molecure

R&D Day

December 7, 2022

Fate can be altered

Molecure SA (”MOC") and its Board and employees make no warranties or assurances regarding the accuracy or completeness of any representations or other materials contained herein.

The information and data contained herein reflect the current conditions and assessments of the market situation as at the time of preparation of the document and are subject to change at any time. All predictions and forward-looking statements express current views, subjective judgments, predictions and assumptions about potential and uncertain future events and are subject to risk and uncertainty.

MOC and the Management Board indicate that there is a possibility of unexpected events (in particular unpredictable ones), so there is no guarantee that the situation will develop in accordance with the presented predictions.

The document is provided for informational purposes only. MOC, its affiliates and its management and employees do not accept any liability for direct, indirect or any loss or damage that may arise in connection with the use of this document or the information or data contained therein.

Warsaw, December 2022

Speakers

Marcin Szumowski

PhD, MBA

Chairman of the Board & CEO

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

Nicolas Beuzen

PhD, MBA

Business Development Director

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

R&D leaders

Samson Fung

MD

Chief Medical Officer

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

Zbigniew Zasłona

PhD,

VP Research Biology

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

Speakers Clinical Experts

Professor Rafał Krenke

Head of Department of Internal Medicine, Pulmonary Diseases & Allergy, Medical University of Warsaw

Member of the European Respiratory Society, Member of the Board of Polish Society of Lung Diseases, Polish Society of Internal Medicine

Professor Cezary Szczylik

Head of the Department of Clinical Oncology and Chemotherapy European Health Center Otwock

President of the Foundation for Experimental and Clinical Oncology, Co-founder of the Study of Molecular Medicine, Member of the Polish Society of Oncology

Agenda

Welcome and Agenda
Katarzyna Mucha, CCGroup

Introduction to Molecure
Marcin Szumowski CEO

OATD-01: Sarcoidosis Market Opportunity and Future Focus (Part 1)
S. Fung CMO, Z. Zasłona VP Biology, Prof. Rafał Krenke Pulmonologist, N.Beuzen BD Director

OATD-02: Clinical Development in a Broad Range of Cancers (Part 2)
S. Fung CMO, Z. Zasłona VP Biology, Prof. Cezary Szczylik Oncologist

USP7, YKL-40, UoM, RNA (Part 3)
Z. Zasłona VP Biology

Concluding Remarks
Marcin Szumowski CEO

Q&A, Discussion
Panel after each section

Molecure history 2012-2022

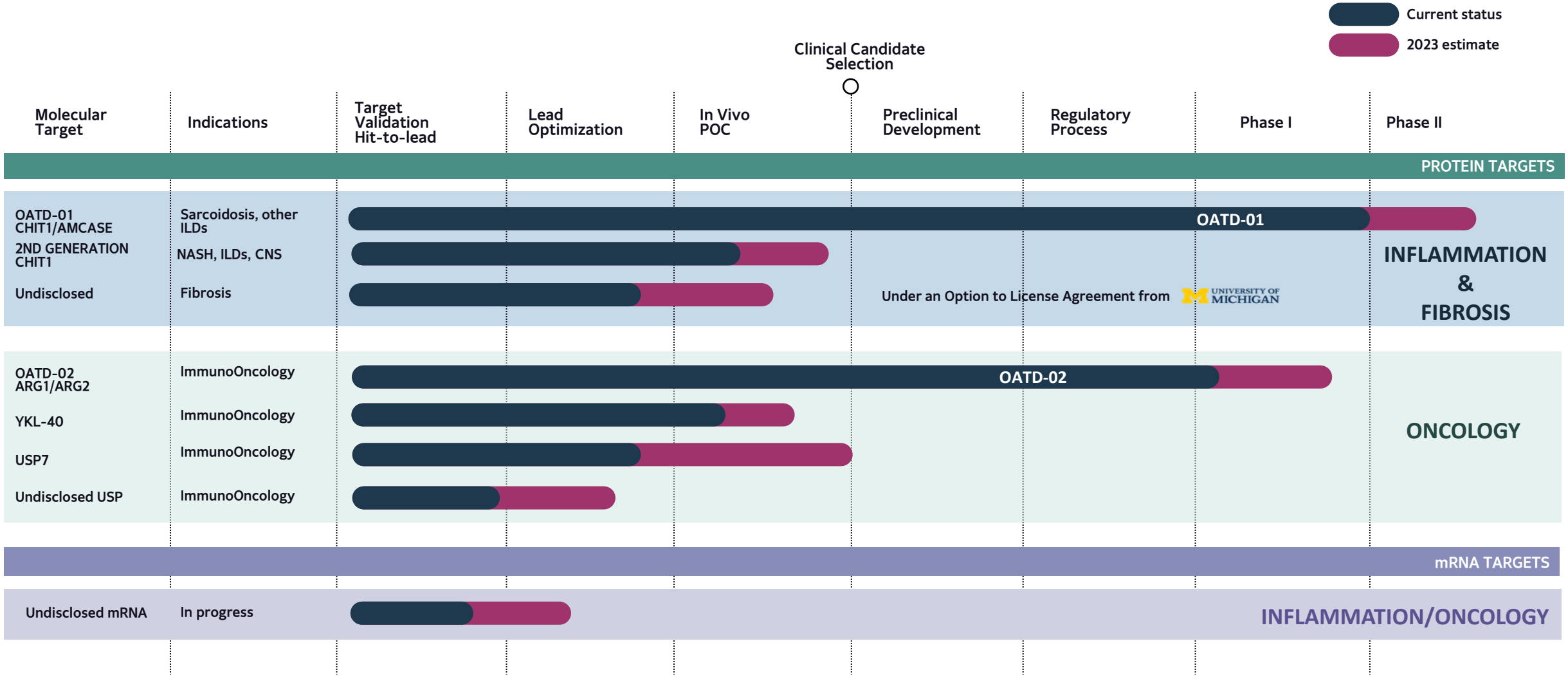
CORPORATE

- **2013** — Seed Round and First Drug Discovery Program
- **JAN 2015** — Exclusive License from Yale and Series A Investment
- **NOV 2016** — President's Award for Best R&D Company in Poland
- **APR 2018** — IPO on the Warsaw Stock Exchange (WSE)
- **NOV 2020** — Global License for OATD-01 with Galapagos NV
- **MAR 2022** — Option to License from the U. of Michigan

PIPELINE

- **2014** — Launch of the First Chitinase Inhibitors Program
- **NOV 2015** — Nomination of First Clinical Candidate OATD-01 (Chitinase Inhibitor)
- **OCT 2017** — First Dosing in a FIH Clinical Trial for OATD-01
- **JAN 2019** — FDA ODD* for OATD-01 in IPF (and Sarcoidosis)
- **JUNE 2021** — RNA Platform: Exclusive Partnership & Research Collaboration with the IIMCB in Warsaw
- **JUNE 2022** — All rights to OATD-01 regained from Galapagos NV
- **NOV 2022** — CTA Approved for OATD-02 FIH trial in Oncology patients

High Value Pipeline



Our Main Achievements to Date

Accelerating clinical development

- Delivering on value generating strategy as a focused small molecule company
- Ongoing commitment to focus on discovery and development of novel small molecule therapies for millions of people with serious and incurable diseases
- Robust pipeline of novel, first in class differentiated assets

Significant pipeline momentum:

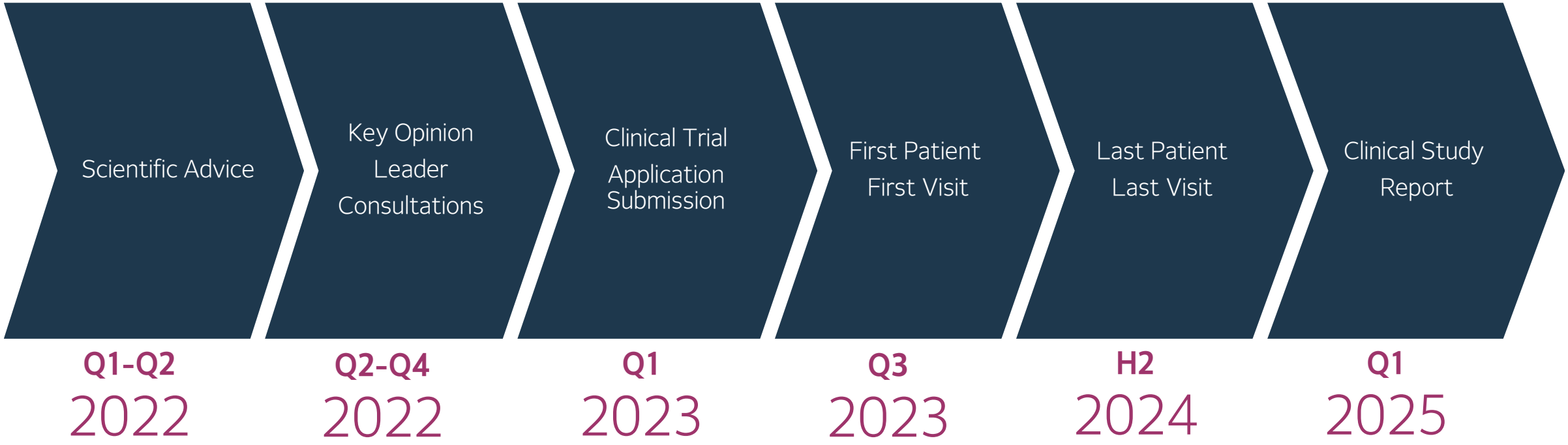
- Lead proprietary candidate, OATD-01 a novel chitinase inhibitor in sarcoidosis expected to advance into a Phase II PoC study in mid-2023
- Plan to evaluate OATD-01 in other indications
- Following the recent CTA approval in November, our 2nd proprietary candidate, OATD-02, a first in class arginase inhibitor for a broad range of cancers will be administered to first patients in early Q1 2023

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

OATD-01: disease modifying potential in sarcoidosis

OATD-01 in sarcoidosis on-track to enter Phase II in 2023

Clinical Trial Application submission package filing expected Q1 2023



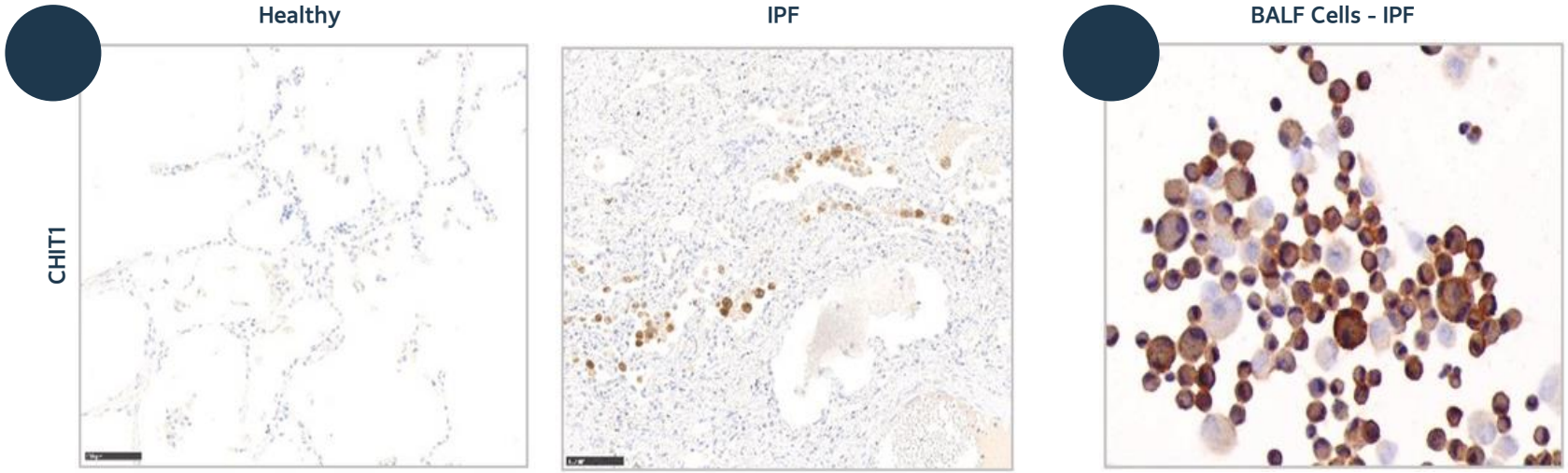
OATD-01 Targets CHIT1 (Chitotriosidase 1)

Biological & Medical Significance of this novel target

Targeting CHIT1

- CHIT1 is the most prominent chitinase in humans, can cleave chitin, participates in the **body's immune response and is associated with inflammation**, tissue damage and remodeling processes

- CHIT1 is expressed mostly by activated macrophages



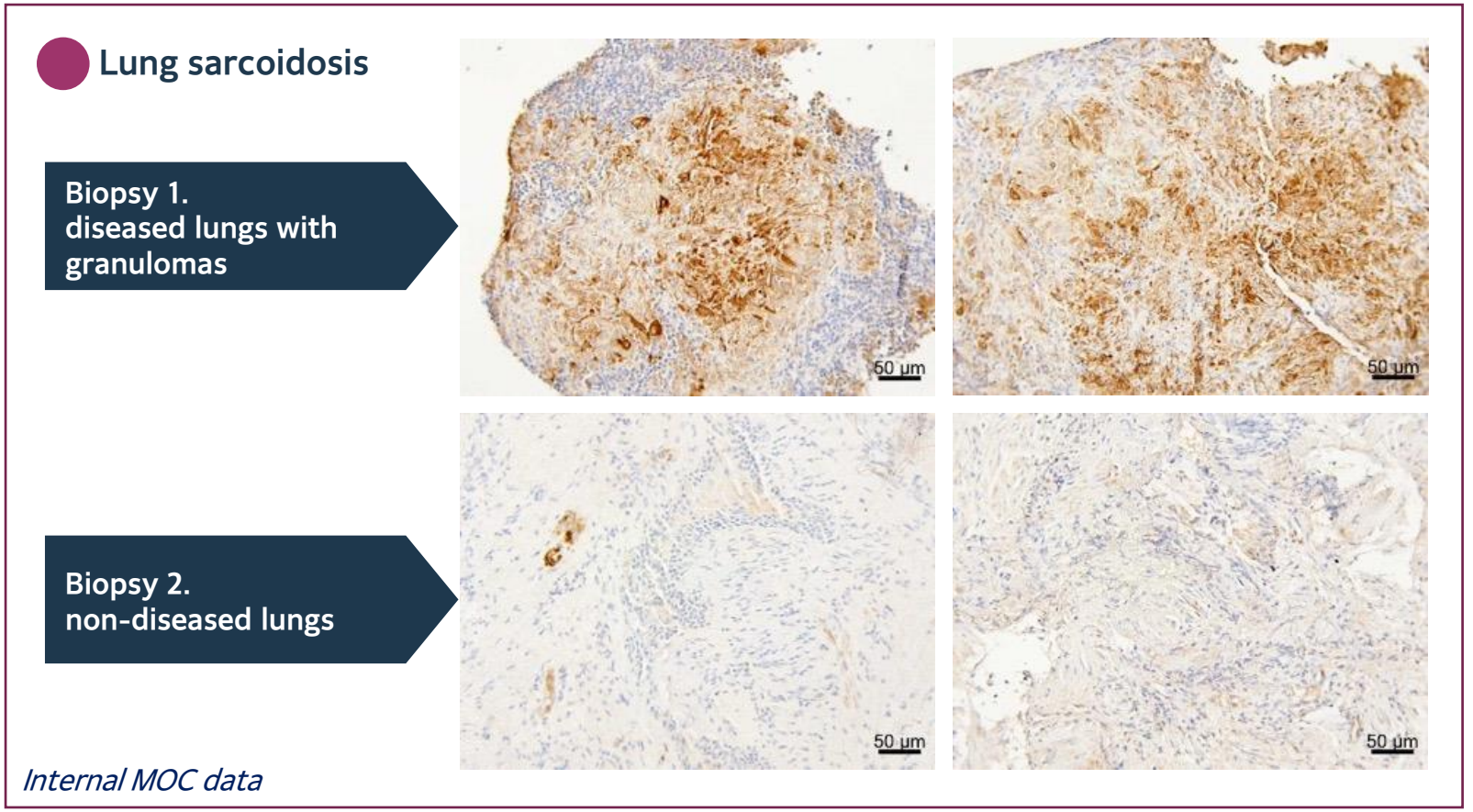
CHIT1 is highly expressed in lungs of patients with sarcoidosis

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

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 confirms that the main CHIT1-positive cell type in BALF are macrophages (80%), additionally lymphocytes stained positive (30-40%).



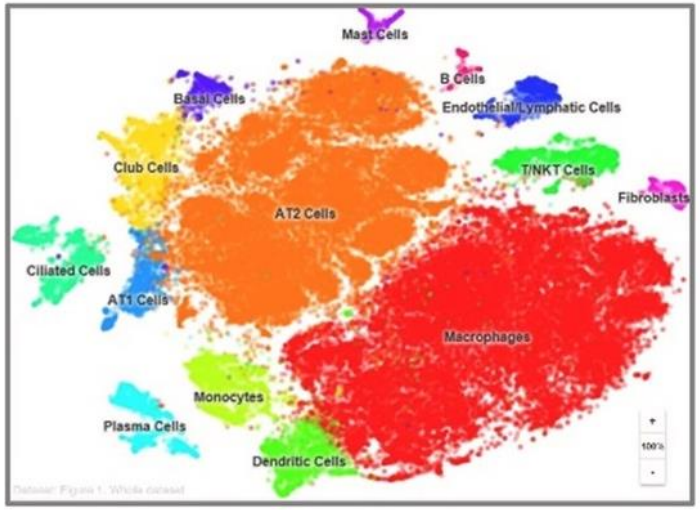
Internal MOC data

CHIT1 is expressed in a subset of fibrosis-specific lung macrophages of IPF patients

