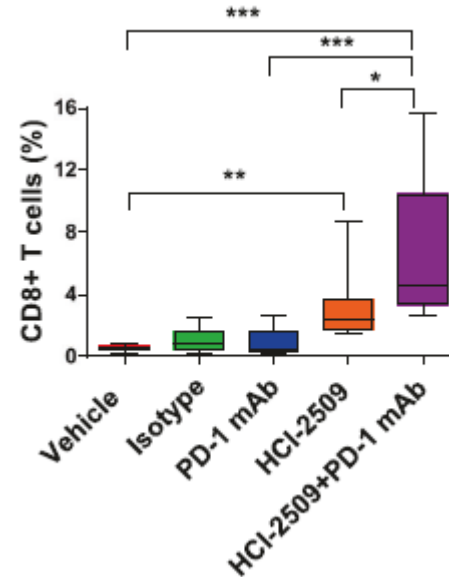
Secclidemstat Analog Shows *in vivo* Synergy with Anti-PD-1

Oncogene

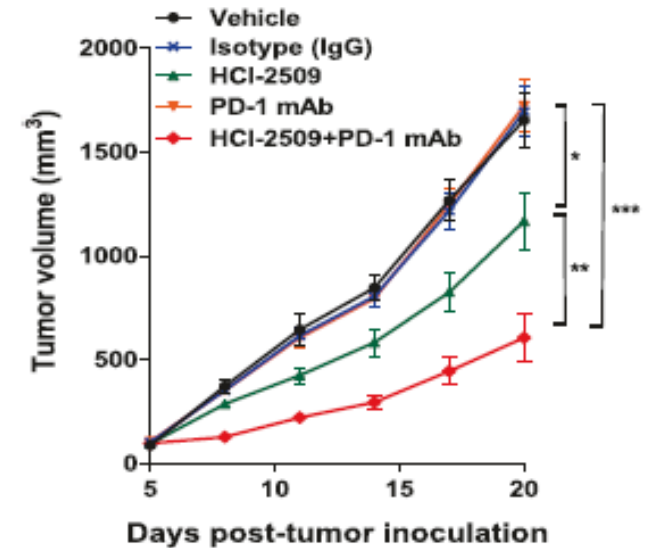
Inhibition of histone lysine-specific demethylase 1 elicits breast tumor immunity and enhances antitumor efficacy of immune checkpoint blockade

- Fewer than 20% of TNBC patients respond to checkpoint inhibitors
- *In vivo* studies showed significant increase in CD8+ T cells and tumor growth suppression for single agent therapy
- Salarius compound sensitizes refractory tumor to checkpoint inhibition

CD8+ T cell infiltration



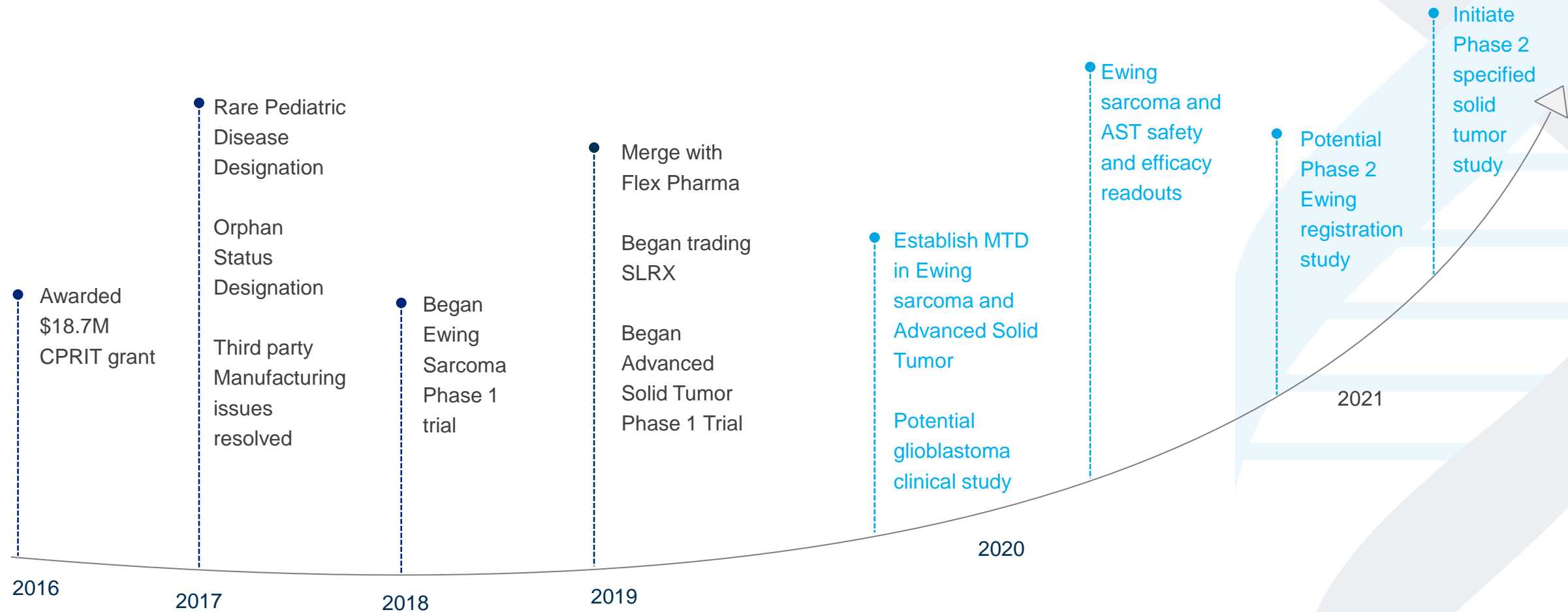
EMT6



Salarius' Development and Future Milestones

Completed

Upcoming



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Thank you!



Appendix A. Seclidemstat Is Eligible To Receive A Pediatric Priority Review Voucher (PRV) Upon Ewing Approval, ~\$100M Value

Date Voucher Awarded	Company Voucher	Held or Sold	Status
2014	BioMarin	Sold July 2014 to Sanofi \$67M	Redeemed
2015	United Therapeutics	Sold August 2015 to AbbVie \$350M	Redeemed
2015	Asklepios Pharmaceuticals	Transferred to Retrophor and Sold May 2015 to Sanofi \$245M	Redeemed
2015	Wellstat Therapeutics	Transferred to AstraZeneca	Unused
2015	Alexion Pharmaceuticals	Held	Redeemed
2015	Alexion Pharmaceuticals	Held	Unused
2016	Sarepta Therapeutics	Sold February 2017 to Gilead for \$125M	Redeemed
2016	Ionis Pharmaceuticals	Held	Unused
2017	Marathon Pharmaceuticals	Held	Unused
2017	BioMarin	Sold November 2017 for \$125M	Unused
2017	Novartis	Held	Redeemed
2017	Ultragenyx Pharmaceutical	Sold December 2017 to Novartis \$130M	Redeemed
2017	Spark Therapeutics	Sold April 2018 to Jazz \$110M	Unused
2018	Ultragenyx	Sold July 2018 for \$81M	Unused
2018	GW Pharma	Sold March 2019 to Biohaven for \$105M	Unused
2018	Leadiant Bioscience Inc.	Held	Unused
2018	Sobi and Novimmune	Sold August 2019 to Astra Zeneca for \$95M	Unused
2019	Vertex	Held	Unused
2019	Alexion	Held	Unused
2019	Novartis	Held	Unused

Average PRV value: \$144M Median PRV value: \$118M

