molecure

Fate can be altered

July 21, 2022

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Warsaw, July 2022

Presenting Team

Samson Fung
MD
Chief Medical Officer

Experienced pharmaceutical executive with significant expertise in translational science, clinical development, strategic marketing and business development.

Roche · morphosys · NOVARTIS

Zbigniew Zasłona
PhD,
VP Research Biology

Biologist with extensive experience in anti-inflammatory drug development programs (molecular, cellular and in vivo).

Trinity College Dublin, The University of Dublin · sitryx

Piotr Iwanowski
MD, PhD
Clinical Research & Operations Expert

20 years of experience in managing , monitoring and guiding drugs through the clinical development pathway.

SERVIER · Bristol Myers Squibb · WOCKHARDT

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PhD, MBA
Chairman of the Board & CEO

Entrepreneur and investor with 20-year experience in the life science industry.

ILLINOIS · MEDICALgorithmics · LSI LIFE SCIENCE INNOVATIONS FUND

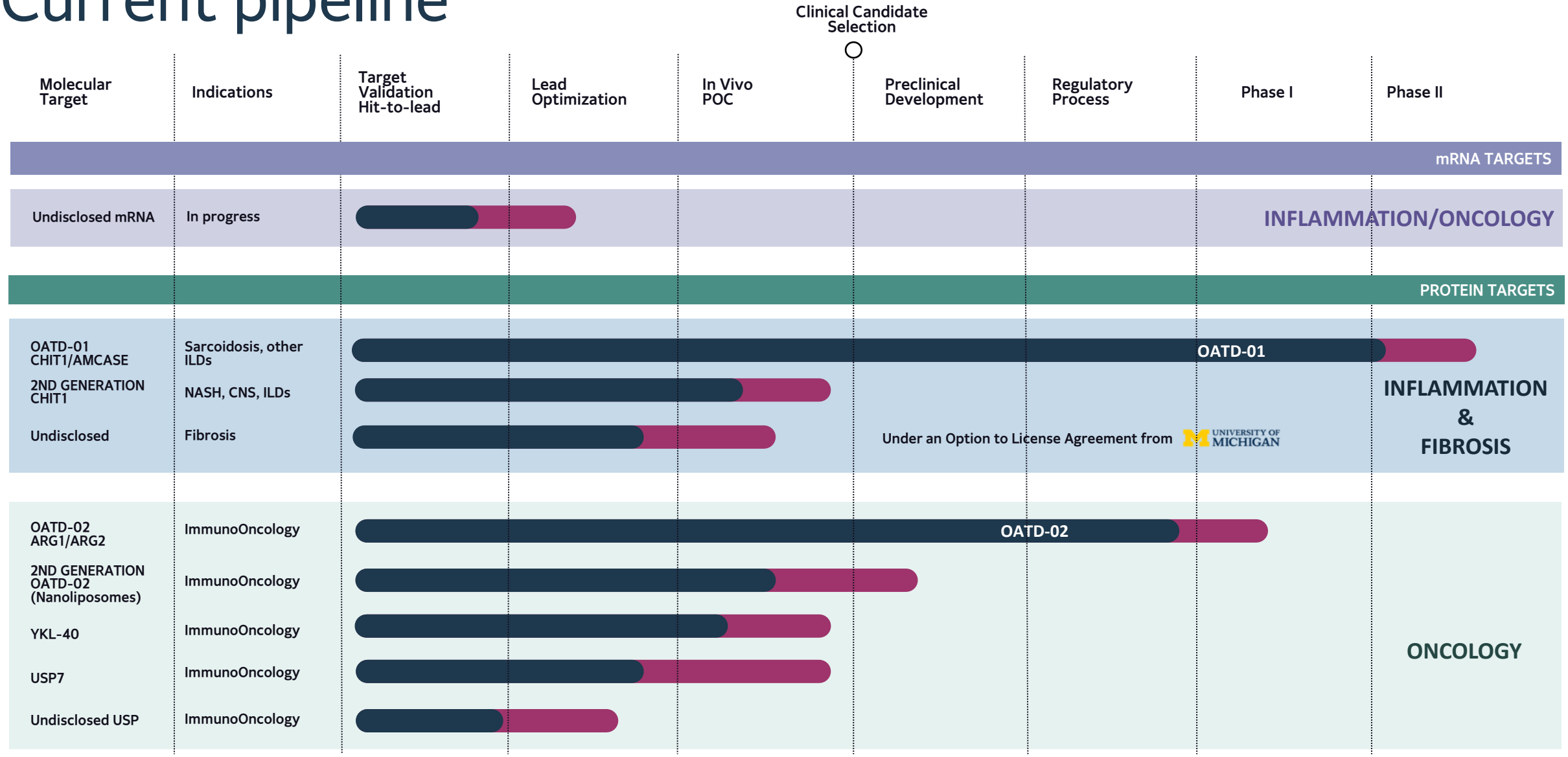
Nicolas Beuzen
PhD, MBA
Business Development Director

20 years of experience working with high performance, international R&D teams.