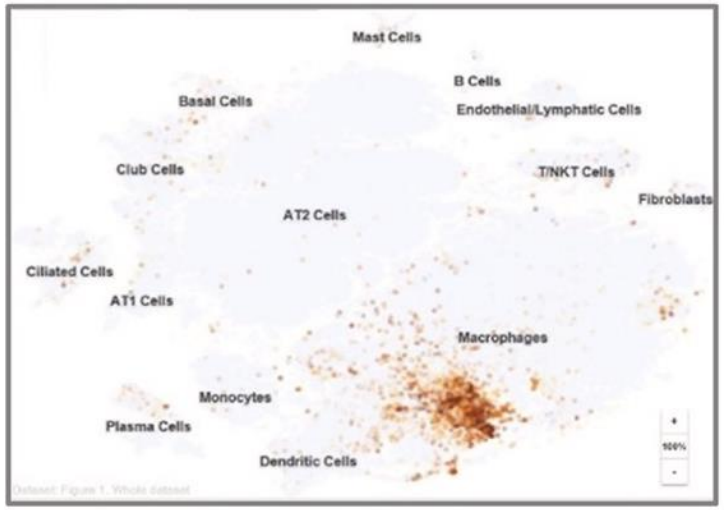
In a differential single cell atlas of pulmonary fibrosis, CHIT1 is expressed in profibrotic alveolar macrophages exclusively present in patients with fibrosis and not in healthy donors

https://www.nupulmonary.org/resources

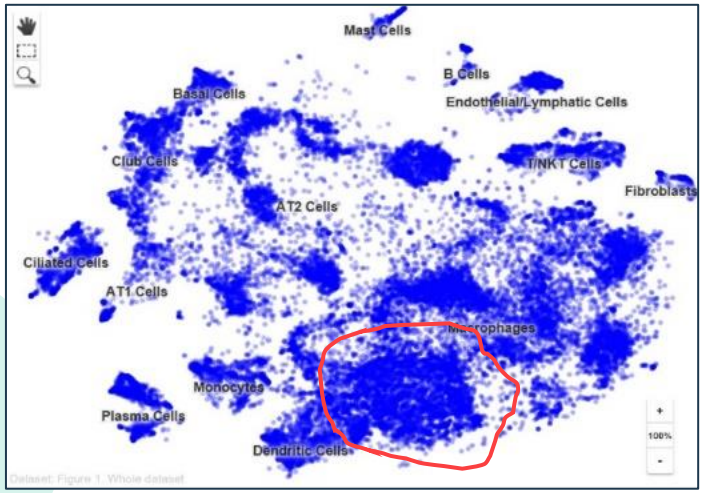
Lung cell clusters



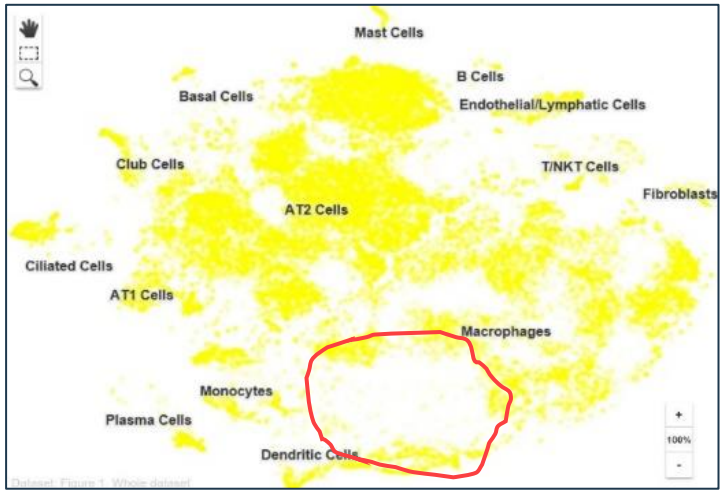
CHIT1



Fibrosis



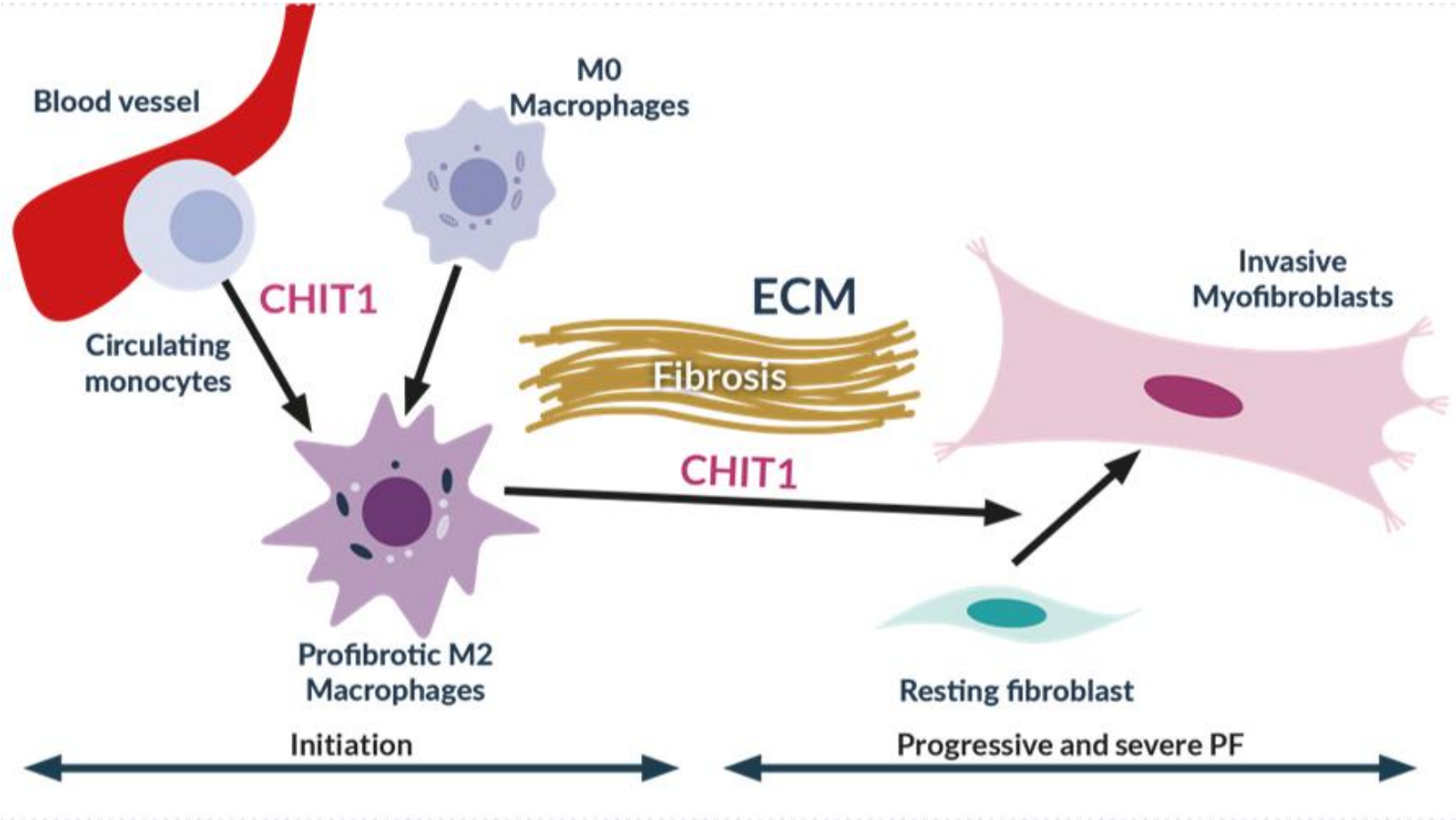
Donor



Role of profibrotic macrophages in the pathogenesis of pulmonary fibrosis

Macrophages are long lived cells capable of shaping the inflammatory microenvironment with plasticity allowing for therapeutic interventions

Macrophage polarization determines the phenotype of fibroblasts in progressive pulmonary fibrosis

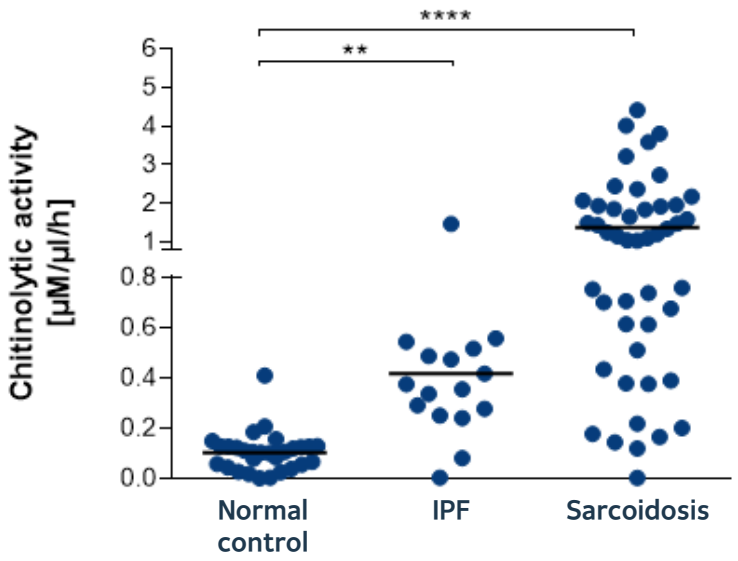


Adapted from Front. Pharmacol., 17 March 2022 Sec. Respiratory Pharmacology

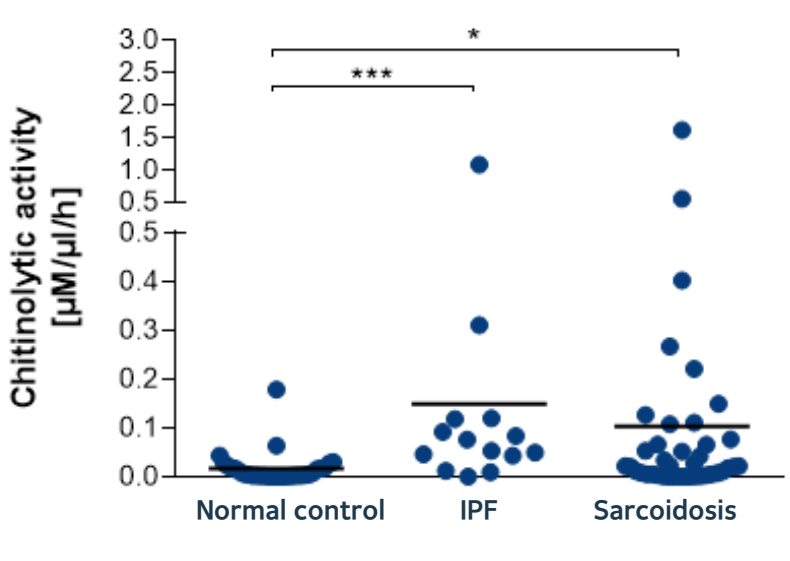
Translational Biomarker Studies

CHIT1 activity in serum, induced sputum and BAL fluid samples from IPF and sarcoidosis patients

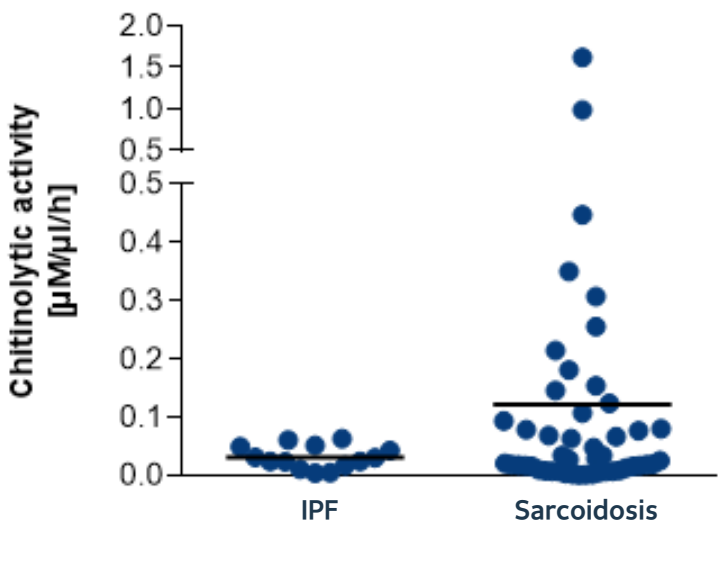
Serum



Induced sputum



BALf

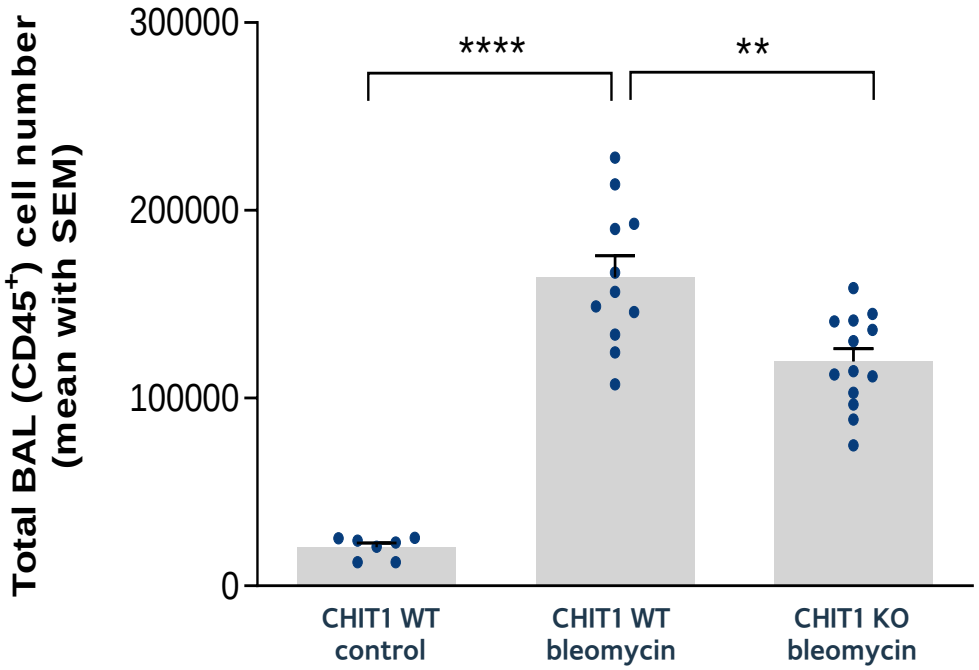


The analysis of chitinolytic activity in samples collected from patients demonstrated **significantly increased chitinolytic activity in serum, induced sputum and BALf** in patients with IPF and sarcoidosis when compared to normal controls.

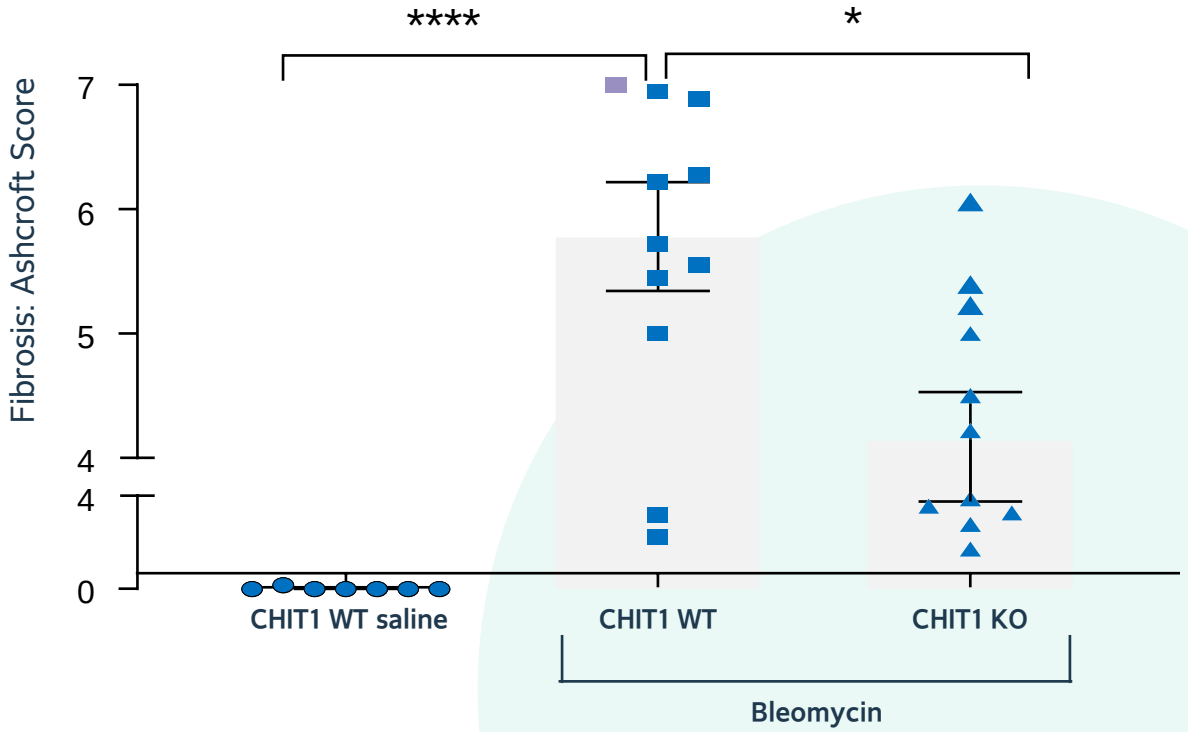
These results are in accordance with the published data and enable biomarker-based patient selection, as well as surrogate efficacy readout in clinical studies

Reduced Pulmonary Fibrosis and Inflammation in Bleomycin-Induced IPF Model in CHIT1 Knock-Out Mice

Inflammation



Pulmonary Fibrosis



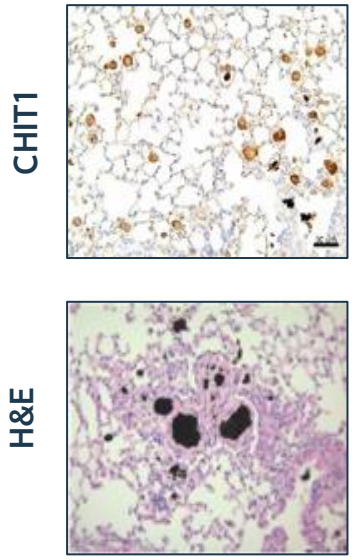
Creating Significant Value with OATD-01

Supportive pre-clinical data

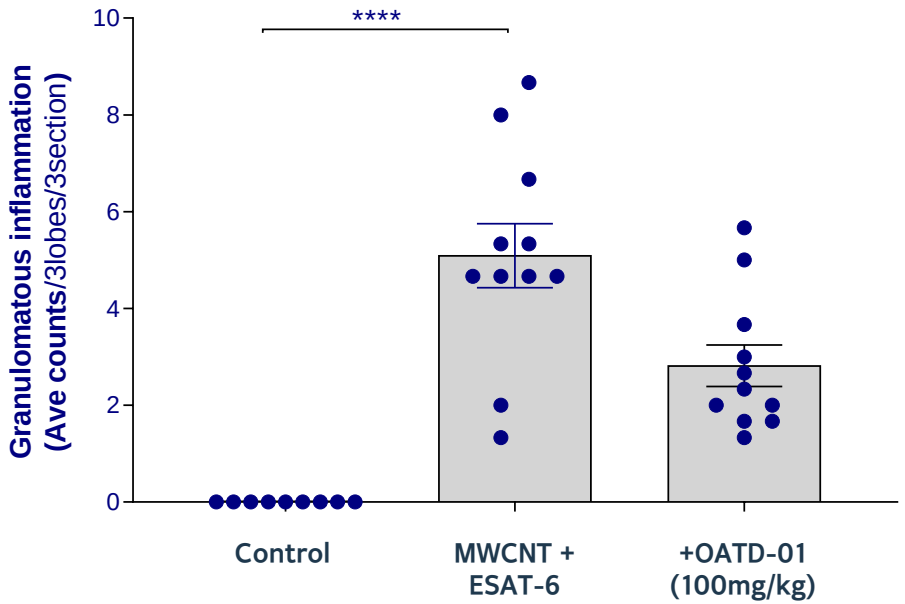
Efficacy of OATD-01 in MWCNT-induced granulomatous inflammation model in mice

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

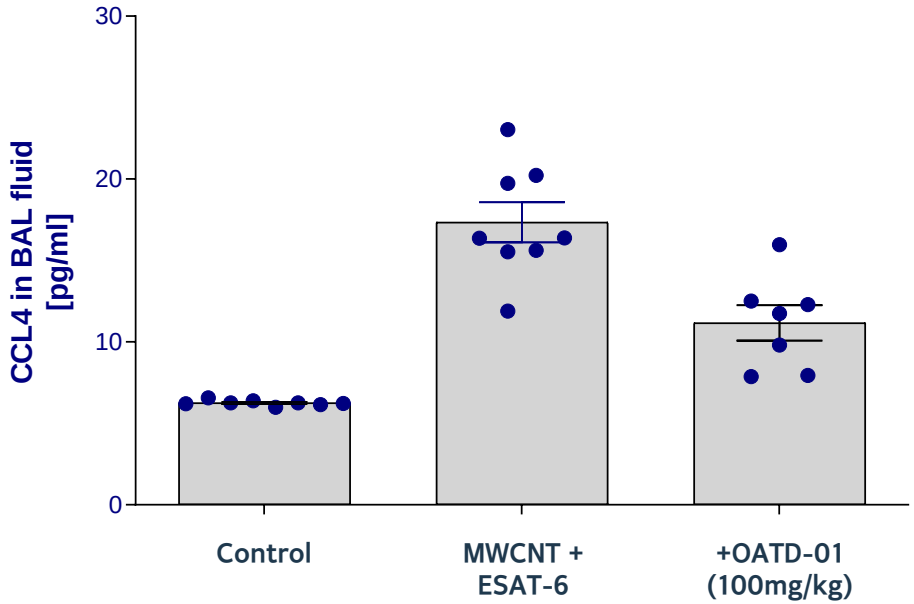
40 days post MWCNT+ESAT-6



Organized granulomatous structures

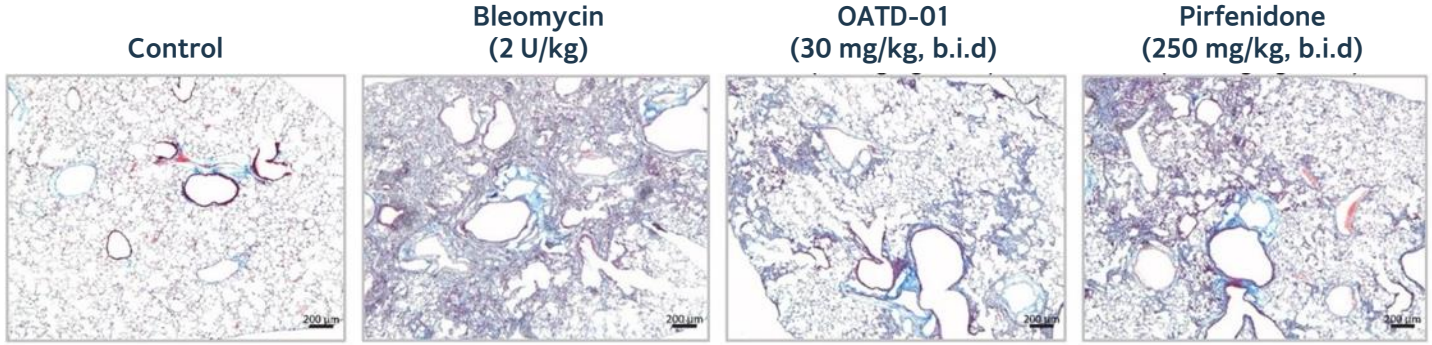


Day 10



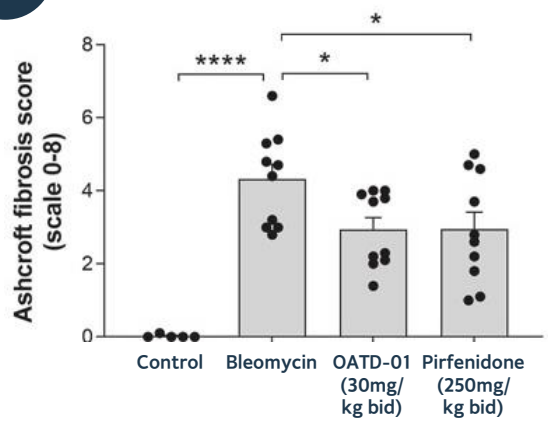
OATD-01 attenuates lung fibrosis in mice

