Molecure

An important year for R&D approaches

In Molecure's recent R&D day presentation, management highlighted the progress of OATD-01 and OATD-02 as the company prepares to begin important clinical trials for sarcoidosis and solid tumours, respectively, in 2023. Details from the presentation show Molecure is planning to maximise the potential of both assets, in our view. Pre-clinical animal model data for OATD-01 suggest it could have potential use in non-alcoholic steatohepatitis (NASH), a fibrotic disease with unmet needs, however we note that animal data is not generalisable to humans. Further, the trial design for the upcoming Phase I study for OATD-02 confirms the company will target cancers where immune checkpoint inhibitors (ICIs) have had limited success, an area where we believe OATD-02/ICI combinations could have an impact. In our view, this is supportive of Molecure's development strategy as the company approaches key trial initiations in 2023.

OATD-01's potential expanding

For OATD-01, the company's first-in-class CHIT1 inhibitor, Molecure presented details on the planned Phase II proof-of-concept trial in sarcoidosis, which it expects to commence in mid-2023. Molecure also presented encouraging pre-clinical rationale for the drug's use in NASH, a fibrotic disease with no medical treatment options and considerable unmet medical needs. We continue to view the demonstration of a disease-modifying profile in sarcoidosis as important in establishing OATD-01's clinical potential

Oncology trials to enrol imminently

The company's second asset, OATD-02, the dual ARG1/2 inhibitor, is expected to begin enrolment for a Phase I solid tumour trial in Q123, following approval from the Polish authorities in November 2022. Details of the trial design confirm that Molecure will target indications where ICIs have low response rates, namely, pancreatic cancer, colorectal cancer, platinum-resistant serous ovarian cancer and renal cell carcinoma. We expect results from this trial will inform the design of a Phase I/II trial in combination with ICIs in solid or potentially hematopoietic tumours.

Pre-clinical pipeline supports long-term goals

Management also highlighted the company's pre-clinical pipeline, which comprises a ubiquitin-specific protease 7 (USP7) programme and novel RNA-targeting small molecule platform, among others. While near/medium-term investor focus will remain clinical development, we view the pre-clinical candidates as potential drivers of longer-term value.

Historical figures

Year end	Revenue (PLNm)	PBT (PLNm)	EPS* (PLN)	DPS (PLN)	P/E (x)	Yield (%)
12/19	124.9	73.7	4.64	0.0	3.30	N/A
12/20	1.2	(13.6)	(0.98)	0.0	N/A	N/A

Source: Company accounts. Note: *EPS are diluted.

Pharma and biotech

8 December 2022

Price	PLN15.3
Market cap	PLN215m

Share price graph

Share details

Code	MOC
Listing	Warsaw Stock Exchange
Shares in issue	14.03m
Cash (PLNm) at 30 September 2022	80.7

Business description

Molecure is a clinical-stage biotechnology company. It uses its medicinal chemistry and biology capabilities to discover and develop first-in-class small molecule drug candidates that directly modulate the function of RNA and underexplored protein targets designed to treat multiple incurable diseases.

Bull

- Two assets to enter clinical development by end-FY23.
- OATD-01 has potential for disease-modifying action in interstitial lung disease.
- Pipeline supported by pre-clinical assets and technology platform.

Bear

- Delays or disruptions to timelines could affect management's estimated cash runway.
- Unvalidated mechanisms of action increase development risk.
- Additional funding needed to complete Phase II development.