University of Glasgow · sanofi pasteur MSD · Ethypharm

Developing first-in-class small molecule drugs to address challenging protein targets

Current pipeline



Molecure now has global rights to OATD-01

1) Molecure regained all rights, associated data, intellectual property and inventory to OATD-01

2) Data generated to date confirm an attractive benefit-risk potential, warranting further development

3) Data and information generated and obtained by Galapagos are highly supportive of further advancing OATD-01 into phase II

4) Molecure has revised its development plan for the potential first indication in sarcoidosis

5) OATD-01 has the potential to become a disease modifying treatment and transform the standard of care

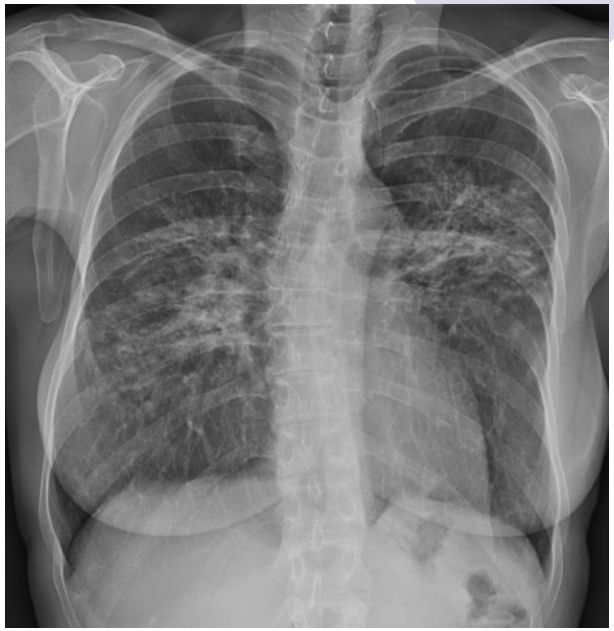
6) Lung sarcoidosis is optimal for first PoC in human and a steppingstone towards other diseases such as other ILDs (including IPF), NASH or IBD (Crohn's disease)

Open to partnerships/licensing deals for further development and commercialization of OATD-01 and long-term collaboration on new therapeutic indications

Why sarcoidosis?

What is sarcoidosis

- Sarcoidosis is a systemic inflammatory disease characterized by formation of immune granulomas in various organs
- Granulomas are tight aggregates of immune cells consisting of centrally located, pathologically activated macrophages, epithelioid and giant cells, surrounded by T cells
- Over 90% of sarcoidosis patients develop pulmonary sarcoidosis with granulomata in lungs
- The most severe complication of sarcoidosis is the occurrence of pulmonary fibrosis
- Sarcoidosis is usually associated with chronic dyspnea and frank impairment of pulmonary function
- Pulmonary fibrosis is the most frequent cause of respiratory failure and results in the majority of deaths related to sarcoidosis in western countries.
- Mortality is up to 8% in western countries, and is due to respiratory failure



Chest radiograph of a 62-year-old woman with stage II pulmonary sarcoidosis
(Mayo Clin Proc Innov Qual Outcomes. 2019 Sep; 3(3): 358–375

Epidemiology

- Sarcoidosis is an idiopathic, global disease
- Affecting both men and women
- Variation in sarcoidosis incidence across ethnic groups is well documented, with African-Americans and northern Europeans having the highest rates of sarcoidosis incidence (up to 3x increase in incidence in these populations).
- Peak incidence for both men and women between 30 and 39 years of age

In 2022, the estimated diagnosed sarcoidosis prevalence is about 320,000 cases in the 7MM (US, EU and Japan) (vs. 212,000 cases for IPF).