A

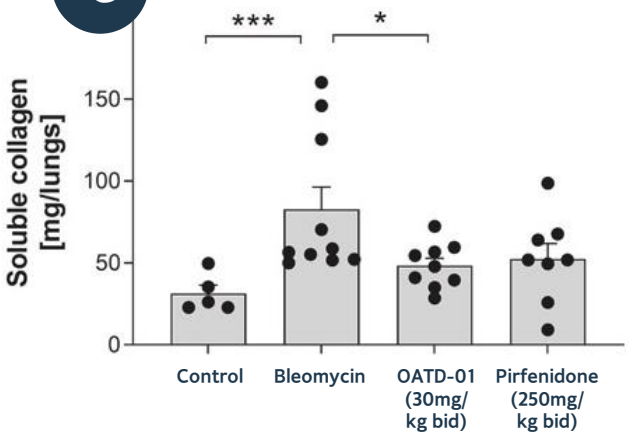


OATD-01 reduces features of pulmonary fibrosis in bleomycin induced model

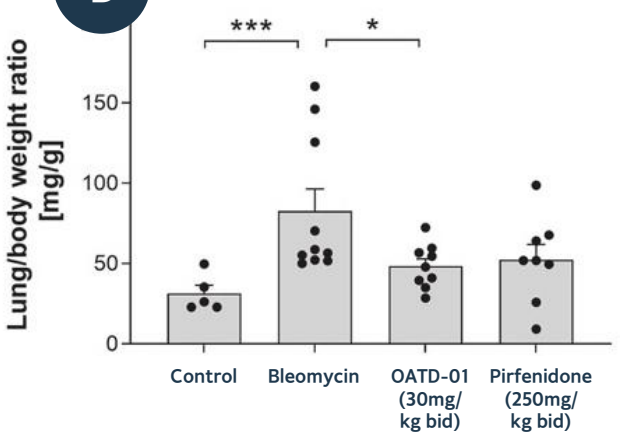
B

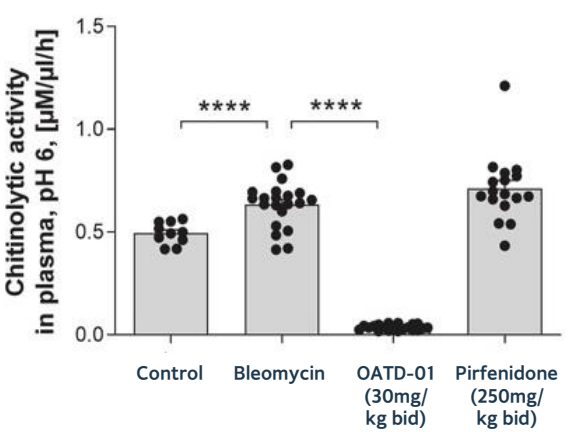


C



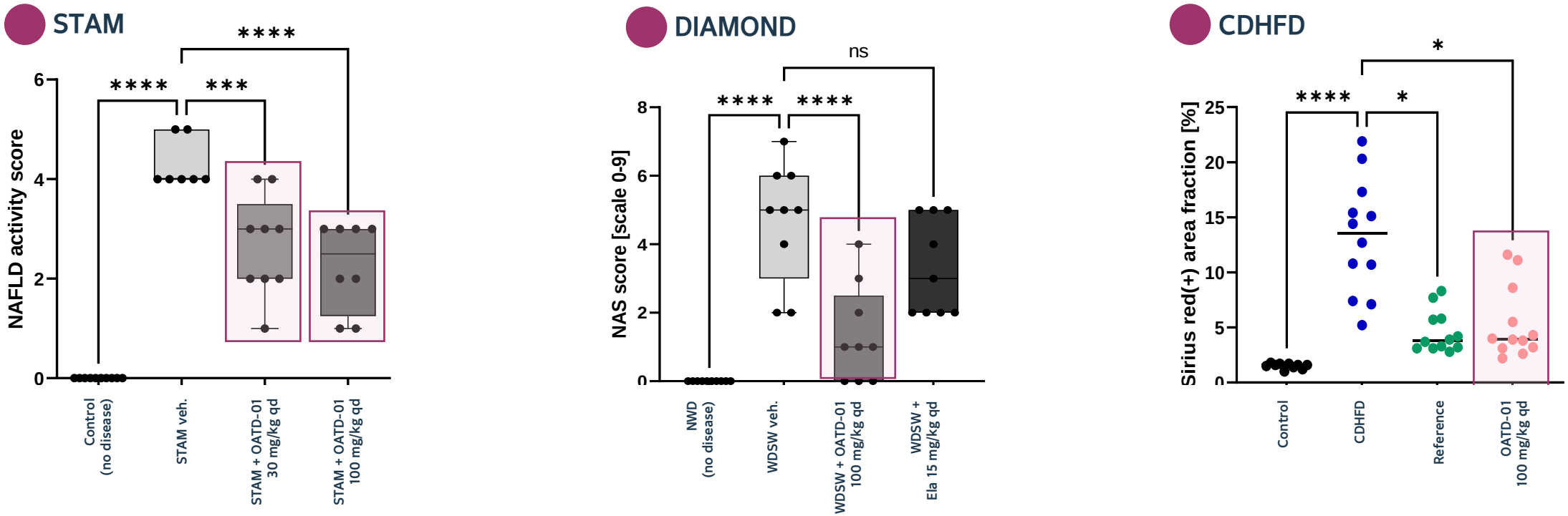
D





Efficacy of OATD-01 in multiple models of NASH in mice and rats

OATD-01 reduced the hallmarks of non-alcoholic liver disease in mice (STAM and DIAMOND) and fibrosis in rats (CDHFD) and mice (STAM)



In both mice models, OATD-01 very significantly reduced complex NAS score (inflammation, ballooning and steatosis)

Top processes regulated in NASH model involve macrophage activation and migration

Most up-regulated pathways
regulation of macrophage migration
regulatory T cell differentiation
neutrophil chemotaxis
extracellular structure organization

Most down-regulated pathways
acetyl-CoA metabolic process
regulation of triglyceride metabolic process

**Collaboration with Galapagos NV*

Major pathways regulated by OATD-01 in NASH model

Most up-regulated pathways
xenobiotic metabolic process
thioester metabolic process
mitochondrial respiratory chain complex assembly
acetyl-CoA metabolic process
alpha-amino acid catabolic process

Most down-regulated pathways
collagen fibril organization
extracellular matrix organization
collagen metabolic process

OATD-01 involve collagen synthesis and extracellular matrix reorganization

**Collaboration with Galapagos NV*

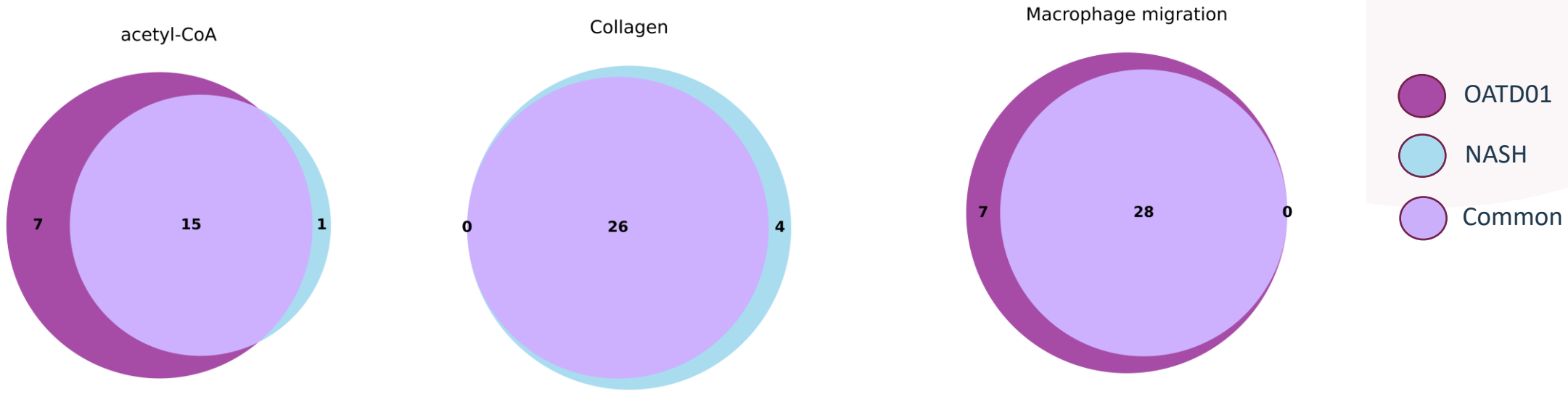
Common pathways and genes regulated by OATD-01

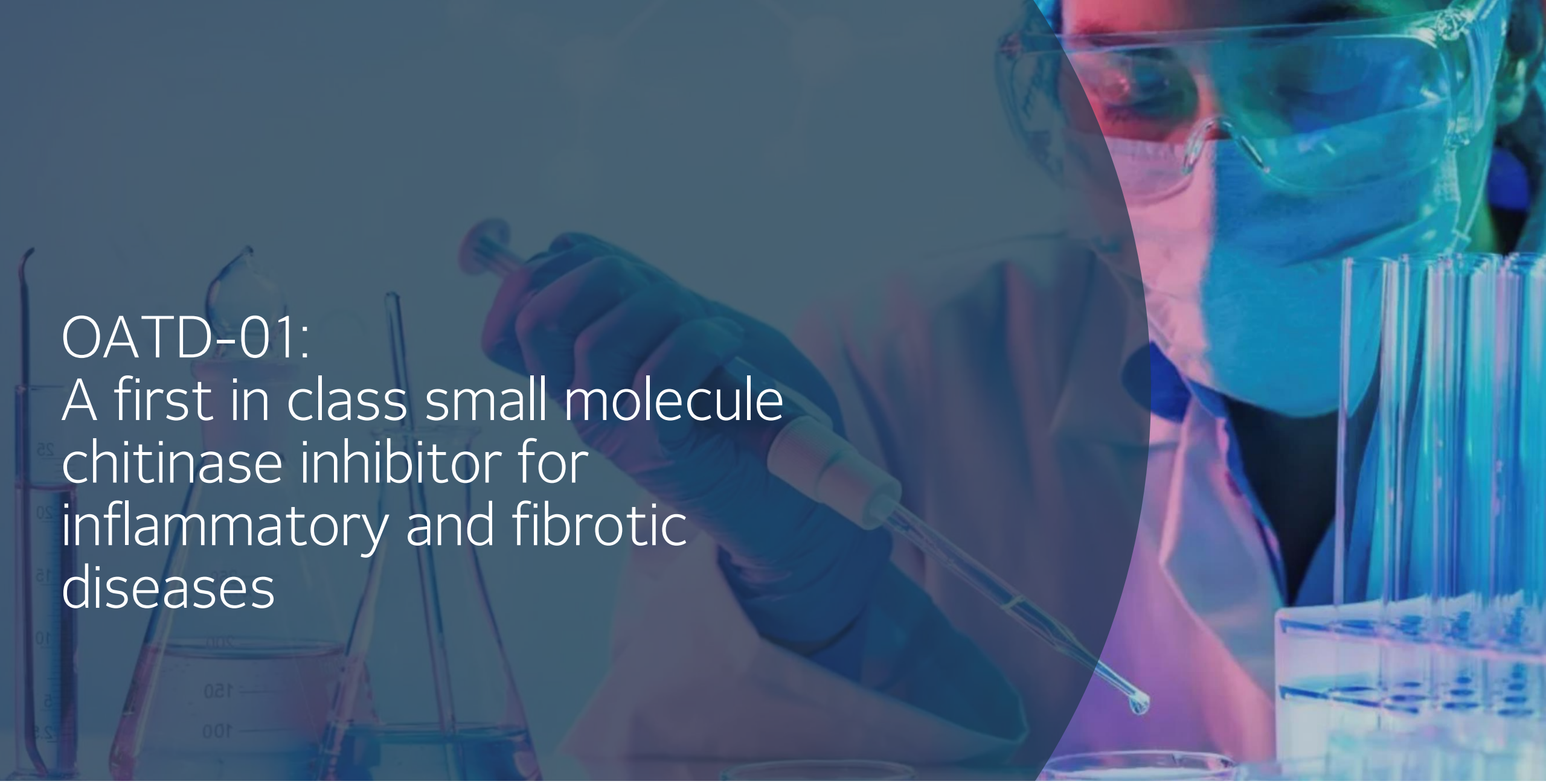
NASH vs control

Most regulated pathways
acetyl-CoA metabolic process
Collagen fibril organisation
Macrophage migration

OATD-01 vs NASH

Most regulated pathways
acetyl-CoA metabolic process
Collagen fibril organisation
Macrophage migration





OATD-01:
A first in class small molecule chitinase inhibitor for inflammatory and fibrotic diseases

Unique Attributes of OATD-01

- OATD-01 is potentially disease modifying agent for interstitial lung diseases, starting with sarcoidosis
- OATD-01 is a novel, single-digit nM, first-in-class small molecule chitinase (CHIT1) inhibitor targeting a key mechanistic pathway involved in inflammation and tissue remodeling
- OATD-01 delivers dual anti-inflammatory and anti-fibrotic activity through a single new chemical entity
- OATD-01 is a once-a-day, direct compression tablet for compliance and ease of use

OATD-01 – Promising clinical data

Compelling Data

- Efficacy proven in multiple animal models of sarcoidosis, chronic and acute asthma, idiopathic pulmonary fibrosis, (IPF) and non-alcoholic steatohepatitis (NASH)
- Compelling translational data
- Excellent pharmacological profile
- Demonstrated safety in animals and human
- Ph I studies in human volunteers and drug-drug interaction studies performed (129 subjects exposed)

Regulatory status

- FDA Orphan Drug Designation (ODD) for IPF and sarcoidosis granted
- Scientific Advice from European Medicines Agency and Pre-IND Written Responses from FDA support further clinical development

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

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

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

Vincent Cottin MD
PhD - FR
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 - US
Chair of the Department of Pulmonary Medicine at Cleveland Clinic's Main Campus

Mark Judson MD
PhD - US
Chief of the Pulmonary and Critical Care Division, Albany Medical College

Clinical Development of OATD-01

A potential disease modifying agent for 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, cost issues

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

OATD-01 Phase I conclusions

- **Clinical phase I completed**
  - Single ascending doses of 25 mg, 50 mg, 100 mg, 200 mg, 400 mg and 600 mg
  - Multiple ascending dose of 25 mg and 50 mg for 12 days
- **OATD-01 was generally well tolerated**
  - No treatment-related Serious Adverse Events (SAE)
  - No alerting safety observations; all safety findings to be routinely monitored in further clinical and non-clinical development
- **Steady state exposures after 25 mg / 50 mg dose were associated with nearly complete inhibition of chitinolytic activity in plasma (multiple ascending dose study)**
- **Dose predictions based on Phase I PK/PD modeling combined with preclinical data suggest that sufficient target engagement in the lungs should already be observed at relatively low doses of 15-25 mg**

Positive results of Drug Drug Interaction (DDI) studies

When co-administered with other drugs commonly used in patients with fibrotic conditions, and midazolam, OATD-01 was well tolerated and did not significantly change the exposure of either drugs

When co-administered with **pirfenidone**, OATD-01 did not result in meaningful changes in pirfenidone exposure demonstrating the absence of interaction with CYP1A2

When co-administered with **nintedanib**, a Pgp substrate with a narrow therapeutic index, no increase of systemic exposure of either drug was observed

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

OATD-01 on-track to enter Phase II in 2023

Trial Design & Sites

Objectives:

- Double-blind, randomized, placebo-controlled multicenter study to assess the safety and efficacy of an oral inhibitor of CHIT1 (OATD-01) for the treatment of patients with active pulmonary sarcoidosis

Major Endpoints:

- Imaging response by PET/CT to a 12-week treatment as a reduction of granulomatous inflammation in pulmonary parenchyma
- Difference in pulmonary function in patients with active pulmonary sarcoidosis (FVC/FEV1)
- Number of patients escaping to corticosteroids
- Change in the quality of life measured by the Kings Sarcoidosis Questionnaire Lung (KSQ LUNG)
- Safety and PK/PD (biomarker) evaluations

Patients:

- ~90 male and female patients with active pulmonary sarcoidosis

Sites:

- 20 to 30 sites in the EU and US

OATD-01: Potential indications beyond sarcoidosis

Sarcoidosis is the entry point to proving the clinical utility of targeting CHIT1

Positive results in the phase IIa proof of concept could pave the way to multiple other indications where chronic inflammation drive tissue remodelling, and where the expression and activity of the target CHIT1 is increased.

In the lung:
Pulmonary fibrosis
Interstitial lung diseases

In the liver
NASH
Liver fibrosis

Prof. Rafał Krenke, pulmonologist

Head of Department of Internal Medicine, Pulmonary Diseases & Allergy, Medical University of Warsaw

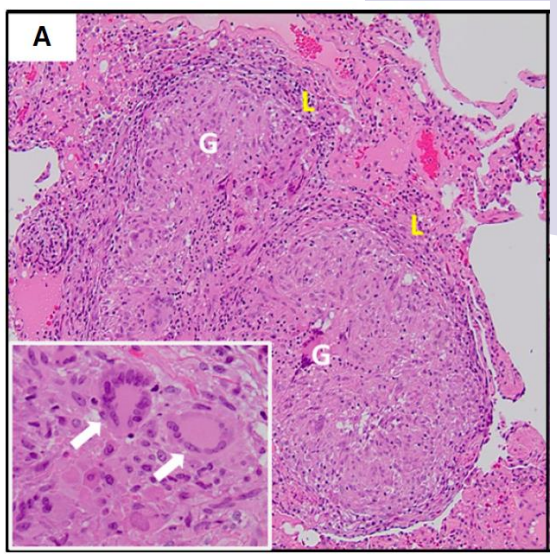
His scientific interest are focused on obstructive pulmonary diseases, pulmonary infections, pleural disorders and endoscopic techniques used in the diagnosis and treatment of lung diseases.

Prof. Krenke is a member of the European Respiratory Society, member of the Board of Polish Respiratory Society, Polish Society of Internal Medicine.

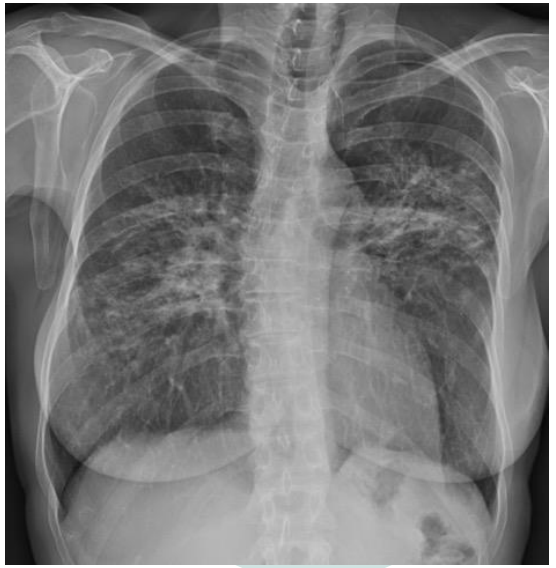
Co-author of 125 original papers, 60 review papers, 50 chapters in monographs and books, with a total IF 476,734 of full text publications.