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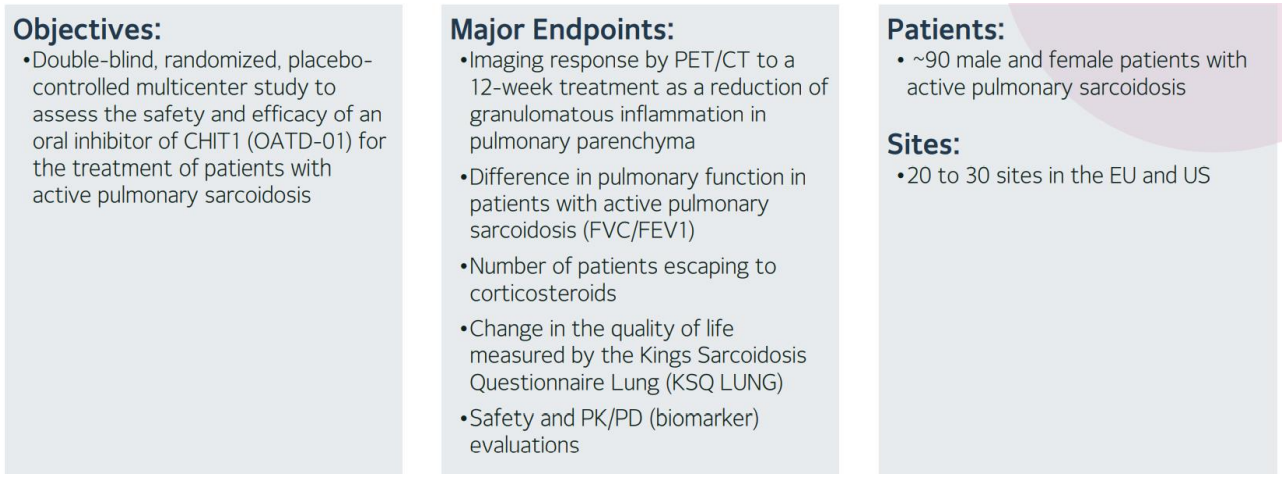
OATD-01 on track to begin Phase II development

OATD-01 is a first-in-class chitinase inhibitor developed by Molecure to be taken as a once-a-day pill for the treatment of inflammatory and fibrotic conditions. Following the return of the global rights for OATD-01 to Molecure in June 2022 by partner Galapagos after a shift in corporate strategy and portfolio review, Molecure will develop the drug's use in sarcoidosis. At its R&D day, Molecure provided details of the trial design (Exhibit 1) for the upcoming global Phase II study, which it believes could provide proof-of-concept not just for OATD-01's use in sarcoidosis but also in other fibrotic diseases. The trial will be a double-blind, randomised, placebo-controlled study and will be run at 20–30 sites in the European Union and United States.

Exhibit 1: OATD-01 Phase II trial design



Source: Molecure R&D day presentation December 2022

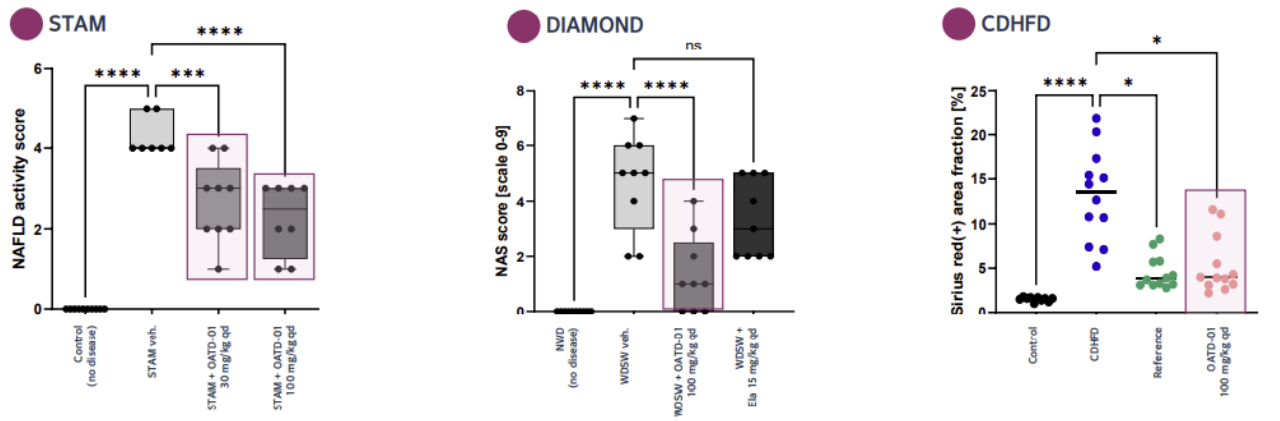
Importantly, management asserts that the inclusion of biomarker imaging endpoints (reduction of granulomatous inflammation as measured by PET/CT) will give the company the best chance of detecting any disease-modifying action, which we believe is crucial to maximising the commercial impact of OATD-01. We note that the inclusion of other endpoints such as corticosteroid escape and quality of life measurements (King's Sarcoidosis Questionnaire) will provide further, clinically relevant data on OATD-01's use. Molecure expects to begin enrolling sarcoidosis patients in mid-2023 (expected full enrolment n=90) and it expects to report top-line data in Q125.