Clear need for new drugs for sarcoidosis

Currently no cure for sarcoidosis and treatments only modify the granulomatous process and its clinical consequences. Furthermore, there is little prospective data to guide therapy strategies

Systemic corticosteroids remain the standard of treatment and although they have short-term benefits, there is little evidence for extended therapeutic efficacy.

Corticosteroids treatment is symptomatic and associated to well known safety and tolerability concerns and poor compliance

- Approximately 40% of newly diagnosed sarcoidosis patients initiate therapy within 96 days of diagnosis
- One-third of patients who initiate treatment progress to a second-line therapy after an average of nearly 4 months on treatment
- 36% of patients in the second line receive an additional third line of therapy after an average of 3 months of treatment.
- Immunosuppressants (e.g. methotrexate) are primarily used in later lines of therapy and in combination with other drug classes (usually corticosteroids)

- Use of anti-TNFα biologics (e.g., infliximab, adalimumab) among newly diagnosed patients is minimal and mostly seen in later lines of therapy. Despite their efficacy, biologics are associated with higher costs.

Creating Significant Value with OATD-01

A potential disease modifying agent for sarcoidosis

OATD-01 – product profile and strengths

- Novel, single-digit nM, first-in-class small molecule chitinase inhibitor targeting a key mechanistic pathway involved in inflammation and tissue remodeling

- Dual anti-inflammatory and anti-fibrotic activity through a single new chemical entity

- Once-a-day pill, direct compression tablet formulation

OATD-01 – scientific and regulatory milestones achieved to date

- Efficacy proven in multiple animal models of sarcoidosis, idiopathic pulmonary fibrosis, (IPF) and non-alcoholic steatohepatitis (NASH)
- Compelling translational data
- Excellent pharmacological profile
- Demonstrated safety in animals and healthy volunteers in preclinical and Ph I studies in human volunteers
- FDA Orphan Drug Designation (ODD) for sarcoidosis and IPF
- Scientific Advice from European Medicines Agency and Pre-IND Written Responses from FDA obtained earlier in 2022 by former partner Galapagos

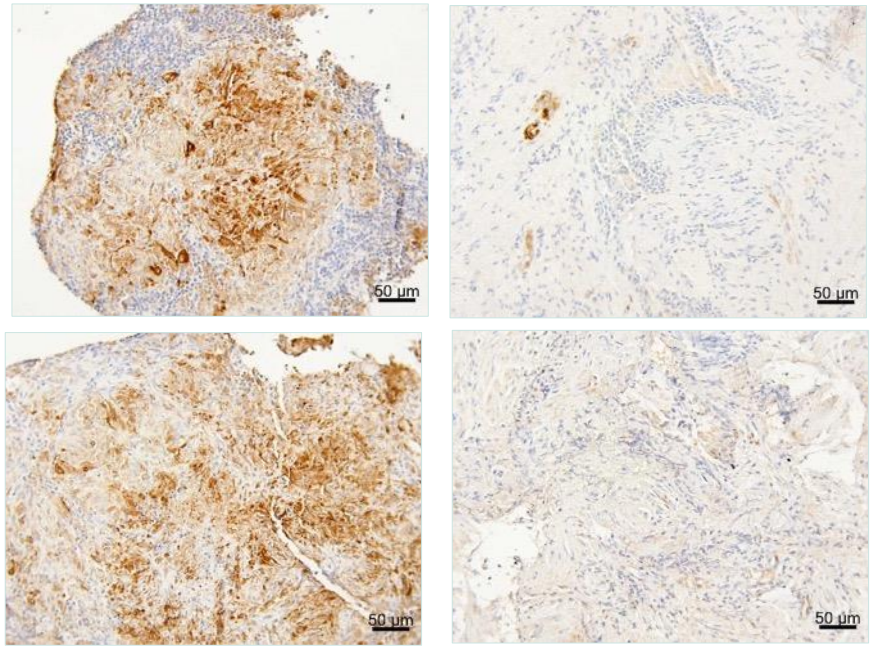
CHIT1 is highly expressed in lungs of patients with sarcoidosis