What is sarcoidosis

- 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 granulomas in lungs



Crouser ED, et al. Am J Respir Crit Care Med 2020; 201 (8): e26–e51

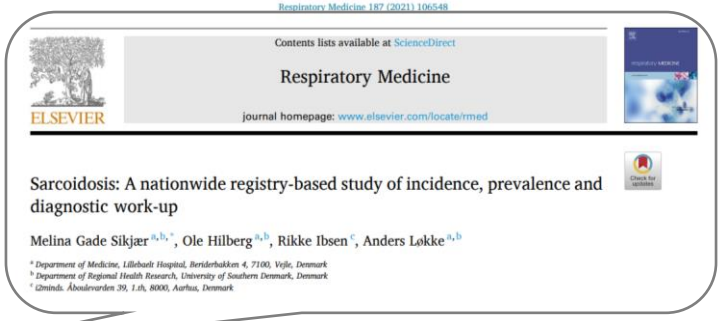


Ungprasert P et al. Mayo Clin Proc Inn Qual Out 2019;3(3):358-375

Burden of sarcoidosis

- Sarcoidosis is classified as a rare disease

- The incidence of sarcoidosis is
  - 0.5 to 1.3 per 100,000 in East Asia,
  - 11.3-14.8 per 100,000 in Scandinavian countries
  - 7 to 11 per 100,000 in the United States and Canada.


Respiratory Medicine 187 (2021) 106548

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

Sarcoidosis: A nationwide registry-based study of incidence, prevalence and diagnostic work-up

Melina Gade Sikjær [a,b,*], Ole Hilberg [a,b], Rikke Ibsen [c], Anders Løkke [a,b]

[a] Department of Medicine, Lillebaelt Hospital, Beriderbakken 4, 7100, Vejle, Denmark
[b] Department of Regional Health Research, University of Southern Denmark, Denmark
[c] i2minds. Åboulevarden 39, 1.th, 8000, Aarhus, Denmark

- Overall, the prevalence of sarcoidosis is 60 to 77 patients per 100,000

- The lifetime risk of sarcoidosis among Black Americans is 2.4 percent, compared with a lifetime risk of 0.85 percent in White Americans

Organ involvement in sarcoidosis (ACCESS study)

Organ involvement	Number*	Percent
Lungs	699	95
Skin¶	117	15.9
Lymph node	112	15.2
Eye	87	11.8
Liver	85	11.5
Erythema nodosum	61	8.3
Spleen	49	6.7
Neurologic	34	4.6
Parotid/salivary	29	3.9
Bone marrow	29	3.9
Calcium	27	3.7
ENT	22	3
Cardiac	17	2.3
Renal	5	0.7
Bone/joint	4	0.5
Muscle	3	0.4

ENT: ear, nose, and throat.

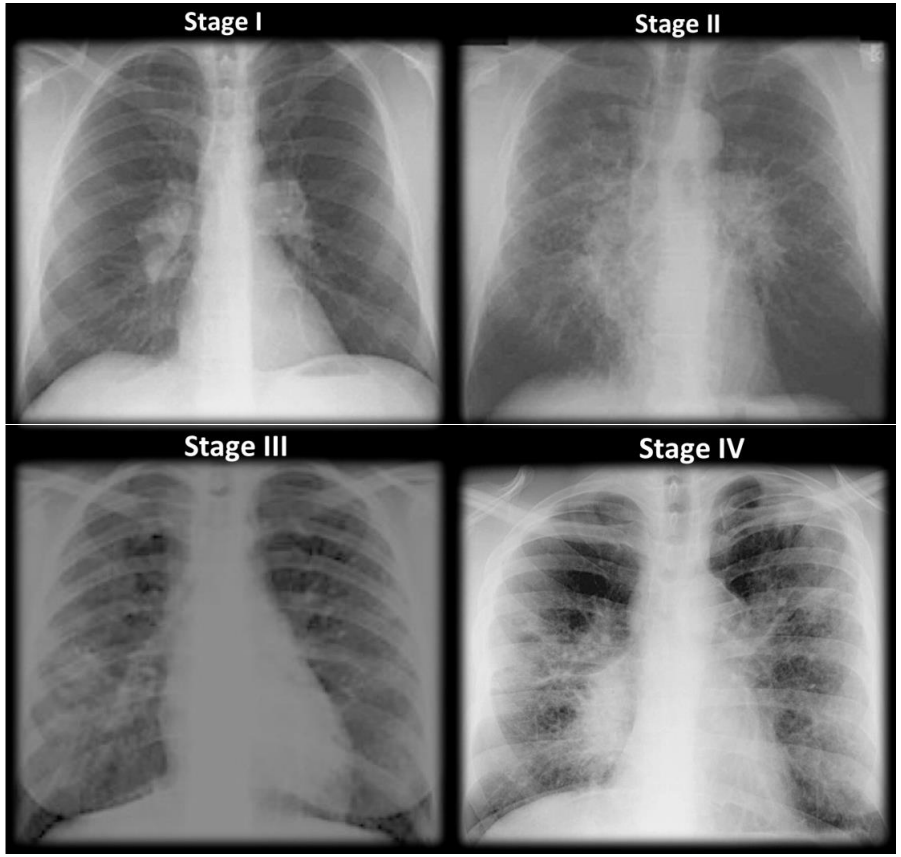
* Total n = 736.

¶ Excluding erythema nodosum.

Sarcoidosis is a multiorgan disease that may present with a numer of different faces!!

Baughman, RP, Teirstein, AS, Judson, MA, et al. Am J Respir Crit Care Med 2001;164:1885

Clinical features and organ involvement in sarcoidosis



Jara-Palomares L, et al. Clinical Manifestations of Sarcoidosis. In: Eishi, Y. , Editor. Sarcoidosis. London: IntechOpen; 2013

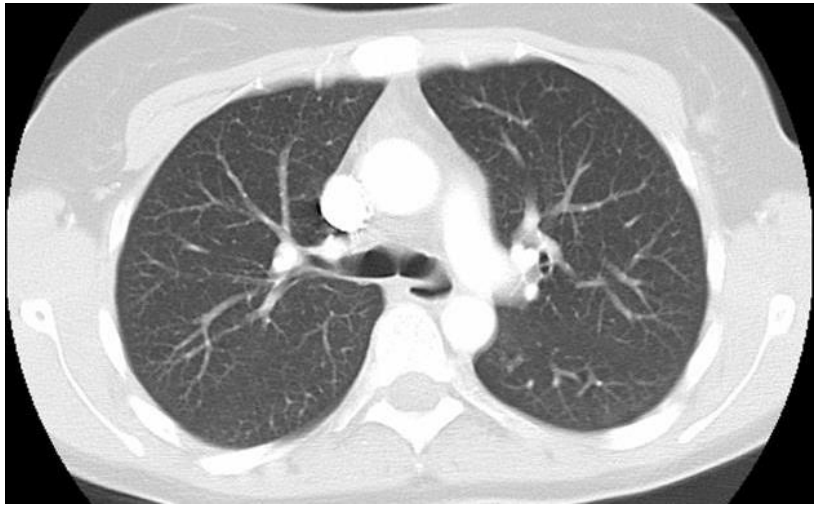
Features and frequency of pulmonary sarcoidosis stages

Stage	Radiographic features	Frequency at presentation (%)
I	Medistinal and hilar adenopathy with no pulmonary infiltrates	40-50
II	Medistinal and hilar adenopathy with pulmonary infiltrates	30-40
III	Pulmonary infiltrates without adenopathy (adenopathy already regresses	15-20
IV	Pulmonary fiborsis with volume loss. No adenopathy	2-5

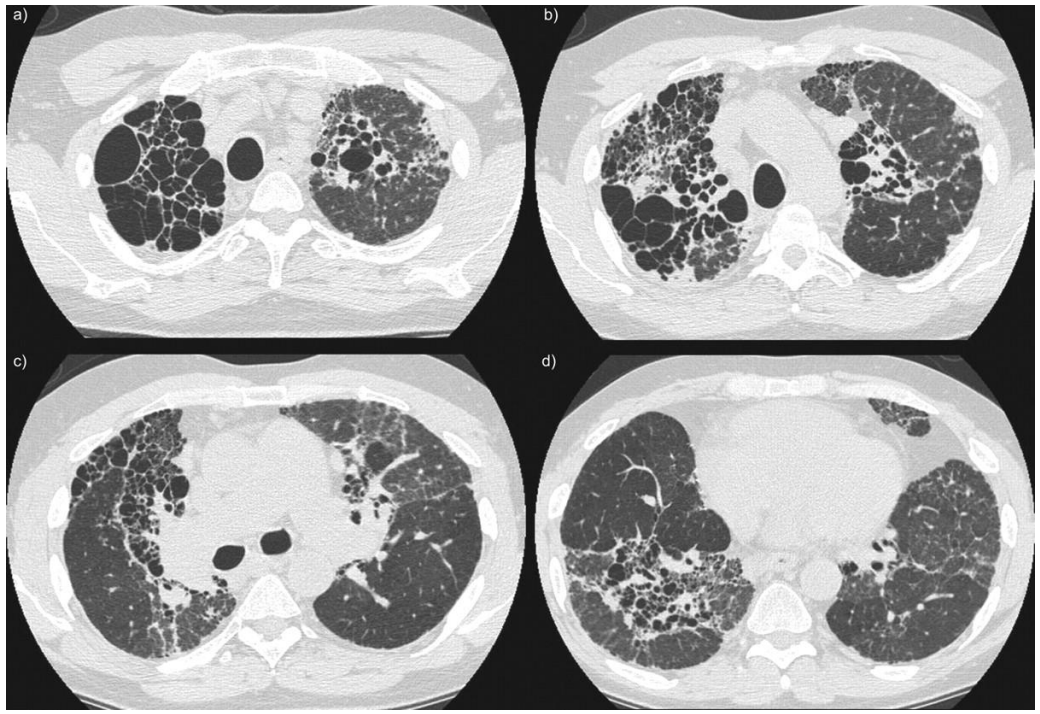
After: Ungprasert P et al. Mayo Clin Proc Inn Qual Out n September 2019;3(3):358-375

Patients with sarcoidosis may show very different stages of pulmonary involvement!

Clinical features and organ involvement in sarcoidosis

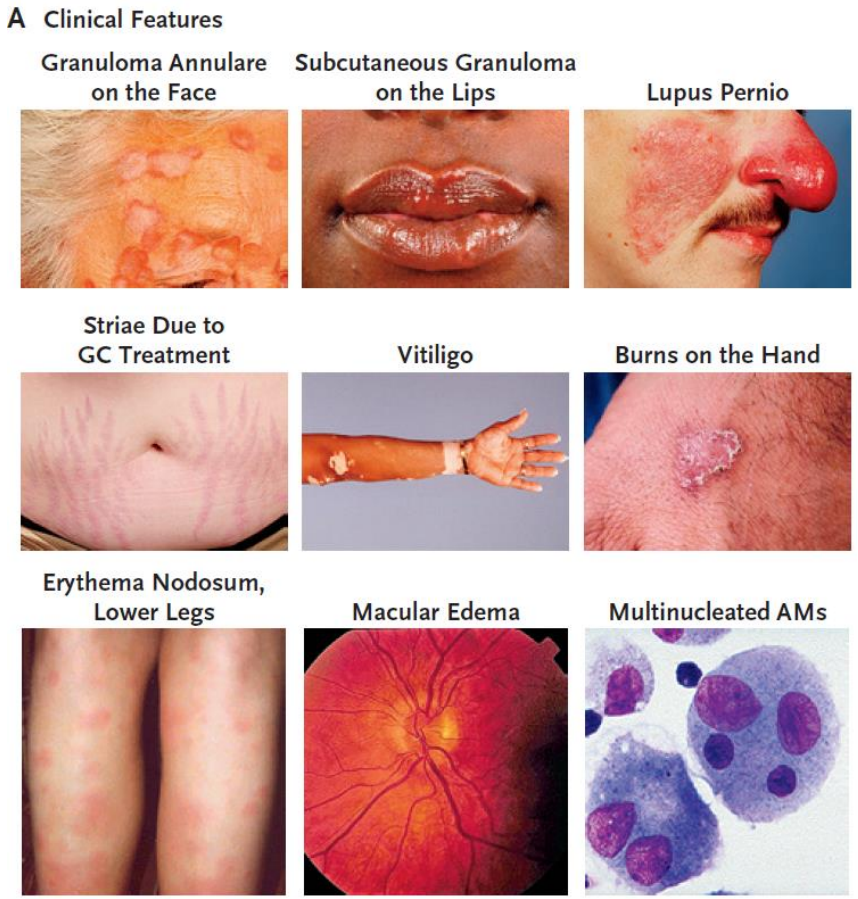


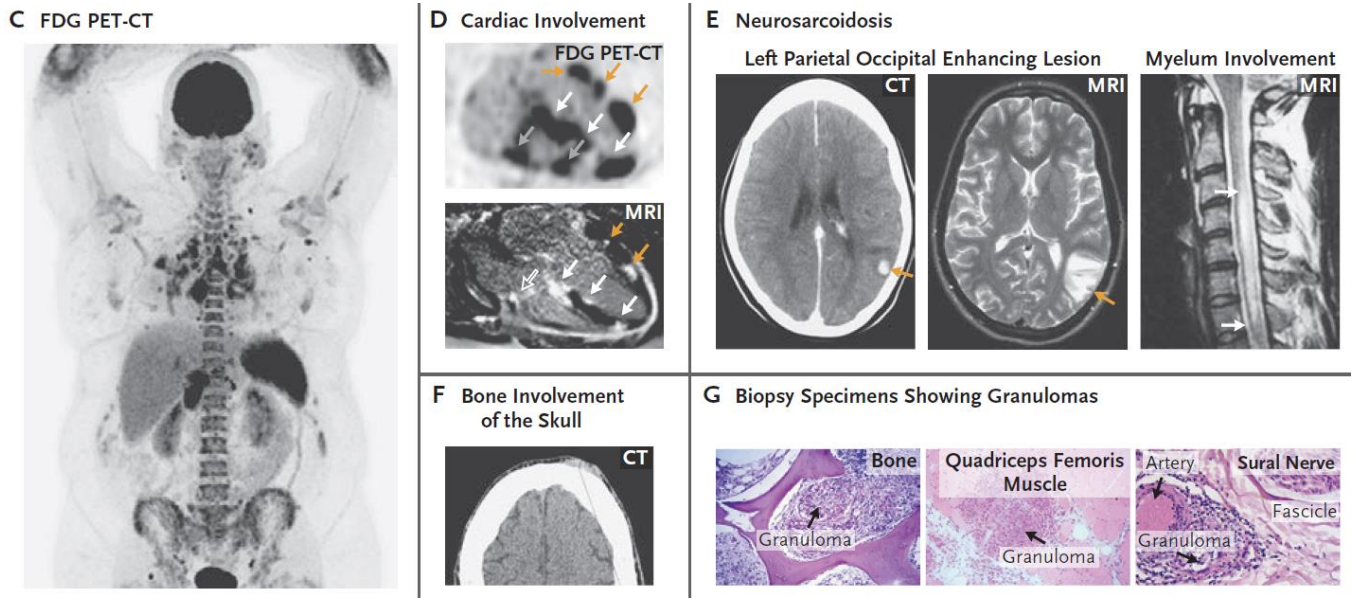
Shlobin AO, Nathan SD. Eur Respir J 2012, 39: 1520-1533



Patients with sarcoidosis may show very different stages of pulmonary involvement!

Clinical features and organ involvement in sarcoidosis





Drent M, et al. N Engl J Med 2021;385:1018-32.

The clinical course of sarcoidosis

Not easily predictable

Spontaneous remission in patients with stage I - 60-80%

but

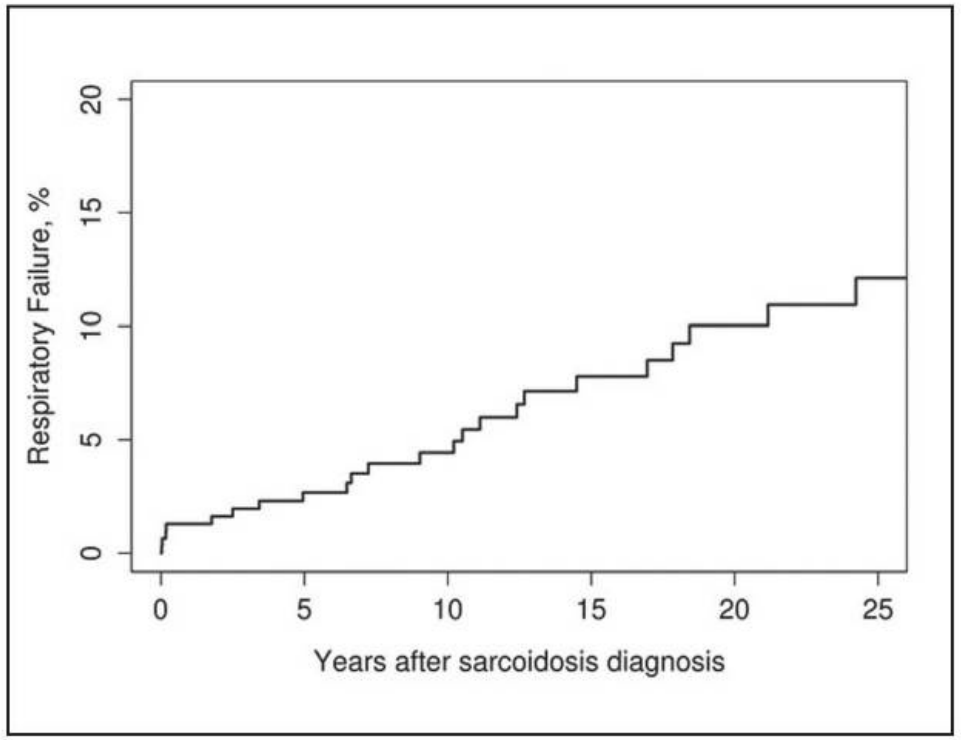
only approximately 30% in patients with stage II and III

Ungprasert P, et al. Sarcoidosis Vasc Diffuse Lung Dis. 2018; 35(2): 123–128.

The clinical course of sarcoidosis
(Rochester Epidemiology Project (REP), Olmsted Country, MN, US)

Stages at diagnosis: stage I disease (54%), stage II (29%), III (15%) and IV (2%). The median length of follow-up 13.8 years.

The 10-year chronic respiratory failure rate = 4.4% (95% CI, 1.9.-6.9)



The hazard ratio (HR) for chronic respiratory impairment of patients with

- stage II pulmonary sarcoidosis compared with stage I disease 5.29 (95% CI, 1.65-16.96)
- stage III and IV pulmonary sarcoidosis compared with stage I disease was 8.36 (95% CI, 26.3-26.52).

Ungprasert P, et al. Sarcoidosis Vasc Diffuse Lung Dis. 2018; 35(2): 123–128.

Risk factors and favorable factors in sarcoidosis

Table 1. Selected Adverse and Favorable Prognostic Factors in Sarcoidosis.*

Variable	Adverse Prognostic Factors†	Favorable Prognostic Factors
Demographic characteristics	Age ≥40 yr at onset[10] Black race[11] Black race and female sex Lower income[4,11]	Age <40 yr at onset[10]
Pulmonary involvement[12,13]	Scadding stage III (absence of lymphadenopathy) or stage IV (signs of fibrosis) on chest radiography‡ Severe dyspnea or hypoxemia with minimal exertion at presentation[13] Clinically significant lung functional impairment Pulmonary hypertension[13]	Asymptomatic Scadding stage I or II (presence of lymphadenopathy) on chest radiography‡
Bronchoalveolar lavage fluid	Neutrophilia at presentation[14] Elevated metalloproteinases (MMP12)	Lymphocytosis without increased eosinophils or neutrophils or both[15] Increased CD4:CD8 ratio[15]
Extrapulmonary involvement	Lupus pernio: nasal mucosal involvement[10] Vitiligo Chronic uveitis[10] Cardiac involvement Hepatomegaly Splenomegaly Neurologic involvement Osseous involvement[10] Hypercalcemia[10] Nephrolithiasis or nephrocalcinosis[10] Small-fiber neuropathy–associated symptoms[16,17]	Acute inflammatory manifestations (e.g., Löfgren's syndrome: acute onset with fever, erythema nodosum, bilateral ankle arthritis, and bilateral hilar lymphadenopathy)[1] Isolated cranial-nerve palsy
Requirement for treatment	Risk of disease progression and organ failure or death[12]	No risk of disease progression or organ failure
Associated genetic variants§	*HLA-DRB1*14*, *HLA-DRB1*15*+[1] Presence of a *TNF-α* rs1800629 G/A variant allele¶ Presence of a *BTNL2* rs2076530 G/A variant allele[18]¶ Presence of an *ANXA11* rs1049550 C/T variant allele	*HLA-DRB1*03*+, *HLA-DQB1*0201* Absence of a *TNF-α* variant allele Absence of a *BTNL2* variant allele Absence of an *ANXA11* variant allele

Sarcoidosis consequences and complications

- Pulmonary fibrosis is the most severe complication of sarcoidosis
- Usually associated with chronic dyspnea and 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
- Approximately 50% of patients require systemic treatment
- Mortality is 4 to 8% in western countries, mainly due to respiratory failure

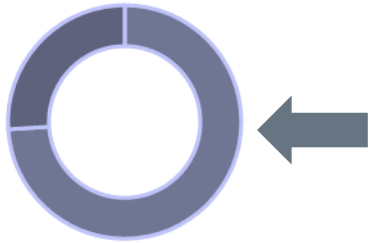
Patients presenting with sarcoidosis

Three fourths of these patients would require treatment

The main aim of treatment is to preserve organ function and improve patient symptoms. Steroids and immunosuppressants are the preferred treatments

Approximately **26% of patients do not require treatment** as they are the "wait and see patients": asymptomatic and have just presented with sarcoidosis

Patients who require treatment



On average, **74% of patients require treatment** as they have Stage 2 or 3 disease
(Range: 60-90%)

Treatment goals

- Improve symptoms
  - reduce the granulomatous inflammation to restore respiratory function
- Boost lung function/ prevent lung dysfunction
  - FVC and radiographic sarcoidosis
- Stop disease progression and organ damage
- Improve QoL

Current ERS guidelines

EUROPEAN RESPIRATORY JOURNAL
ERS OFFICIAL DOCUMENTS
R.P. BAUGHMAN ET AL.

