at a glance™

Salarius PHARMACEUTICALS

Of Note: With three potential sarcoma indications in the Phase 2 portion of a Phase 1/2 trial, a second Phase 1/2 underway and a third announced, Salarius is taking on a leadership position in novel therapies to inhibit LSD1, an epigenetic target receiving increasing validation in a broad range of difficult to treat cancers. Expect potential data releases during the remainder of this year and into 2022.

Key Highlights

- **Salarius' lead compound, seclidemstat, is an oral tablet that targets the LSD1 enzyme, a well-validated target for treating a variety of solid and blood-borne cancers, including sarcomas, prostate, breast, and gynecological cancers, plus a range of blood malignancies.**
- **The company's Phase 1/2 trial treating three different patient groups with soft tissue sarcomas has progressed to the Phase 2 stage, and enrollment has just begun in an investigator-initiated Phase 1/2 trial at MD Anderson Cancer Center, researching two different patient groups with hematologic, or blood cancers.**
- **In addition, the company expects the HonorHealth Research Institute to start an investigator-initiated Phase 1/2 trial soon to study seclidemstat in combination with Merck's category-leading checkpoint inhibitor, Keytruda®, in select gynecological cancers.**
- **The company's sarcoma program targets Ewing sarcoma, myxoid liposarcoma and FET-rearranged sarcomas. It is designed to fulfill a 'fast to market' strategy by developing a novel therapy for rare cancers.**
- **Seclidemstat has already received Fast Track, Orphan Drug and Rare Pediatric Drug designations from the FDA for the Ewing sarcoma indication.**
- **Ewing sarcoma is a rare and deadly pediatric cancer that afflicts about 500 new patients each year in the U.S. Current first-line Ewing sarcoma therapy fails about 40 percent of patients. There is no standard second-line therapy and between 70 percent and 90 percent of patients who have relapsed or failed first-line treatment die within five years.**
- **Myxoid liposarcoma and FET-rearranged sarcomas-- also rare cancers—afflict three times as many new patients (about 1,500 total) as Ewings sarcoma each year in the U.S. and also represent potential "fast to market" indications.**
- **The company believes combination therapies for certain indications may lead to better patient outcomes, faster approvals, and larger addressable markets.**
- **For example, in the Phase 2 portion of the Ewing sarcoma trial, Salarius is teaming seclidemstat with approved cancer agents which have shown significant synergy with seclidemstat in a validated preclinical model.**
- **All the company's current trials are open label. Expect data releases at meaningful intervals through the remainder of 2021 and into 2022.**
- **At June 30, Salarius' cash and cash equivalents stood at $33 million.**

Salarius Pharmaceuticals
(Nasdaq: SLRX)

52 Week Range:	**$0.63-$3.50**
Shares O/S:	**45 Million**
Approx. Mkt Cap:	**$40 Million**
Fiscal Year Ends:	**Dec. 31**

Analyst Coverage: Benchmark, H.C. Wainwright, Ladenburg-Thalmann

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Overview

Interest in the field of epigenetics, especially LSD1 inhibitors, has heated up in recent years, drawing in a slew of companies including Salarius, Bristol Myers Squibb/ Celgene (BMS), Oryzon (ORY.MC), and newly public Imago Biosciences (IMGO), all with mid-stage programs in difficult-to-treat cancers.

LSD1 inhibitors, as a class, work by disrupting the body's gene signaling communications that turn healthy cells cancerous.

Salarius believes its LSD1 inhibitor is one of the few, if not the only one, now in the clinic that is engineered to achieve three of the most advantageous binding and activity mechanisms for a drug in this class.