Expression of CHIT1 in lungs and serum of patients with confirmed sarcoidosis

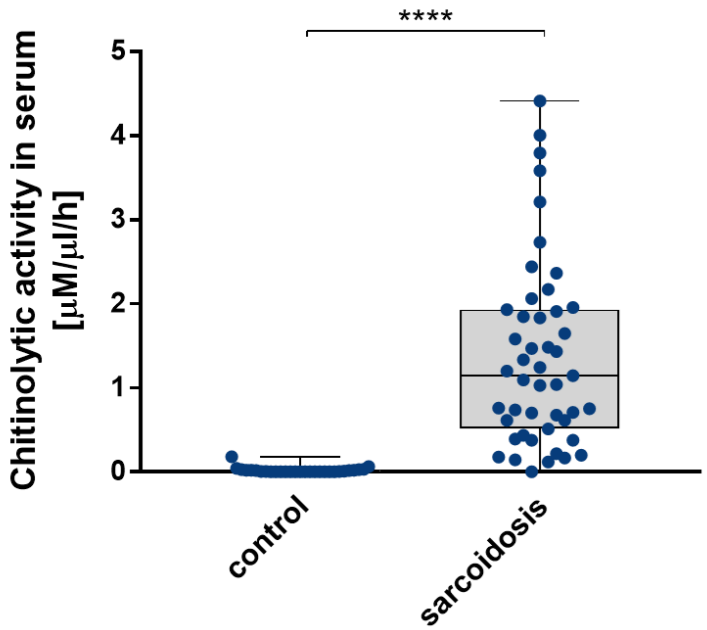
Lung sarcoidosis

Biopsy 1. – diseased lungs with granulomas

Biopsy 2. – non-diseased lungs



Serum



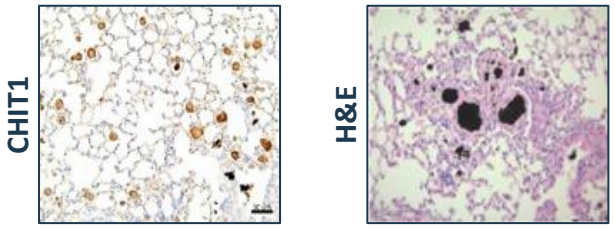
Lung biopsies from sarcoidosis patients show very strong expression of CHIT1 specifically restricted to granulomas and not present in the unaffected areas.

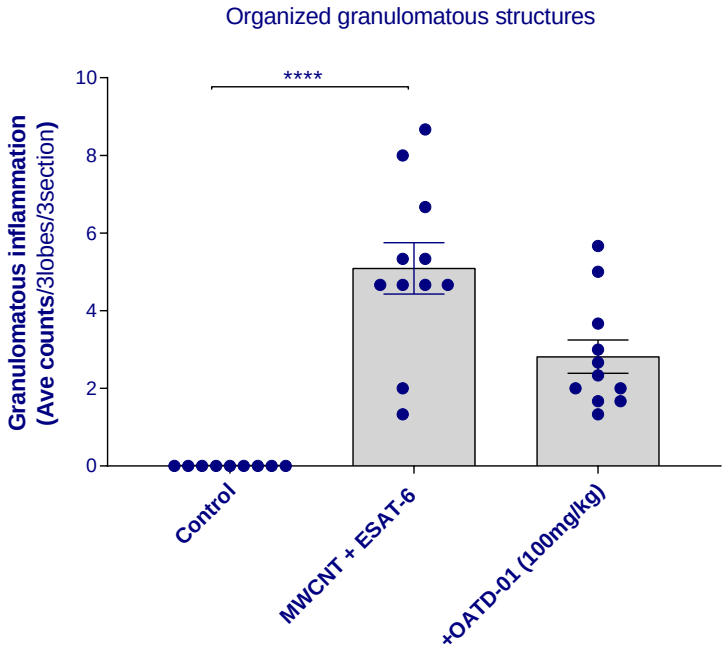
In patients, 65-75% of broncho-alveolar lavage fluid (BALF) cells expressed CHIT1. Cytological analysis confirmed that the main CHIT1-positive cell type in BALF are macrophages (80%), additionally lymphocytes stained positive (30-40%).