ERS clinical practice guidelines on treatment of sarcoidosis

Robert P. Baughman[1], Dominique Valeyre[2], Peter Korsten[3], Alexander G. Mathioudakis[4], Wim A. Wuyts[5], Athol Wells[6], Paola Rottoli[7], Hiliaro Nunes[8], Elyse E. Lower[1], Marc A. Judson[9], Dominique Israel-Biet[10], Jan C. Grutters[11,12], Marjolein Drent[11,13,14], Daniel A. Culver[15], Francesco Bonella[16], Katerina Antoniou[17], Filippo Martone[18], Bernd Quadder[19], Ginger Spitzer[20], Blin Nagavci[21], Thomy Tonia[22], David Rigau[23] and Daniel R. Ouellette[24]

Eur Respir J 2021; 58: 2004079

Decision making on sarcoidosis treatment

The decision of who and when to treat an individual sarcoidosis patient depends on two major factors:

- risk for death or organ failure,
- impairment of quality of life (QoL).

About 5% of patients die from the disease and pulmonary and cardiac disease are the most common reasons for death from sarcoidosis. Irreversible organ damage to the brain, eyes or kidneys can also cause significant morbidity. Recent studies have identified features associated with increased risk for death from pulmonary disease

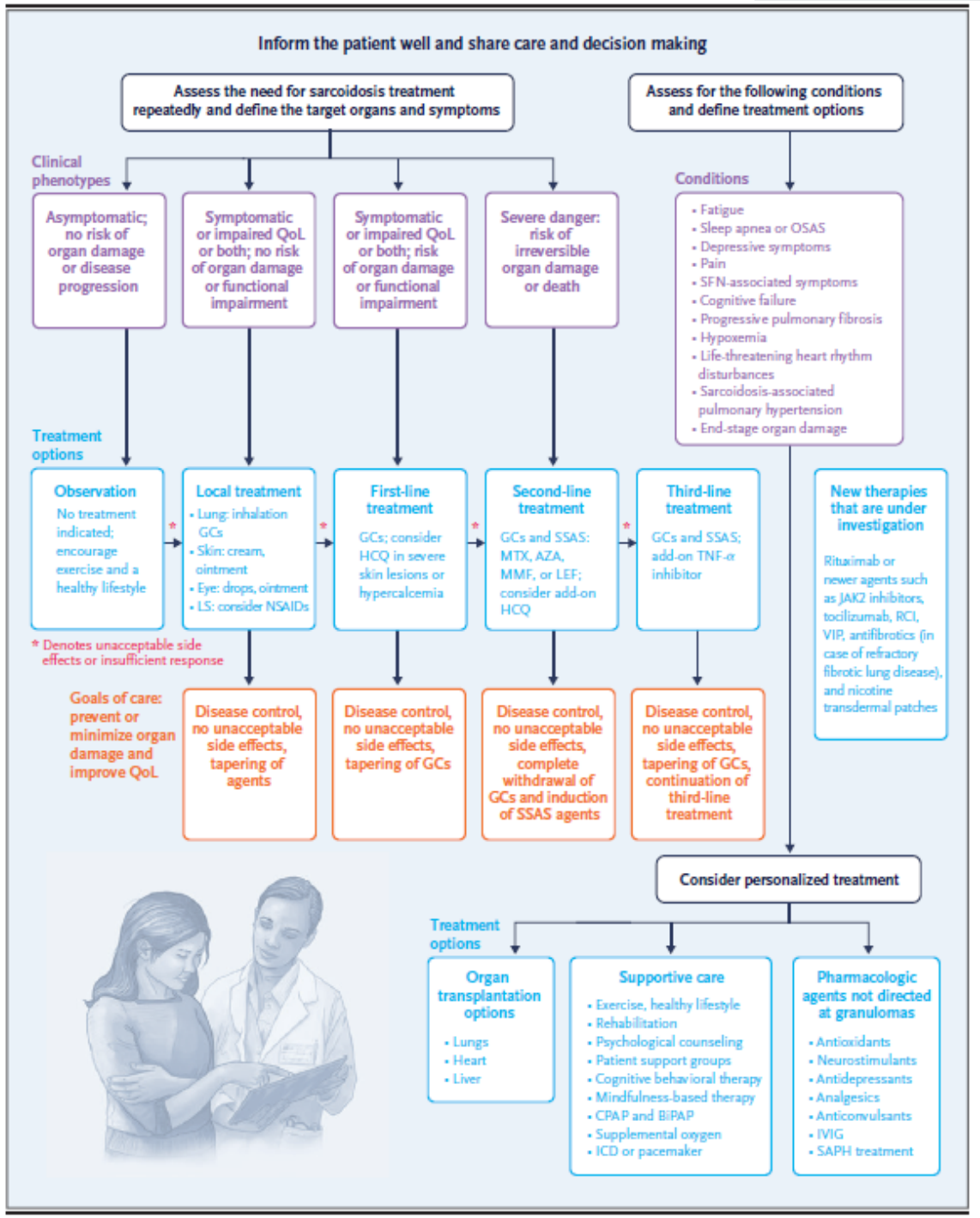
Baughman RP, et al. Eur Respir J. 2021; 58: 2004079

Decision making on sarcoidosis treatment

- Fatigue is a very common symptom in sarcoidosis (reported in up to 90% of patients) and is strongly associated with a lower QoL.
- It is not always related to organ involvement induced bysarcoidosis and may persist for many years, even after apparent remission of active granulomatous inflammation.
- Other causes of fatigue have to be ruled out before SAF can be diagnosed
- Studies have shown poor agreement between physicians' and patients' assessment of SAF, highlighting the importance of using patient-reported outcome measures for the evaluation of effects of interventions in clinical trials and clinical practice.

Baughman RP, et al. Eur Respir J. 2021; 58: 2004079

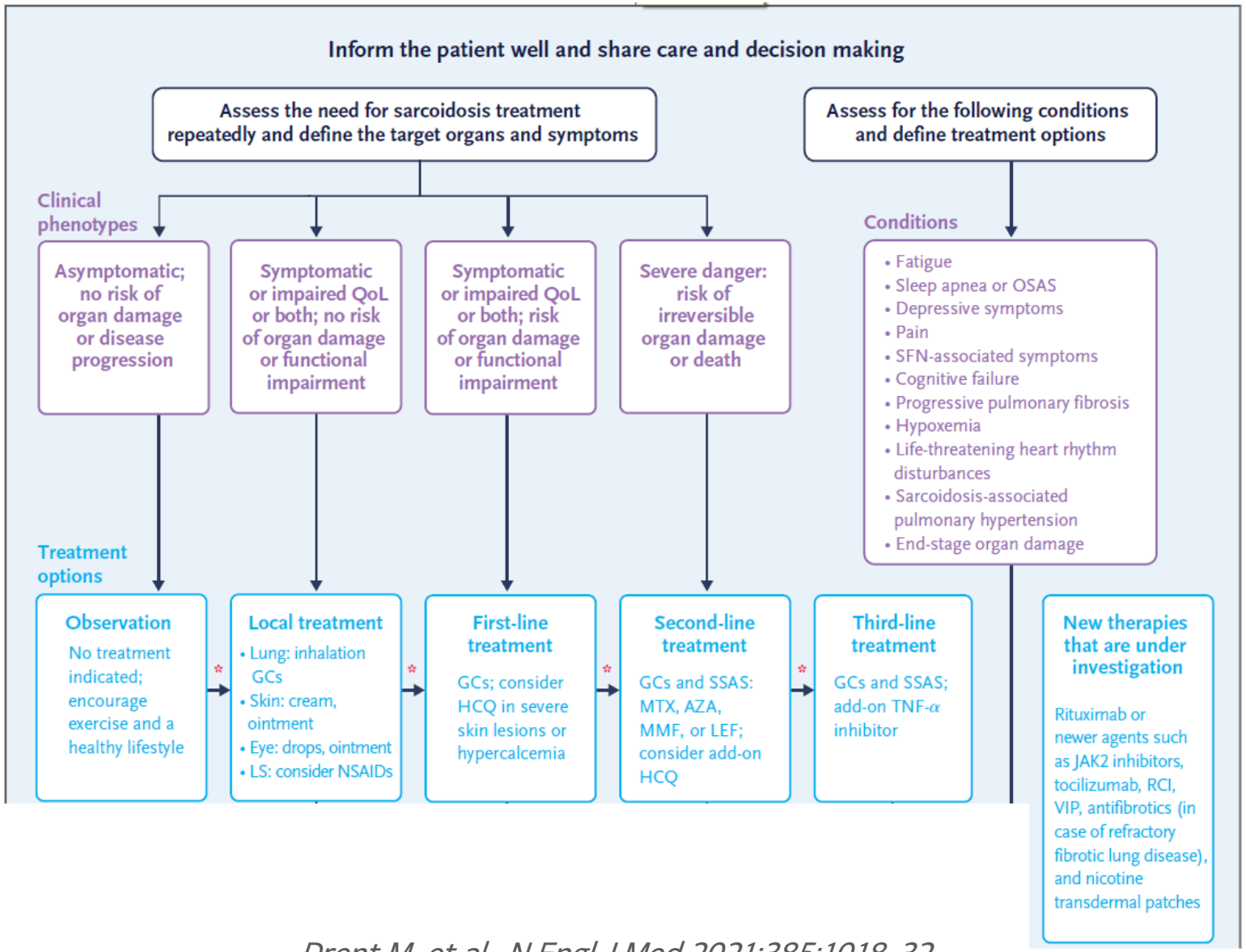
Current algorithm for sarcoidosis treatment



Drent M, et al. N Engl J Med 2021;385:1018-32.

molecu

Current algorithm for sarcoidosis treatment



Drent M, et al. N Engl J Med 2021;385:1018-32.

Current treatment paradigms

- No cure for sarcoidosis, treatments only modify the granulomatous process and its clinical consequences - major opportunity for a new disease modifying therapy
- Little data to guide therapy strategies despite guidelines
- Systemic corticosteroids remain the standard of care with short-term benefits only; importantly there is little evidence for their extended therapeutic efficacy
- Corticosteroid treatment is symptomatic; well known safety and tolerability concerns and poor compliance

1st Line- Systemic steroids

- ✓ Usually prednisolone
- ✓ Start working very rapidly (within 1 month)
- ✗ Used short-term (6-12 months) or at low doses due to side effects
- ✗ Tapered-off over 3-6 months, long-term immunosuppressants introduced

2nd Line- Immunosuppressants

- ✓ Methotrexate & azathioprine preferred, sometimes mycophenolate mofetil also used
- ✓ Steroid-sparing agents
- ✓ Long-term use: less side effects
- ✗ Take a long time to induce effect (2-6 months)

3rd Line- Biologics

- ✓ Infliximab or adalimumab usually used
- ✓ Used in refractory cases where immunosuppressants/steroids are not useful anymore
- ✗ In China, 2nd and 3rd line are not available

Current immunsuppressive therapies for sarcoidosis

Drug	Usual dosage	Major toxicities	Recommended monitoring	Comments
Prednisone/ prednisolone	Initial 20 mg once a day; follow-up 5–10 mg once a day to once every other day	Diabetes; hypertension; weight gain; osteoporosis; cataracts; glaucoma; moodiness	Bone density; blood pressure and serum glucose	Cumulative toxicity
Methotrexate	10–15 mg once a week	Nausea; leukopenia; hepatotoxicity; pulmonary	CBC, hepatic, renal serum testing	Cleared by kidney, avoid in significant renal failure
Leflunomide	10–20 mg once a day	Nausea; leukopenia; hepatotoxicity; pulmonary	CBC, hepatic, renal serum testing	Cleared by kidney, avoid in significant renal failure
Azathioprine	50–250 mg once a day	Nausea; leukopenia; infections; malignancy	CBC	
Mycophenolate mofetil	500–1500 mg twice a day	Diarrhoea; leukopenia; infections; malignancy	CBC	Less experience in sarcoidosis than other agents
Infliximab or biosimilars[#]	3–5 mg·kg^{-1} initially, 2 weeks later, then once every 4–6 weeks	Infections; allergic reaction	Screen for prior TB; monitor for allergic reactions; contraindicated in severe CHF, prior malignancy, demyelinating neurologic disease, active TB, deep fungal infections	Allergic reactions can be life threatening
Adalimumab[#]	40 mg every 1–2 weeks	Infections	Screen for prior TB; monitor for allergic reactions; contraindicated in severe CHF, prior malignancy, demyelinating neurologic disease, active TB, deep fungal infections	Less toxic than infliximab
Rituximab[#]	500–1000 mg every 1–6 months	Infections	Screen for viral hepatitis; check IgG level with chronic therapy	High risk for viral reactivation; can lead to IgG deficiency
RCI[#]	40–80 units twice a week	Diabetes; hypertension; oedema; anxiety	Monitor glucose and blood pressure	Most of toxicity is on day of injection
Hydroxychloroquine	200–400 mg once a day	Loss of vision	Ocular exams periodically depending on age and renal function	Minimal impact on cardiac and neurologic disease

More details regarding dosages, major toxicities and monitoring are given in supplement S1 in the supplementary material and adapted from prior reports [4, 39–48]. CBC: complete blood count; TB: tuberculosis; CHF: congestive heart failure; RCI: repository corticotropin injection. [#]: use reserved for patients who have failed prior treatments with steroids and/or antimetabolites.

Baughman RP, et al. Eur Respir J. 2021; 58: 2004079

OATD-01 Opportunity Assessment

A potential disease modifying agent for sarcoidosis

Opportunity assessment – Citeline study

Objectives

Current treatment paradigms and unmet needs

- Understand the main treatment goals and expectations in sarcoidosis
- Identify which therapies are preferentially used amongst KOLs
- Gauge KOL and payer opinions on the unmet needs of sarcoidosis patients, with a focus on the available drug therapies

Opportunity assessment and pricing considerations

- Document KOL and payer opinions OATD-01, and identify the drivers and barriers to uptake of this product
- Identify the patient populations the product would be most suitable for
- Understand payer expectations and assessment considerations for OATD-01

KOL interviews
45-60 min virtual discussions

KOL requirements

- Treat sarcoidosis patients
- Have clinical trial experience

Payer interviews
45-60 min virtual discussions

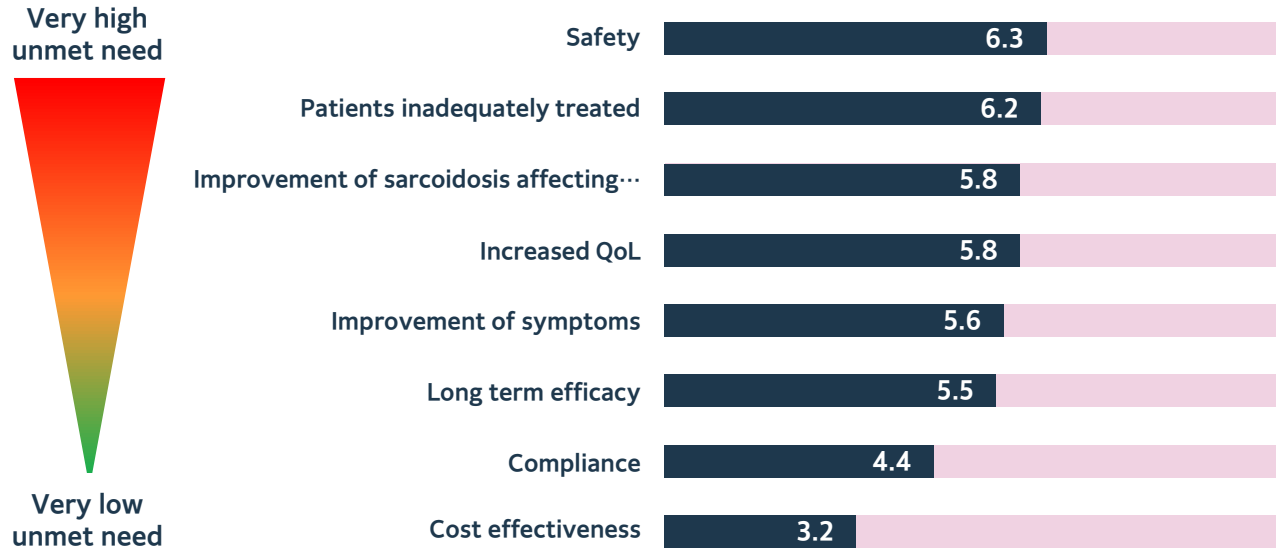
Significant unmet needs, a KOL perspective

The main need in sarcoidosis is a safer treatment that could halt disease progression, whilst still being cost-effective

Most significant unmet needs

- Need for quick, accurate & non-invasive diagnosis
- Some patients don't respond to current treatment
- Current treatments lack efficacy data
- Lack of treatment guidelines
- Sarcoidosis manifestations inadequately managed
- No safer alternatives to steroids that could halt progression

Satisfactory score for current options: 6/10



KOLs and payers are moderately satisfied with the current treatment options

Source: Citeline

Disease modifying therapies in sarcoidosis are eagerly awaited

As well as stopping disease progression, KOLs hope that new disease-modifying therapies can offer a safe and effective alternative to steroids

Key desirable disease-modifying drug attributes

- ✓ More efficacious than steroids
- ✓ Halt disease progression
- ✓ Cost-effective
- ✓ Safer than current treatment options
- ✓ Offer a replacement /alternative to steroids
- ✓ Self-administered drug to ensure compliance

40% **Of patients would be offered OATD-01 by KOLs based on current data**

Perceived strength of OATD-01

- Oral, once daily
- Could replace steroids, therefore less side effects
- No drug-drug interactions
- Promising in vivo efficacy

Up to 75% **Of patients would be offered OATD-01 by KOLs based after clinical outcome**

If these attributes are confirmed:

- Efficacy
- Side effect profile
- Exact patient population
- Cost of drug reasonable

Source: Citeline

Significant market opportunity for disease-modifying profile

Global sarcoidosis market is currently catered for with old, genericized drugs such as steroids and other immunosuppressive drugs are inexpensive

However, the market is likely to completely change in the coming years.

The two most advanced compounds are:

- **namilumab** (anti-GM-CSF (biologics); Ph2 studies; Kinevant)
- **efzofitimod** (neuropilin-2 modifier (biologics); Ph3 studies; aTyr Pharma)

Molecure estimates a value for the sarcoidosis market at maturity for a disease-modifying treatment could be over US$1.5bn**.