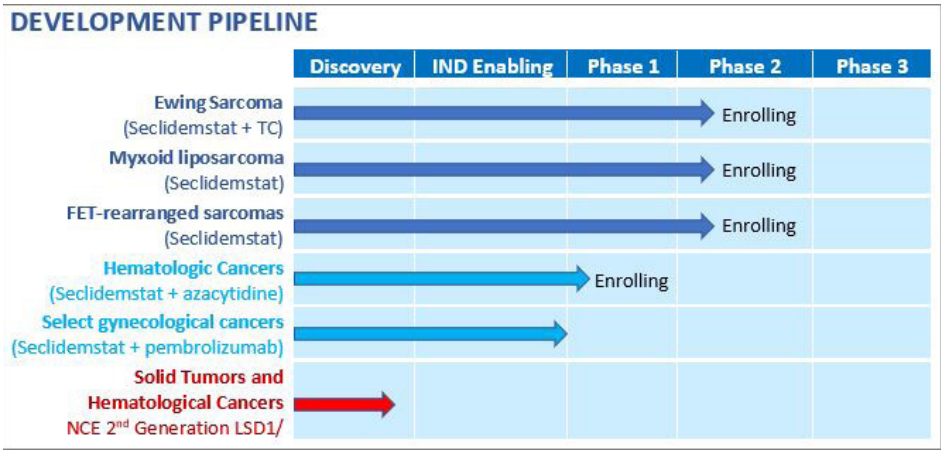
-Seclidemstat is an oral tablet and reversible LSD1 inhibitor, enabling a reduced likelihood of causing the known, potentially dose-limiting blood toxicities of irreversible LSD1 inhibitors.

-Seclidemstat mechanistically inhibits the protein-protein scaffolding associated with LSD1's cancer-causing activity, supporting better efficacy in treating solid tumors. This gives seclidemstat a distinctive feature not shared by all LSD1 inhibitors: it is a treatment candidate for both solid and liquid tumors.

-Seclidemstat has been shown to have a beneficial impact on the tumor microenvironment, heating it up, and potentially increasing the efficacy of checkpoint inhibitors such as Keytruda.

Robust Clinical Program

One Phase 1/2 clinical trial has progressed



to the Phase 2 stage, a second Phase 1/2 trial just started, and a third Phase 1/2 trial is expected to get underway during the second half of 2021.

Early results from dose-escalation portion of the current sarcoma trial for seclidemstat in heavily pretreated patients provided encouraging efficacy signals and showed a manageable safety profile. Based on safety and pharmacokinetics, the recommended phase 2 dose (RP2D) was selected to be 900 mg twice daily. The safety profile is predominantly GI-related and a GI management protocol has been put in place.

Interim data presented at this year's ASCO showed that seven patients with advanced solid cancers, including sarcomas, achieved stable disease (3 greater than six months) with median time to progression ranging from 4.3 to 9.4+ months (three patients). Interestingly, these patients were treated at doses below the RP2D. The combined outcomes are suggestive of disease control and stand as clinically relevant endpoints for soft tissue sarcoma.

Upcoming

2H21 –Potential clinical updates from on-going trials

2H21—Expected start of Ph. 1/2 trial in gynecological cancers in combination with Merck's Keytruda immunotherapy

1H22—Early Ph. 2 data from Ewing and FET-rearranged sarcomas

2H22—Full Ph. 2 data from Ewing and FET-rearranged sarcomas

2022—Early Ph. 1/2 data from gynecological and blood cancer combination trials

Combination Therapies

Early trial findings of this nature, although in a small number of patients, are encouraging for seclidemstat as a single agent and point to its potential as an agent to combine with other drugs for a 1+1=2+ or more synergistic outcome.

With that in mind, Salarius ordered in vitro profiling of seclidemstat's potential synergies with a range of approved chemotherapeutic agents, targeted drugs, and checkpoint inhibitors in a variety of solid tumors and blood cancers.

More is likely to come on this subject, but to date the company has initiated a Phase 1/2 sarcoma clinical trial combining seclidemstat with chemotherapy agents. MD Anderson Cancer center has initiated Phase 1/2 blood cancer trial with a chemotherapy agent and Honor Health selected Keytruda as its combination checkpoint inhibitor teammate in a third indication.

Combined with a checkpoint inhibitor, seclidemstat's expected role is not only to reduce new cancer growth through LSD1 inhibition, but also to unmask tumors, making them more visible to anti-cancer effects of the immune system and allowing checkpoint therapies to reach their full therapeutic potential.