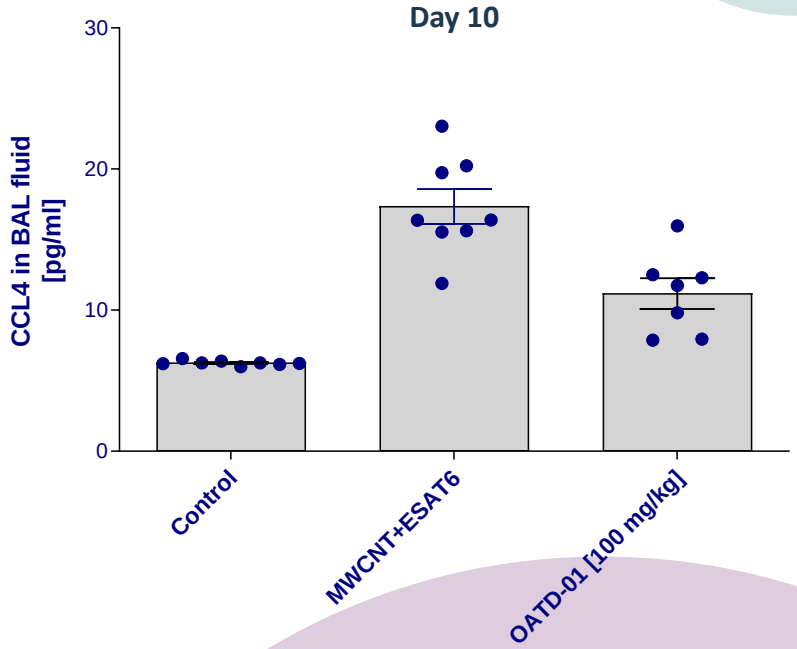
Internal OAT data

Efficacy of OATD-01 in MWCNT-induced granulomatous inflammation model in mice

40 days post MWCNT+ESAT-6







OATD-01 suppressed development of the organized granulomatous structures in lungs and CCL4 levels in BALF in the MWCNT (multi wall carbon nanotubes) + ESAT-6-induced model of sarcoidosis

OATD-01 – translational and clinical data to support a PoC study in sarcoidosis

Very strong clinical correlation of CHIT1 activity with the disease process

- 10-100 fold elevated CHIT1 activity in serum and BALF in sarcoidosis patients
- Correlation with the clinical stage and progression of the disease, and with requirement for a more aggressive therapy
- CHIT1 is considered the best marker of disease progression

Unmet medical need: no effective therapy, advanced disease is debilitating with 8% mortality

- Standard of Care: steroids, no long-term benefits, side effects
- Anti TNFa: modest clinical benefits, organ specific

Clinical Phase I results

- Full and sustained pharmacodynamic (PD) effect achieved with OATD-01
- Reduction of baseline chitinolytic activity in plasma to 10% or less
- The observed PK, PK/PD and safety profile justify further clinical development

GLPG4716-CL-102 (NCT05030857) conclusions

Drug-drug Interaction and Food-effect Study With OATD-01 and Midazolam in Healthy Subjects

Conclusions:

- **OATD-01 when co-administered with midazolam was well tolerated.**
- **Repeated dosing of OATD-01 did not result in meaningful changes in midazolam exposure, demonstrating the absence of interaction of OATD-01 with CYP3A4.**
- **Food decreased the rate of absorption without impacting the bioavailability of OATD-01.**

The second drug-drug interaction study, with GLPG4716 and nintedanib and pirfenidone in healthy subjects is not yet completed – clinical study report *expected* 4Q22.

OATD-01 on-track to enter Phase 2 clinical study H1 2023

A double-blind, randomized, placebo-controlled multicentre study to assess the anti-granulomatous efficacy and safety of an oral inhibitor of CHIT1 (OATD-01) in patients with active pulmonary sarcoidosis

- 6 to 10 out-patient sites in the US and EU
- Relatively short recruitment: 12 months; patient availability confirmed with key opinion leaders (KOL) clinicians
- 70-90 male and female patients with active pulmonary sarcoidosis, treatment-naïve or currently untreated
- 3-month treatment
- Strong interest of KOL clinicians confirmed in EU and US

- Well-defined end points:
  - primary endpoint related to evaluation of granulomatous inflammation in lungs
  - secondary endpoints related to pulmonary function, escape to corticosteroids (in case of lack of efficacy), quality of life measurement, and others
  - exploratory endpoints related to extrapulmonary manifestations of sarcoidosis, disease biomarkers, and others

Timelines & budget estimates for Phase 2 PoC

Submission package filing expected Q1 2023

Estimated budget: $10 mln

Potential sources of funding:

- Foundation for Sarcoidosis Research FSR in the U.S.: $2-5 mln
- NIH: $ 2 mln
- Grants from domestic sources,
- European Union i.e.: EIC Accelerator Programme under Horizon Europe: 2,5 mln EUR grant

Key Opinion Leaders supporting the clinical development of OATD-01 in sarcoidosis

- Prof. Michael Kreuter MD PhD
- Head of the Center for Interstitial and Rare Lung Diseases in the Thoracic Clinic of the University Hospital Heidelberg