*EvaluatePharma;. **Company estimates

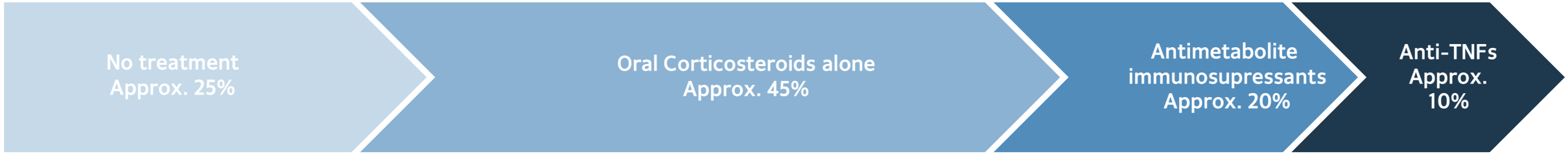
Significant market opportunity for Sarcoidosis alone

US 200,000 patients

EU / UK 150,000 patients

JP 20,000 patients

Patients Treatment Segmentation



Core target population
Steroid sparing agent or replacing steroids

Upside target population
Sarcoidosis patients at risk of progression

Target OATD-01 population in major markets represents 150,000 – 200,000 patients

Source: Citeline, Cortellis, Company estimates

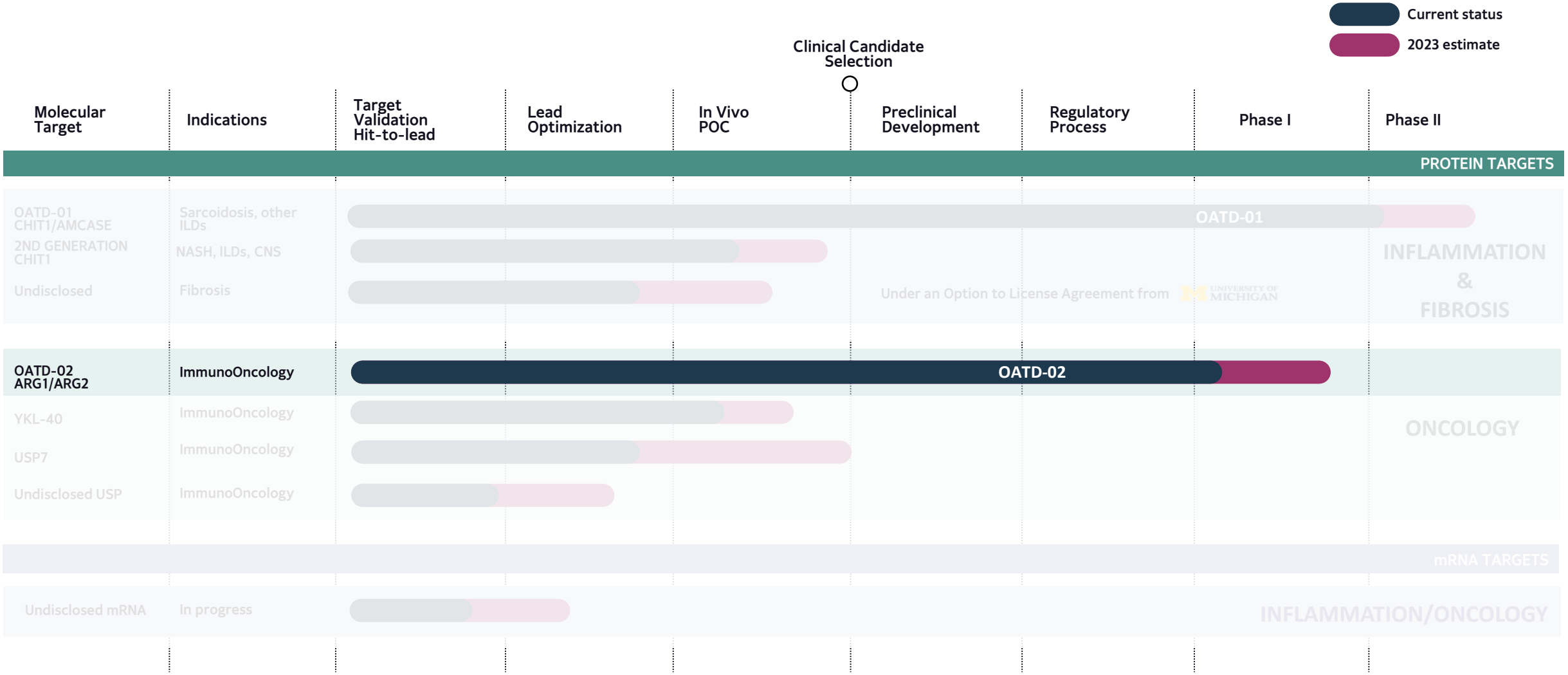
OATD-01 a potential major step forward in therapy

- Molecure is committed to solving unmet medical needs of patients with interstitial lung diseases, starting with sarcoidosis
- OATD-01 potentially a new disease-modifying therapy that can offer a safe and effective alternative to steroids
- Demonstrated safety in Phase I studies in human volunteers
- Strong interest of KOL clinicians confirmed in EU and US (5 top centers)
- Clinical trial design with well defined end points, patient availability
- IND filing with the FDA expected in 1Q 2023
- Efficacy proven in multiple animal models of sarcoidosis, IPF and non-alcoholic steatohepatitis NASH – possibility to extend to additional therapeutic area during / after clinical PoC


Q&A

OATD-02: A first in class dual arginase inhibitor for cancer applications

High Value Pipeline



OATD-02 targeting a broad range of solid tumors

Pursuing first in class dual arginase inhibitor (Arginase 1 and Arginase 2) targeting solid tumors

Leadership position in arginase discovery, in particular modulating the intra-cellular ARG2

High arginase activity has been found in patients with a wide spectrum of cancers, both in plasma and in tumors and correlated with a poor prognosis

Favorable Competitive landscape

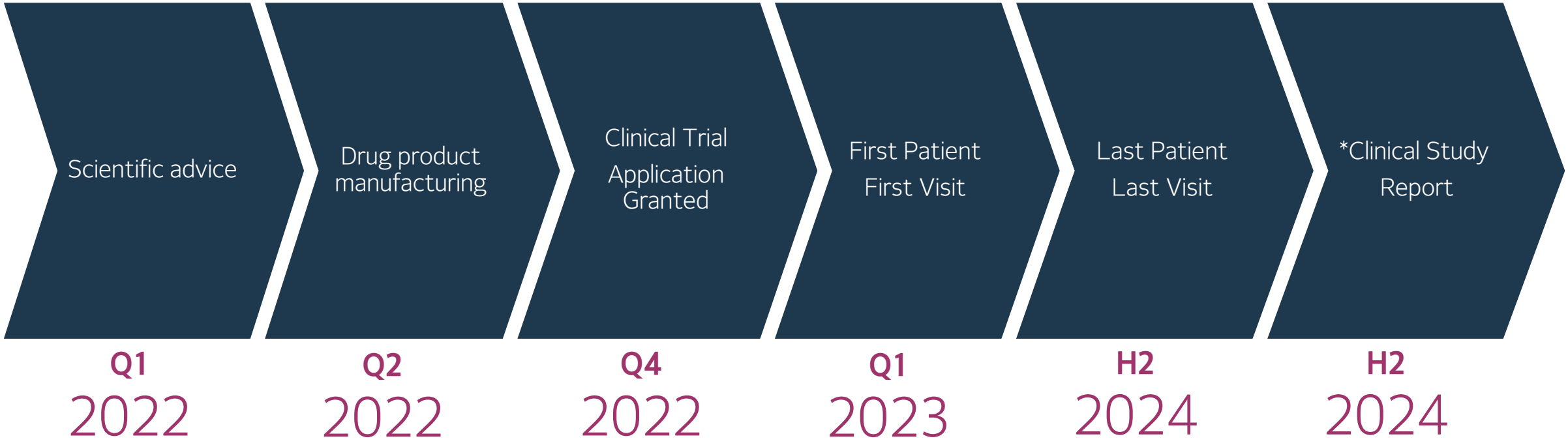
3 main competitors in Oncology with small molecules.

- Incyte / Calithera INCB001158 – Phase II
- AstraZeneca AZD-0011 – Preclinical
- Merck & Co – Discovery

2 companies also developing small molecule arginase inhibitors in other indications

- Calithera – CB280 – Phase Ib - cystic fibrosis
- Chemical Diversity Research Institute – Selective ARG2 inhibitor ZB-49-0010 – Discovery - cardiovascular diseases

OATD-02 Key Milestones, 2022-2024

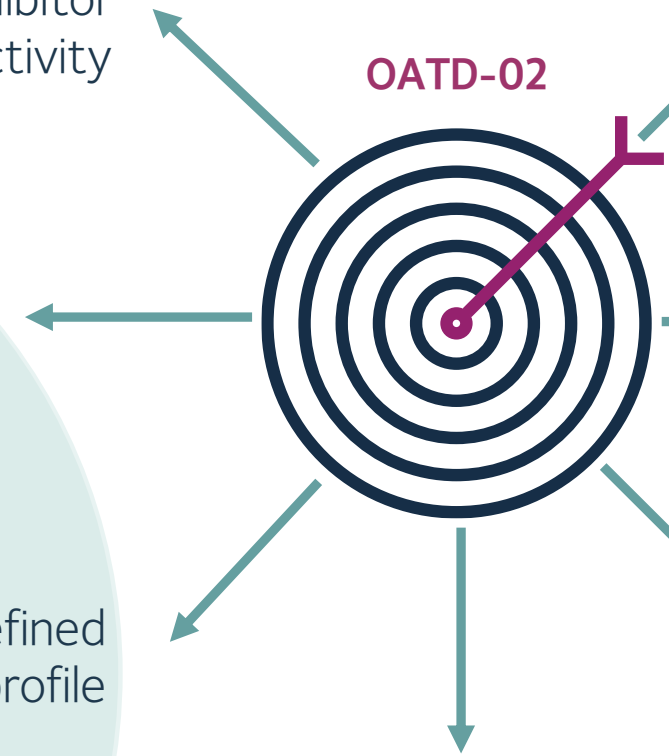


*Clinical Study Report

OATD-02: Unique mechanism of action

OATD-02 is a first-in-class dual ARG1-ARG2 inhibitor

Molecure is the only company offering a dual arginase inhibitor with high intracellular activity



Highly potent, orally active dual ARG1/ARG2 inhibitor with intracellular activity

Significant anticancer efficacy as monotherapy and in combinations in multiple tumor models with no toxicity

Restored arginase-suppressed T cell-mediated immune functions

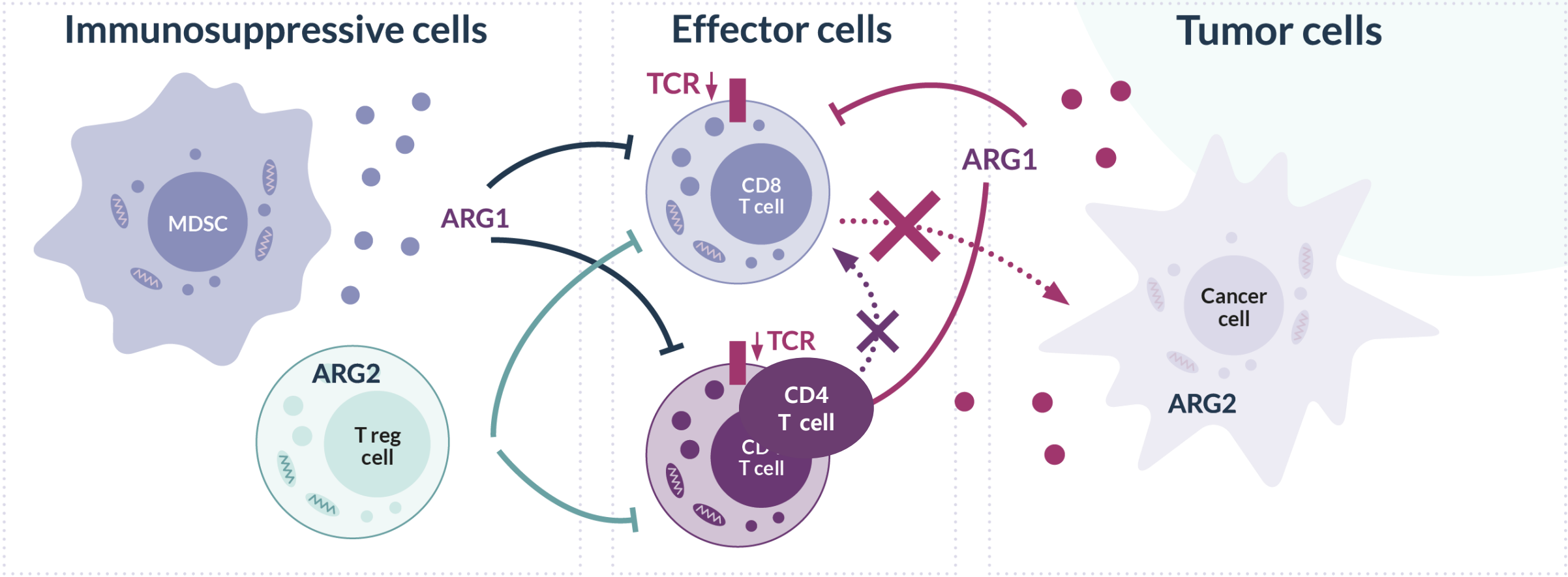
Predicted favorable human PK

Clearly defined pharmacological profile

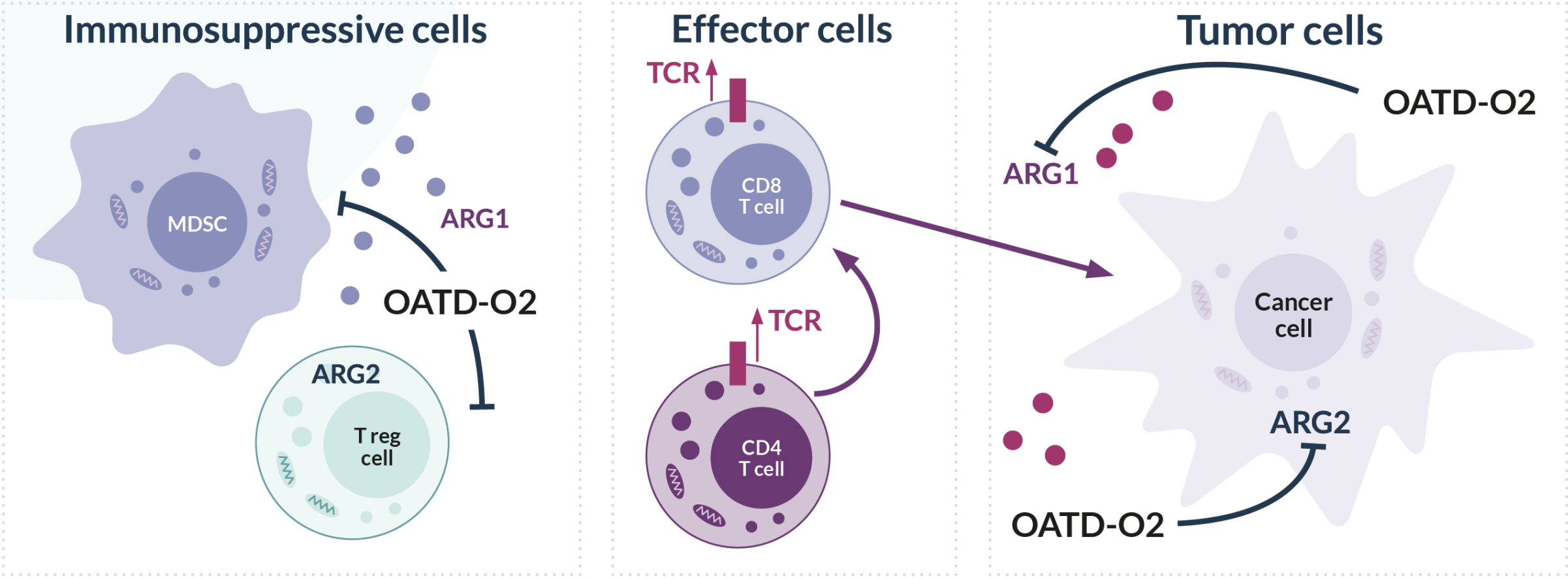
Patent protection until 2037

Expected to enter the clinic in 2022

Increased of ARG1 & ARG2 suppress anti-tumor immune responses



OATD-02 restores effective anti-tumor immune responses via inhibition of ARG1 and ARG2



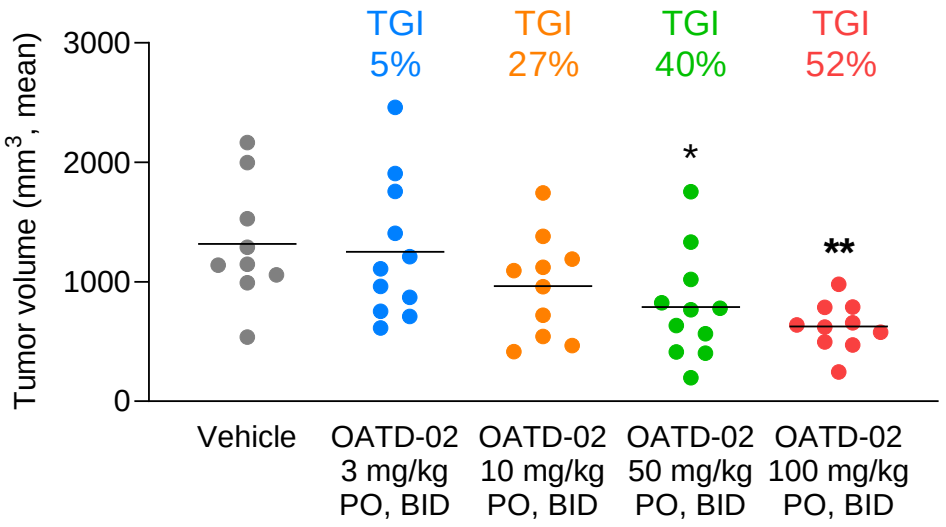
OATD-02 Compelling pre-clinical data

OATD-02 demonstrated dose-dependent therapeutic effect in colorectal cancer model

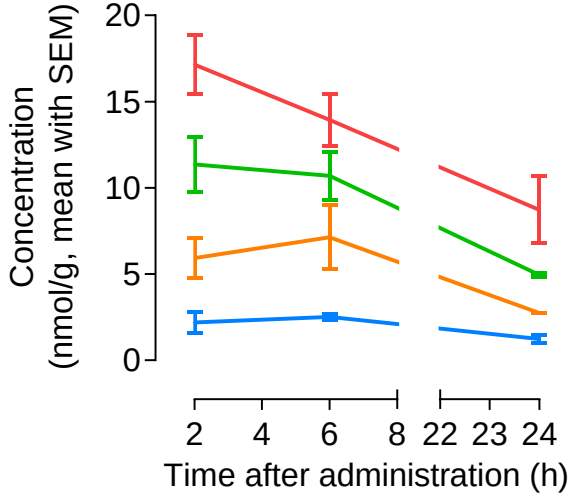
Significant dose-dependent effect was demonstrated in the CT26 model*

High concentrations of OATD-02 detected in plasma and tumors correlated with dose OATD-02 induced significant PD effect – arginine levels were elevated up to ca. 6-fold vs. control animals

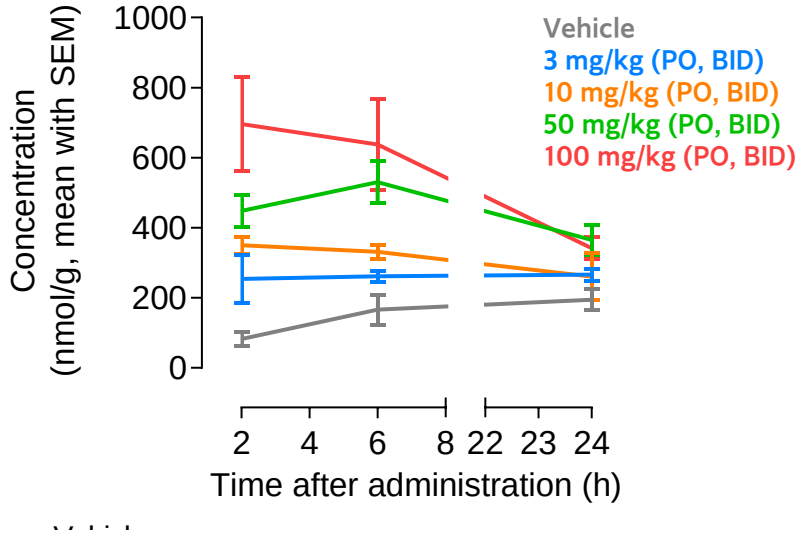
Syngeneic CT26 model of colorectal cancer