As a combo drug with chemo agents, the synergy would be created by seclidemstat's single-agent activity and the prospect that it can extend tumor response beyond that normally associated with the chemo agent(s) alone.

The Phase 2 potion of the Phase 1/2 trial in Ewing sarcoma was recently expanded by teaming seclidemstat with topotecan and cyclophosphamide (TC), two chemo agents currently used as second-line and third-line therapies to treat the disease. This allows Salarius to treat earlier-line patients than it treated in the dose escalation phase.

The investigator-initiated trial at MD Anderson targets blood cancers and teams seclidemstat with azacytidine, an approved drug in the treatment of MDS and CMML, two precursors of AML.

The investigator-initiated trial planned by HonorHealth targets select gynecological cancers and partners seclidemstat with Keytruda.

FDA Designations

Seclidemstat has received Orphan Drug Designation, Fast Track Designation, and Rare Pediatric Drug Designation from the FDA for Ewing sarcoma with a potential accelerated path to approval. If seclidemstat is approved by the FDA for Ewing sarcoma, Salarius believes it will be eligible for a priority review voucher which provides for an FDA priority review of a subsequent marketing application for a different product. The voucher can be sold, with recent prices reportedly in the $100 million range.

Market Opportunities

Salarius' clinical strategy is to first seek approval of seclidemstat in Ewing sarcoma, a mainly childhood and adolescent cancer with roughly 500 new cases diagnosed each year in the U.S.

Analysts estimate that if seclidemstat is approved for Ewing sarcoma, it could generate global sales in the neighborhood of $200 million annually. Approval for myxoid liposarcoma and/or FET-rearranged sarcoma could generate additional global sales also in the neighborhood of $200 million annually

As a point of reference, Vitrakvi, an approved treatment from Eli Lilly (LLY) for another rare cancer (NTRK-mutation), currently costs $393,000 annually.

By expanding to other indications, especially in combination with other drugs, Salarius expects to participate in much larger markets including the checkpoint inhibitor market and hematologic market.

Acute myeloid leukemia (AML), for example, is a leading blood cancer with nearly 20,000 newly diagnosed cases each year in the U.S. alone, according to 2020 data from the American Cancer Society. The current trial at MD Anderson could lead the company to this indication.

The pending clinical trial of seclidemstat in gynecological cancers will study the safety and efficacy of combining secleidmstat with Keytruda, the leader in the $25 billion checkpoint inhibitor market, which is projected to grow substantially, especially as new combination therapies come online.

Literally any program that plays into the growth calculus of checkpoint inhibitors (i.e., combo therapies) draws attention. Salarius' clinical program should be no exception, especially since it potentially creates the one thing checkpoint inhibitors need most: hot tumors.

Summary

- **Salarius is a leading developer of drugs to inhibit LSD1, a validated target that is often overexpressed and responsible for the unchecked growth of a variety of solid tumors and blood cancers.**
- **Salarius and BMS/Celgene are the only two public companies known to be developing an LSD1 inhibitor with a reversible binding mechanism. This is an important safety feature in treating blood cancers, reducing the potential of problematic toxicities such as neutropenia and thrombocythemia.**
- **Based on encouraging single-agent safety and activity in Ewing sarcoma and FET-rearranged sarcomas, Salarius expanded its clinical programs to address broader cancer markets in combination with potentially synergistic drugs.**
- **Two trials in combination with chemo agents are underway and a third combination trial, set to start soon, will team seclidemstat with Keytruda, to study the combination's safety and efficacy in certain gynecological cancers.**
- **Data releases from on-going Phase 1/2 clinical trials are expected to issue during the remainder of this year and into 2022.**
- **On June 30, 2021, Salarius' cash and cash equivalents stood at $33 million.**

For additional information, contact:

Redington, Inc. • CT 203 222-7399 • NY 212 926-1733 • www.redingtoninc.com

Salarius Pharmaceuticals • 832 834-6992 • www.salariuspharma.com