Potential in other fibrotic diseases could broaden utility

In addition to the clinical update, Molecure has presented pre-clinical data highlighting OATD-01's potential utility in NASH, an inflammatory liver disease that can result in fibrosis, cirrhosis and liver failure/cancer. Currently there are no drugs available to treat NASH and the disease is commonly managed through a combination of weight loss and diet modifications. For patients in which the disease has resulted in fibrosis or cirrhosis of the liver, there is no option for reversing the damage and serious cases require a liver transplant. Considering NASH has an estimated annual prevalence rate of 2.8% in the United States, this leaves a considerable unmet medical need.

The data presented by Molecure show that OATD-01 was able to reduce the hallmarks of non-alcoholic liver disease in mouse models (STAM, DIAMOND) and fibrosis in rat and mouse models (CDHFD, STAM), which is shown by the data points highlighted in the purple boxes in Exhibit 2. The company also reported information, gathered during the collaboration with Galapagos, which implies OATD-01 acts on pathways that experience dysregulation in models of NASH, such as the acetyl-CoA metabolic process, collagen fibril organisation and macrophage migration, further suggesting the drug could have applications in these indications.

Exhibit 2: OATD-01 effect in mouse/rat models of NASH



Source: Molecure R&D day presentation December 2022

While the data presented is pre-clinical animal model data, and therefore not generalisable to a human population, it continues to build the case for OATD-01's potential in inflammatory and fibrotic diseases outside of sarcoidosis. We view the drug's potential in NASH and idiopathic pulmonary fibrosis (IPF, discussed in our initiation report) as a considerable opportunity for the company, given the serious unmet medical needs in these conditions. However, a key factor to OATD-01's success will be the demonstration of a disease-modifying profile in these conditions. Hence, we see the PET/CT measured biomarker imaging endpoints from the upcoming Phase II sarcoidosis trial as an important readout for establishing OATD-01's clinical potential.

OATD-02's clinical oncology journey begins

OATD-02, Molecure's dual ARG1/2 inhibitor, was granted Polish regulatory approval in November 2022 to conduct a clinical trial, and management now expects to begin enrolment for a Polish Phase I trial in Q123. The company will investigate OATD-02's use in oncology, where it believes ARG1/2 inhibition could help restore antitumour immune responses by interacting with immunosuppressive tumour microenvironments. Details released at the recent R&D day confirm that the open-label, single-arm Phase I trial will assess the safety and tolerability of OATD-02 as a monotherapy in pancreatic cancer, colorectal cancer, platinum-resistant serous ovarian cancer and renal cell carcinoma patients at three sites in Poland. The study will employ a Bayesian optimal interval design (which management assert may allow the company to reach the recommended Phase II dose faster and with greater confidence) and aims to enrol 30–40 patients. Management expects the study will last for one and a half years before reporting top-line results in H224. Secondary endpoints will focus on efficacy measures (response and survival) and PK/PD biomarker data.

We expect results from this trial will inform the design of a Phase I/II trial of OATD-02 in combination with ICIs in solid or potentially liquid tumours. We note that all the cancer types eligible for enrolment in this Phase I are indications where ICIs have limited use and hence OATD-02 could have a potentially important impact, in our view. Management expects to spend PLN11m over the course of the trial, with PLN4–5m potentially covered by development grants the company expects to apply for in FY23. We see the commencement of this Phase I trial in Q123 as the next catalyst for Molecure.

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