OATD-02 in tumors



Arginine in tumors

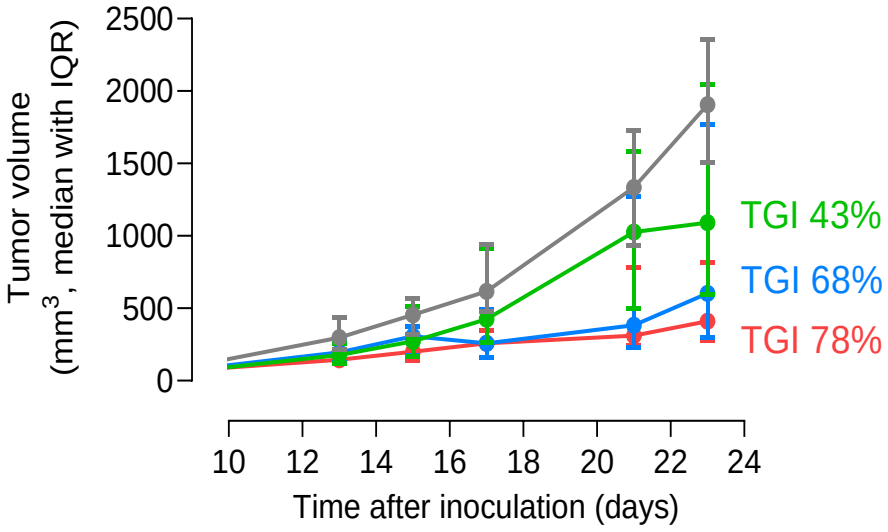


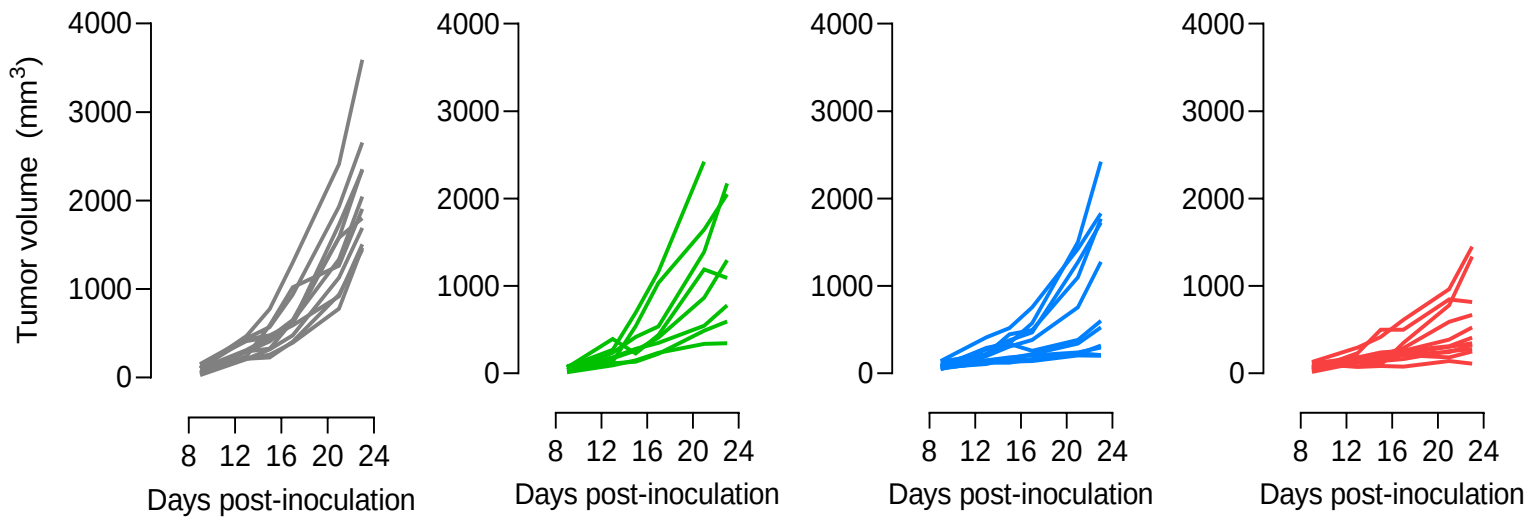
* immunocompetent, C26 tumor bearing mice are commonly used experimental model of colorectal cancer

OATD-02 improved the efficacy of immune checkpoint inhibitors

OATD-02 enhanced the efficacy of anti-PD-L1 antibodies in colorectal cancer model

Syngeneic CT26 model
OATD-02 + anti-PD-L1 antibody

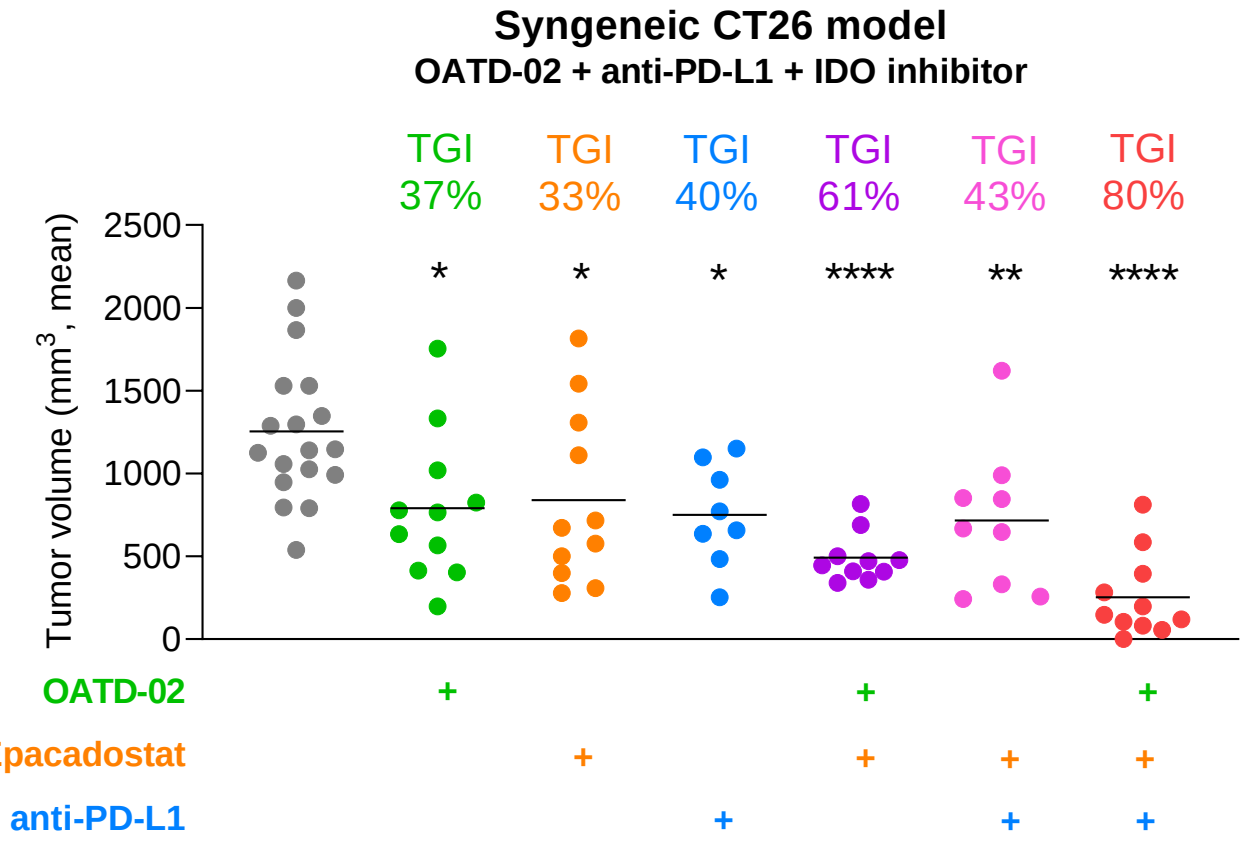




OATD-02 showed superior activity in a triple therapy combined with anti-PD-L1 antibody & epacadostat (IDO inhibitor)

OATD-02 showed superior antitumor activity in combination with IDO inhibitor (TGI 61% vs. 33% for EPA monotherapy)

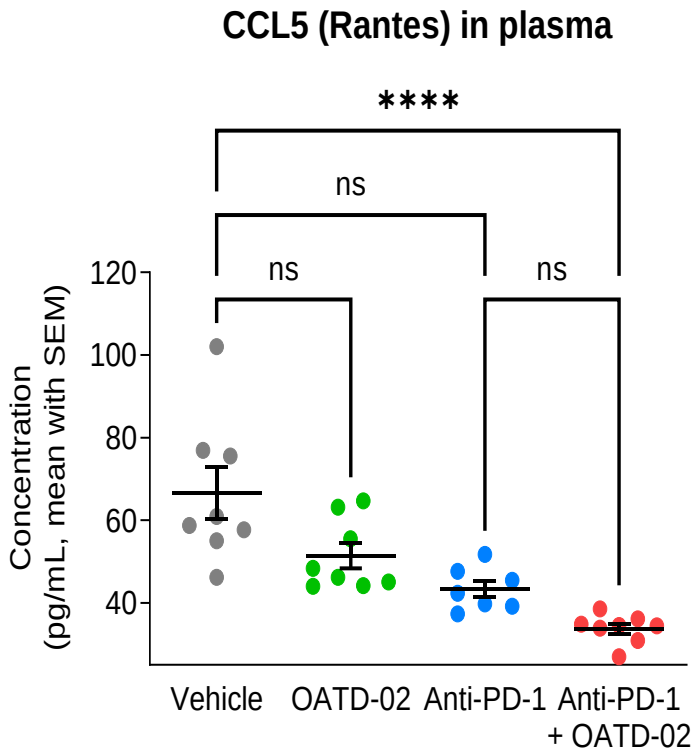
OATD-02 strongly improved the efficacy of the combination of epacadostat and anti-PD-L1 antibody (TGI 80% vs. 43% for dual combo) without apparent toxicity



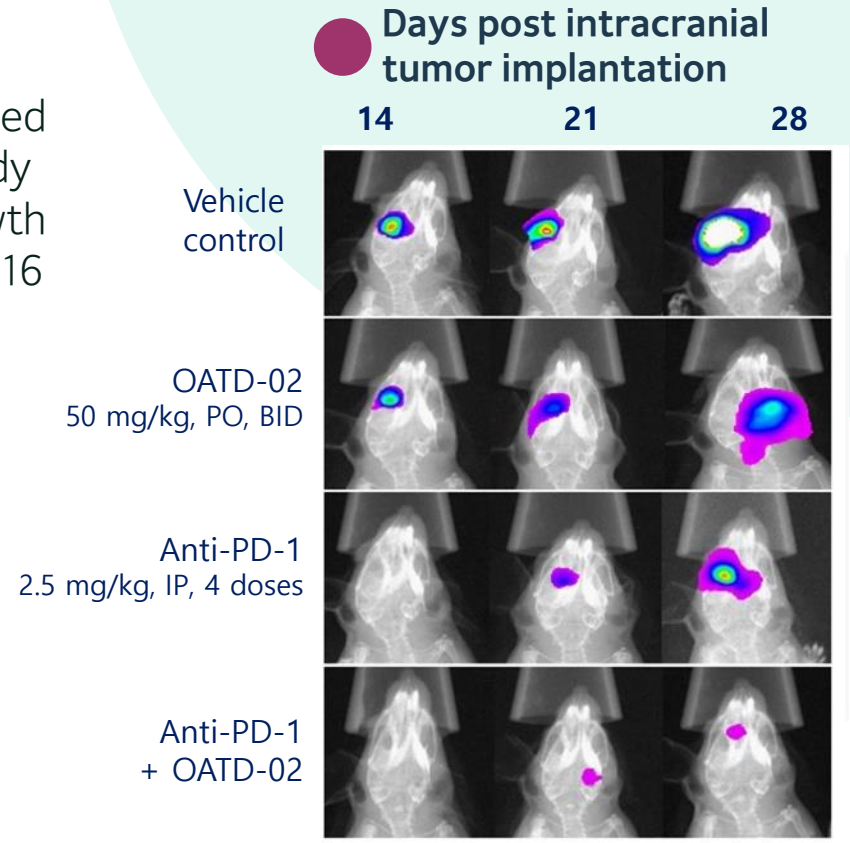
OATD-02 dosed at 50 mg/kg (po, bid from day 1). Epacadostat dosed at 30 mg/kg (po, bid from day 1). Anti-PD-L1 dosed at 2.5 mg/kg (ip, qd, days 8, 10, 12, 14 & 16)

OATD-02 combined with PD-1 antibody reduced the growth of syngeneic GL216 glioma in the orthotopic model

CCL5 is highly expressed in glioma and is associated with poor prognosis in patients. OATD-02 significantly decreased the levels of CCL5 chemokine which participates in driving tumor heterogeneity, formation of cancer stem cells and the promotion of invasion and metastases.

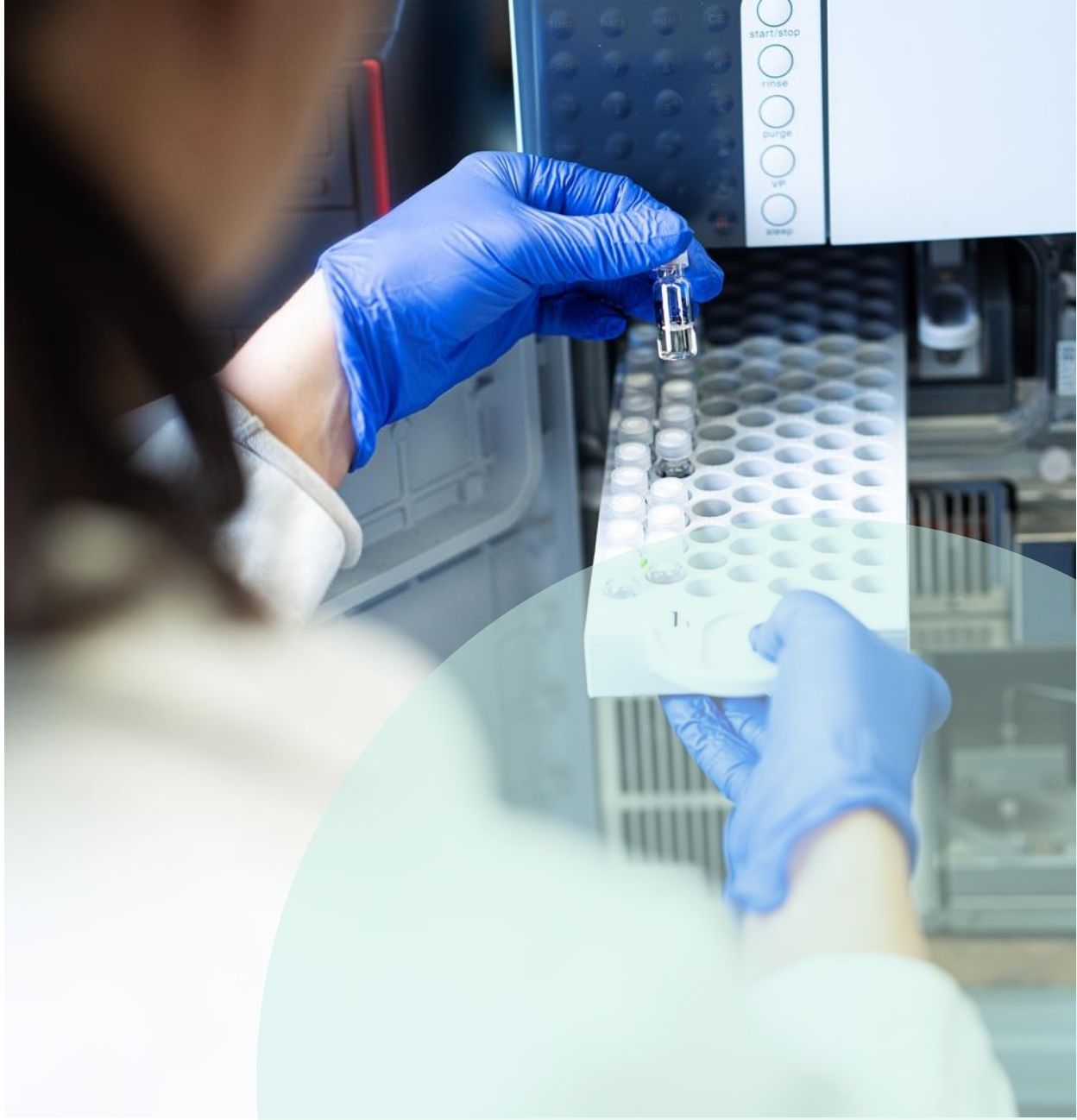


OATD-02 combined with PD-1 antibody reduced the growth of syngeneic GL216 glioma in the orthotopic model



OATD-02 compelling efficacy in animal studies

- Demonstrates dose-dependent therapeutic effect & immune activation response in a C26 tumor model – CRC
- Improved the efficacy of immune checkpoint inhibitors
- Enhanced the efficacy of anti-PD-1 and anti-PD-L1 antibodies
- Showed a superior activity in a triple therapy combined with anti-PD-L1 antibody & epacadostat (ido inhibitor)
- In mouse model effective as a maintenance therapy
- Converted the immunosuppressive environment and enhanced anti-PD-1 immunotherapy in murine model of glioma



OATD-02 displays an attractive target product profile

Biological effect	INCB001158	OATD-02
Extracellular activity	hARG1 80 nM	**hARG1 20 nM**
Intracellular Activity	**Low/none**	**Tregs, ARG2 dependent cancer cells, tumor associated fibroblasts**
Efficacy in syngeneic models	average	**high**
Efficacy in xenograft models	Low / None	**high**

Drug-like properties	INCB001158	OATD-02
Residence on target	1.5 hrs	**>3 hrs**
Plasma half-life	6 hrs	**>30 hrs (predicted)**
Volume of distribution	Rat 0.76 L/kg Mouse 0.4 L/kg Human 0.6 L/kg	**Rat 2.57 L/kg** **Mouse 1.8 L/kg** **Human (predicted) 6.9 L/kg**

V_{ss} < 0.7 L/kg – unable to target the cells in TME
$T_{1/2}$ = 6h is not sufficient to generate high PD response

Easy TME penetration and intracellular ARG1 and ARG2 inhibition for extended period of time

Clinical Development Plan

Professor Cezary Szczylik, Oncologist

Head of the Department of Clinical Oncology and Chemotherapy
European Health Center Otwock

His scientific interest concentrates on hematology and clinical oncology.

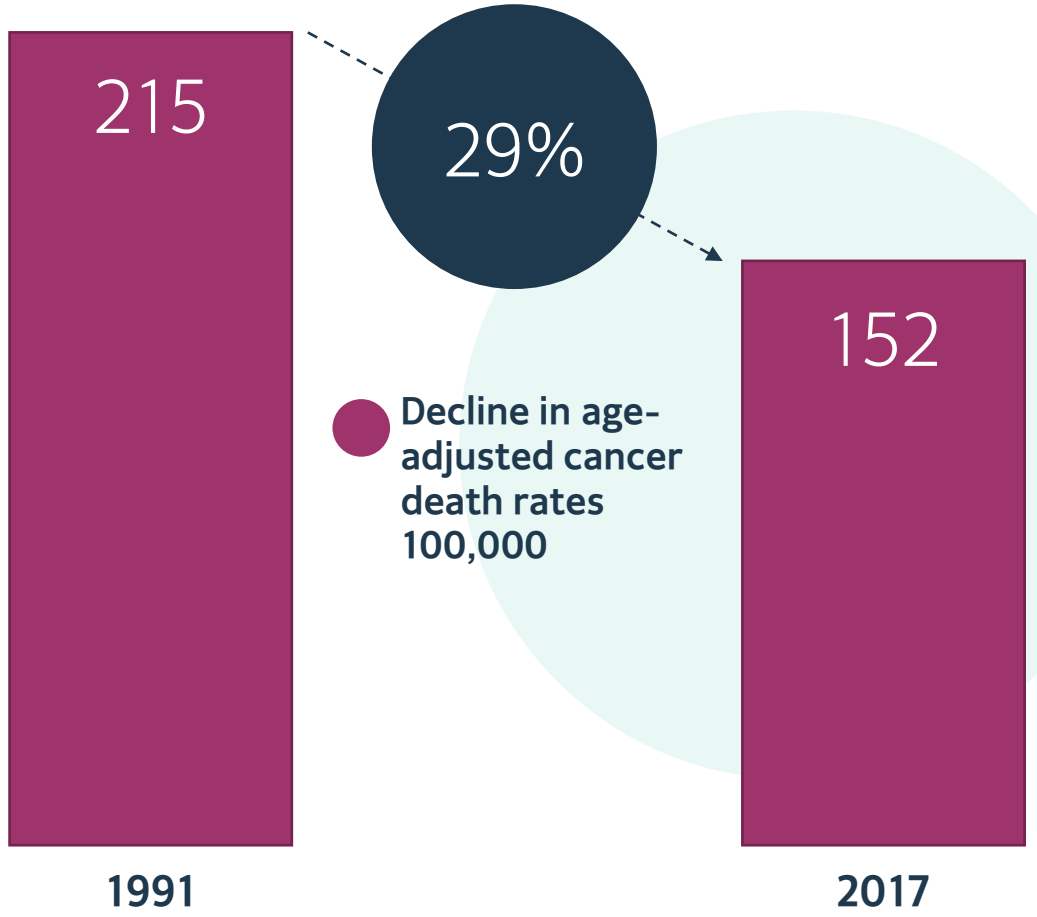
Prof. Szczylik is a President of the Foundation for Experimental and Clinical Oncology, co-founder of the Study of Molecular Medicine and Member of the Polish Society of Oncology.