- Marlies Wijsenbeek – Lourens MD PhD
- Pulmonologist, Chair Centre for Interstitial Lung Diseases and Sarcoidosis Erasmus MC

- Vincent Cottin MD PhD
- Hospices Civils de Lyon (Centre Hospitalier Universitaire de Lyon) | CHU Lyon National Reference center for Rare pulmonary diseases, department of respiratory medicine, MD PhD

- Daniel Culver MD PhD
- Chair of the Department of Pulmonary Medicine at Cleveland Clinic's

- Prof. Marc Judson MD PhD
- Chief, Division of Pulmonary and Critical Care Medicine Albany Medical College

Prof. Michael Kreuter

Prof. Dr. Michael Kreuter is Head of the Center for Interstitial and Rare Lung Diseases in the Thoracic Clinic of the University Hospital Heidelberg.
This is an ILD center certified by the European Reference Network (ERN) and a sarcoid expert center recognized by WASOG*.

Prof. Kreuter is a specialist in internal medicine and specializes in pneumology and hematology/internal oncology. After his clinical training in Münster and a science scholarship at the Harvard Medical School in Boston, USA, he has been working in the thoracic clinic since 2005.

Prof. Kreuter's clinical and scientific focus includes interstitial and rare lung diseases. In this field he carries out numerous scientific projects on comorbidities, epidemiology, biomarkers as well as diagnostics and therapy of interstitial lung diseases.

* World Association of Sarcoidosis and other Granulomatous Disorders

Market

- Currently the sarcoidosis market is fragmented due to the lack of standard of care
- Annual cost or treatment varies form $280 for prednisone alone to over $30,000 for adalimumab
- Disease modifying treatment (DMT) will warrant a premium price, estimated acceptable for the commercial payer at around $22,000 annually
    - Annual cost to society in the US is $1.5bn in work loss and $8.7bn in direct medical cost.

Conservative estimate of the market at maturity with DMT is $1.5bn

Competition

Companies reported developing innovative sarcoidosis molecules with disease modifying potential are:

- Kinevant Sciences (Phase II) - GM-CSF ligand inhibitor
- MorphoSys / Novartis (Phase II) - Interleukin 18 ligand inhibitor
- Kyorin / aTyr Pharma (Phase I b/II a) - Neuropilin 2 modulator
- Pfizer (Phase I) – JAK 1/3 inhibitor
- AI Therapeutics (Pre-clinical) -mTOR inhibitor

OATD–01 potential source of significant value

1) OATD-01 is a novel, first in class dual acting chitinase inhibitor
2) Potentially disease modifying, and could transform standard of care for patients with lung sarcoidosis – no current compelling treatment options
3) Efficacy proven in multiple animal models of sarcoidosis, IPF NASH & IBD (Crohn's) so its first clinical PoC can be a steppingstone towards a number of other diseases
4) OATD-01 has been generally well tolerated in animal experiment and in human
5) FDA Orphan Drug Designation (ODD) for sarcoidosis and IPF
6) Large market opportunity and unmet need in sarcoidosis due to poor disease management with steroids

Open to partnerships/licensing deals for further development and commercialization of OATD-01 and long-term collaboration on new therapeutic indications for chitinase and CLP inhibitors

Questions & answers

Abbreviations used:

- ADME: Absorption, Distribution, Metabolism, And Excretion
- BALF: Broncho-alveolar Lavage Fluid
- BID: Bis In Die – Twice A Day
- CHIT1: Chitotriosidase
- CSR: Clinical Study Report
- CTA: Clinical Trial Application
- DLT: Dose-limiting Toxicity
- EMA: European Medicine Agency
- FDA: Food And Drug Administration
- FIH: First-in Human
- GLP: Good Laboratory Practices
- FPFV: First Patient First Visit
- IND: Investigational New Drug
- IPF: Idiopathic Pulmonary Fibrosis
- KOL: Key Opinion Leader
- LPLV: Last Patient Last Visit
- MAb: Monoclonal Antibody
- MTD: Maximum Tolerated Dose
- NASH: Non-alcoholic Steatohepatitis
- nM: Nanomolar
- NOAEL: No-observed-adverse-effect Level
- ODD: Orphan Drug Designation
- PK/PD: Pharmacokinetics / Pharmacodynamics
- PO: Per Os - Orally
- PoC: Proof Of Concept