Principal investigator in more than 100 commercial clinical trials for kidney, breast, pancreatic, non-small cell lung cancer, melanoma, lymphoma, colorectal, gastric, prostate, ovarian cancer.

Author of more than 250 scientific papers in journals such as Science and The New England Journal of Medicine

Unmet need in oncology

- Recent advances in diagnosis and treatment of cancer diseases have resulted in declining cancer death rates across most developed countries
- In particular immunotherapies such as checkpoint inhibitors have led to increase in treatment responses and survival
- However, only about 20-25% of patients respond to checkpoint inhibitors
- In addition, with increasing use of immune therapies resistance is building up rapidly
- Thus there remains a significant unmet need for effective treatments in particular therapies to restore immune response



Sources: Siegel RL et al[19]; Seabury SA et al[20]; National Cancer Institute[21]; American Cancer Society[22]

Tumor types with particular unmet need

Pancreatic ductal cancer (advanced, inoperable)

- current standard treatments comprise chemotherapy combinations (taxanes, gemcitabine, platinum derivates, irinotecan etc.)
- ICIs have not yet demonstrated significant efficacy

Metastatic colorectal cancer

- ICI effective in 15-20% subpopulation only (msi high, dMMR+)

Serous Ovarian Cancer

- ICIs not standard of care

Renal Cell Cancer

- Targeted agents standard-of-care, ICIs with limited efficacy

State of oncology in Poland – Statistics

According to the Polish National Cancer Registry (2019):

- Cancer is the **second cause of death** in Poland and a significant health problem primarily in young and middle-aged people (25-64 years)
- 171,218 have been diagnosed, and 100,300 died of cancer
- 85,559 of which occurred in men and 85,659 in women
- In 2019, compared to the previous year, there was a **slight increase in cases**: by 1,989 in men and 1,783 in women; the number of cancer **deaths decreased** among men by 993 and among women by 74
- In women cancer is the leading cause of death before the age of 65, accounting for 31.7% of young deaths and 46.8% of middle-aged women's deaths
- Of particular concern is the impact of **smoking** rates on the trend of lung cancer in the female population – in 2019, the number of women who died as a result of lung cancer exceeded the number of women who died from breast cancer (by more than 1,254).

Krajowy Rejestr Nowotworów (onkologia.org.pl)

State of oncology in Poland – common cancers

♂

- the most common cancer in men is **prostate** cancer (almost 21%)
- **lung** cancer is the second leading cancer in men, accounting for about 27% of deaths
- for almost 15 years a decrease in the incidence and mortality has been observed, associated primarily with a decrease in the percentage of male smokers in recent decades
- **colorectal** cancer is in third place (8% of cases) with an increasing trend of morbidity while stabilizing mortality

♀

- in the female population, the leading cancers are: breast, lung and colorectal
- the incidence of **breast** cancers, which are dominant among women, have been increasing over the past half-century; mortality trends have changed several times over the past thirty years; in the years 1996-2010 there was a decrease in mortality, however in 2010-2019 there was an unfavorable change in this trend
- **lung** cancer remains the first in causes of death in women (17.9%), ahead of breast cancers (15.1%).
- the third leading cause of cancer death in women in the past few years remains **colorectal** cancer

Krajowy Rejestr Nowotworów (onkologia.org.pl)

State of oncology in Poland - treatments

Pancreatic cancer

- Treatment of pancreatic cancer is one of the most difficult and still poses a big challenge for oncologists.
  - Results of the treatment remain unsatisfactory, despite undoubted progress,
  - Mortality rates meet the morbidity rates.
  - Overall, five-year survival rates do not exceed 10%, and in those patients who have undergone surgical treatment, five-year survival rates reach only 20%.
  - Chemotherapy remains the mainstay of care. **More clinical studies are needed to develop completely new therapies**.

Colorectal cancer

- Since **colorectal** cancer affects younger and younger people, there is a proposal to lower the age of groups undergoing screening.
  - Particularly heterogeneous disease, therefore molecular profiling is important in diagnosis and treatment, and it is not possible to treat all patients equally.
  - Immunotherapy is effective in patients with microsatellite instability. **There is high need for novel treatment options, also through the combinations of existing drugs.**

State of oncology in Poland - treatments

Ovarian cancer

- In ovarian cancer, prevention is impossible, and the symptoms are not characteristic.
  - The surgical treatment should take place in experienced centers.
  - Comprehensive care for patients is also needed.
  - Genetic tests are performed too rarely.
  - **Access to modern therapies is also incomplete**. The only type of prevention may be the special care of families in which this disease has occurred.

Renal cancer

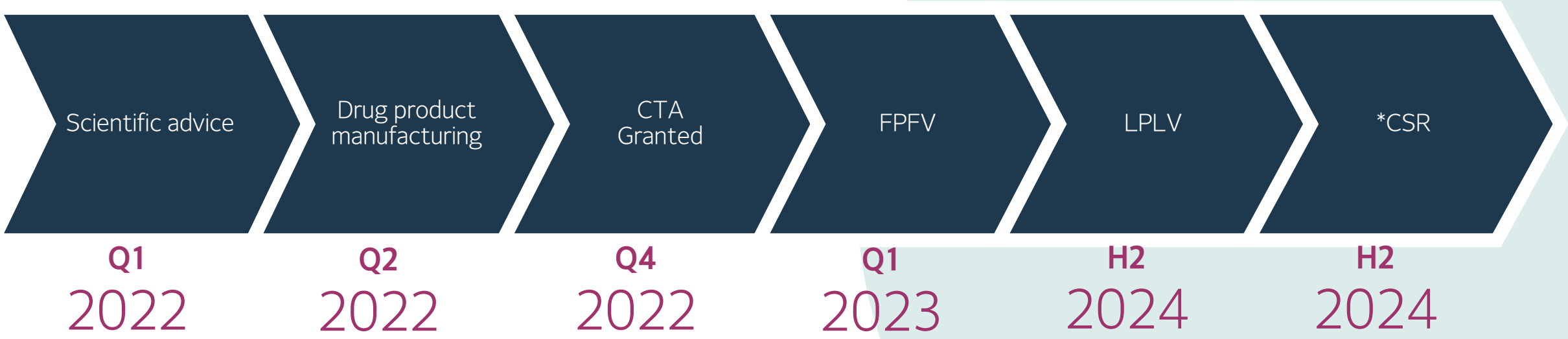
- In half of patients with renal cell carcinoma the disease is spread.
  - An undoubted breakthrough in the treatment is immunotherapy, used after radical treatment.
  - New drug program reflecting recent recommendations of scientific societies, gives the opportunity to **choose the most appropriate treatment strategy**.

OATD-02 on-track to enter the clinic in 2023

CTA granted. Study initiation with first patient first visit expected Q1 2023

Potential best-in-class profile:

- First dual ARG1/ARG2 inhibitor
- Favorable therapeutic window of OATD-02 for improved safety and tolerability
- Better infiltration in tumor microenvironment enhancing therapeutic efficacy
- Possibility to broaden the spectrum of target malignancies



*Clinical Study Report

OATD-02 FIH Phase I/II study (1)

Design

- Open-label single-arm dose-escalation monotherapy study (Bayesian design)

Patient population (30-40 patients)

- Relapsed/refractory advanced and/or metastatic solid tumours

- Colorectal cancer, platinum-resistant serous ovarian cancer, pancreatic ductal cancer, renal cell carcinoma

Study Sites

- 3 sites in Poland: Warsaw, Otwock, Bydgoszcz

Study Duration

- Approx. 1,5 years (Q1, 2023 - H2, 2024)

OATD-02 FIH Phase I/II study (2)

Study Objectives:

- **Primary outcomes:** safety and tolerability, determination of MTD/RP2D
- **Secondary outcomes:** PK, PD (biomarkers), anti-cancer activity (response, survival endpoints)

Data generated will inform design of future additional studies across multiple tumor types (e.g. hem malignancies) and treatment combinations (e.g. with ICIs,)

Key highlights of OATD-02

- First in class dual arginase therapy
- First in human clinical study to start in early 2023
- Potential to treat a broad range of cancer patients
- OATD-02 demonstrates robust efficacy in animal studies
- Novel approach with very limited competition
- Potential as a mono and combination therapy


Q&A

10 minute break

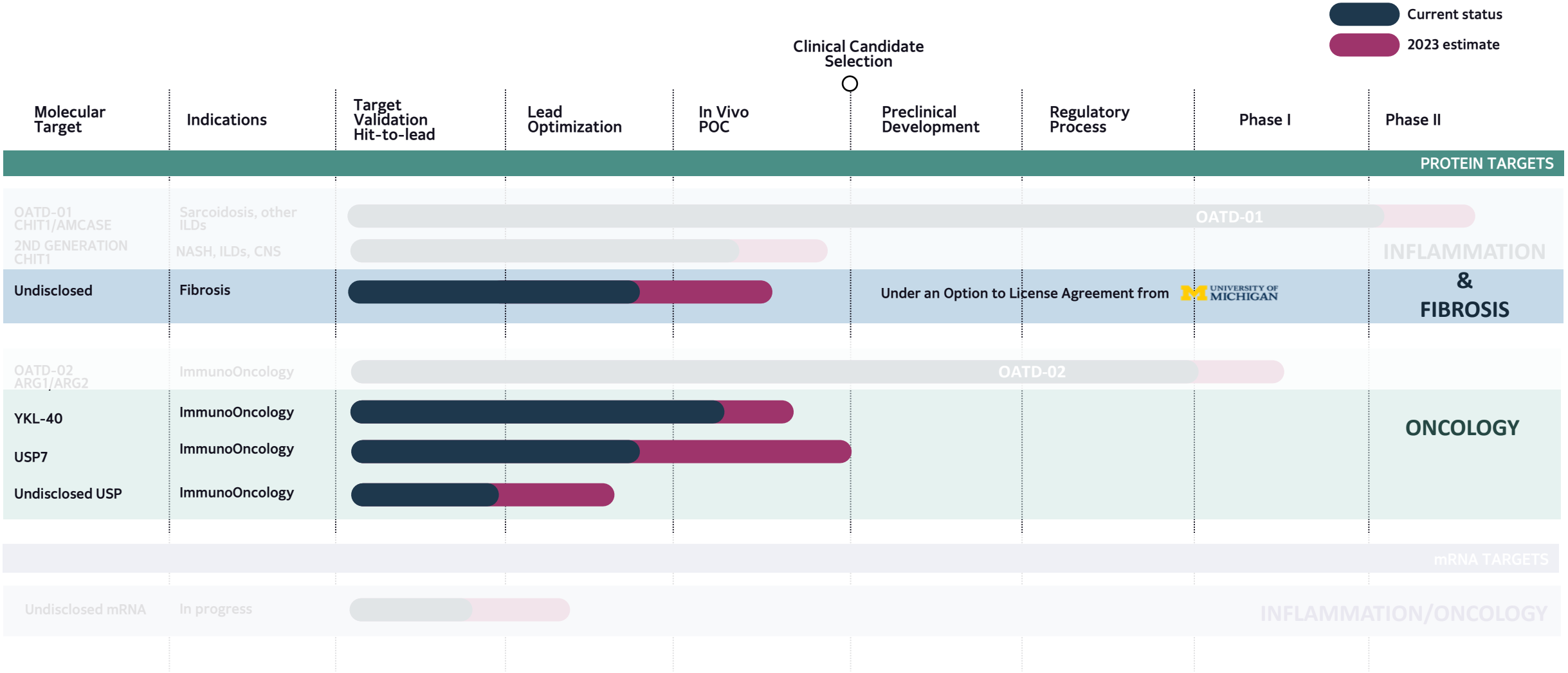
Next session starts at 15:40

Our vision

Our goal is to become a leading biotechnology company, globally recognized for discovering and developing breakthrough small molecule drugs acting on unexplored protein and novel RNA targets to help patients in need of innovative therapeutic solutions

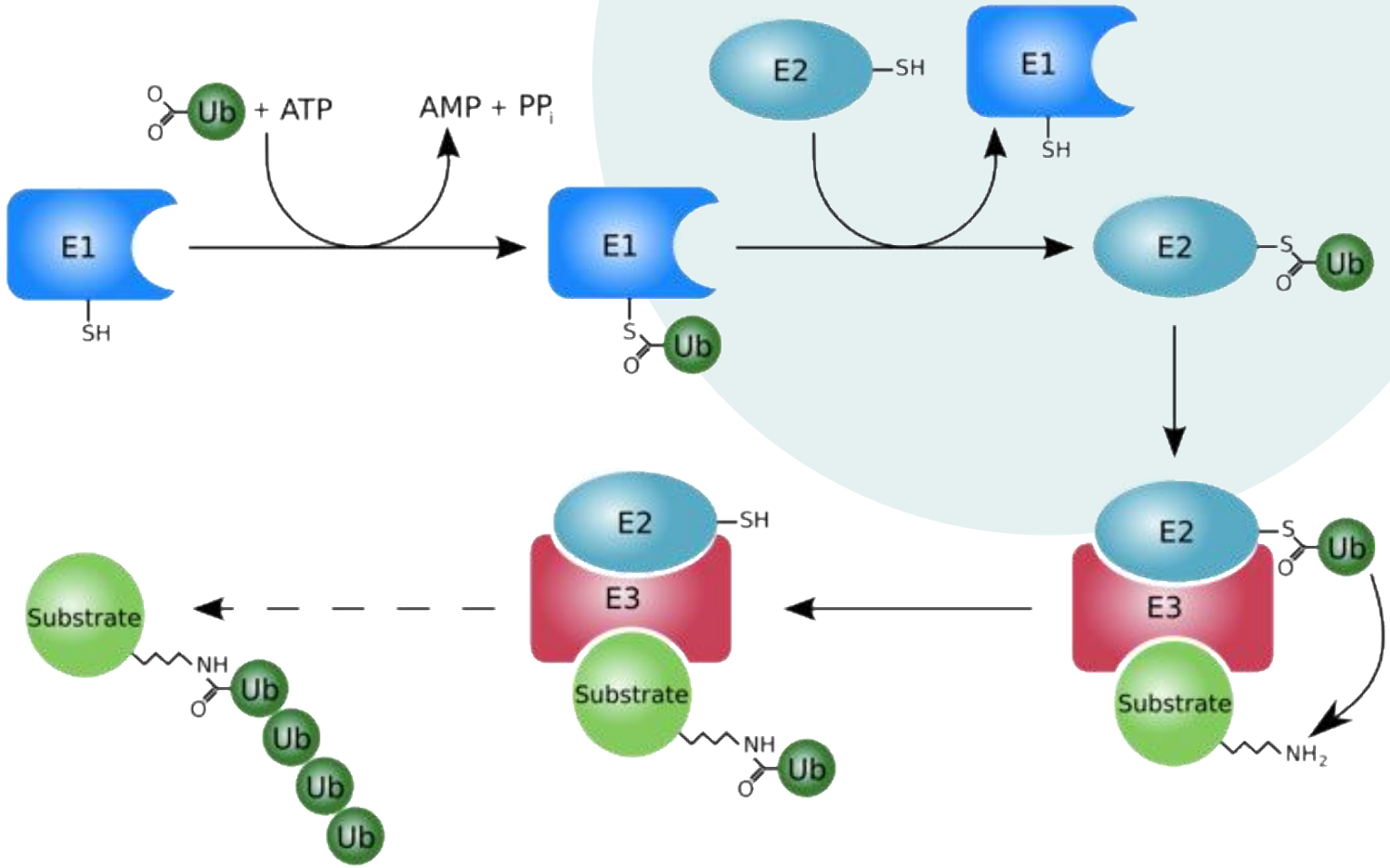

Early programs

High Value Pipeline



Ubiquitin pathway – focus on post-translational modifications

- Ubiquitination is a **post translational modification covalently attaching ubiquitin to targeted proteins**
- Ubiquitination **determines or alters protein's biological activity**, stability or sub-cellular localization

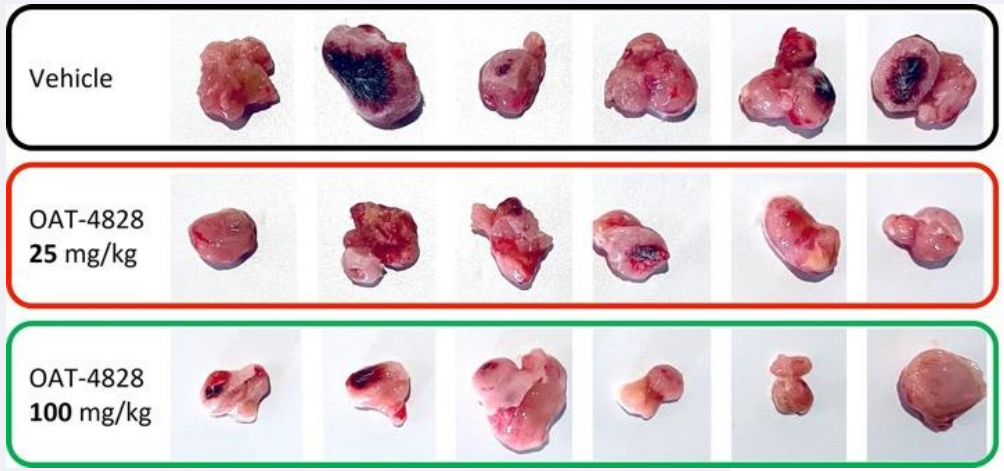


Significance of deubiquitinase inhibition

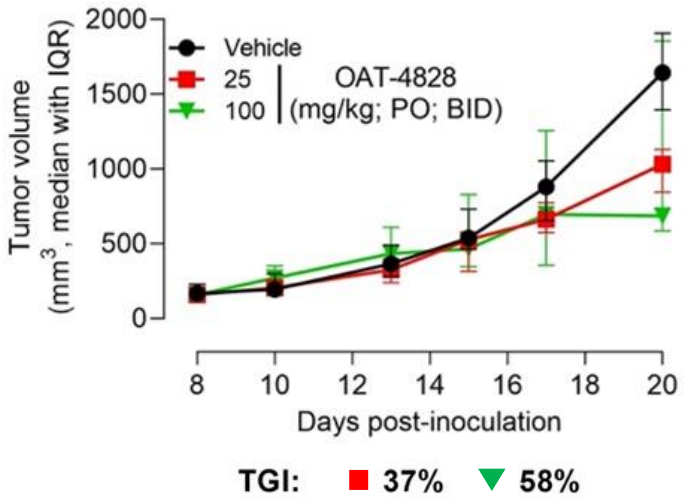
- Deubiquitinating enzymes (DUBs), are proteases that **reverse the post translational modification of proteins by removing ubiquitin** or remodeling ub-chains on target proteins
- **As a result, DUBs have a great influence on many biological processes** and cellular pathways
- Enhanced expression of DUBs can be seen in **both cancer and some inflammatory states**
- This makes DUBs a potentially very **important group of targets** for anticancer therapeutic agents

Molecure is developing inhibitors of DUBs, including selective inhibitors of ubiquitin specific protease 7 (USP7), and another yet undisclosed USP whose high expression is seen to be aberrant in a number of tumor indications, promoting oncogenesis.

Significant tumor size reduction in CT26 model after USP7i (OAT-4828) treatment

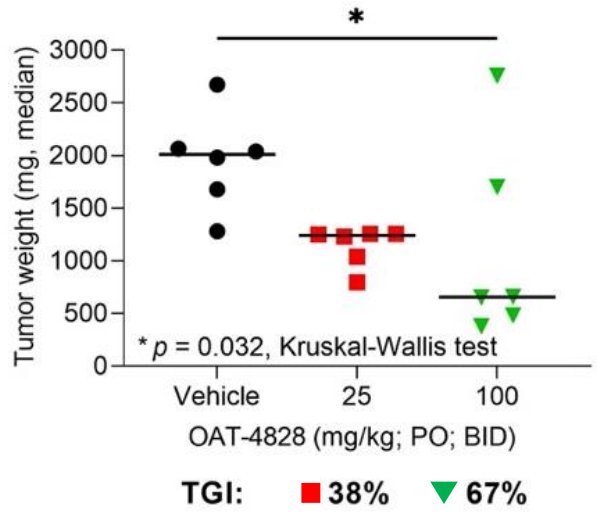


CT26 tumor growth kinetics



TGI: ■ 37% ▼ 58%

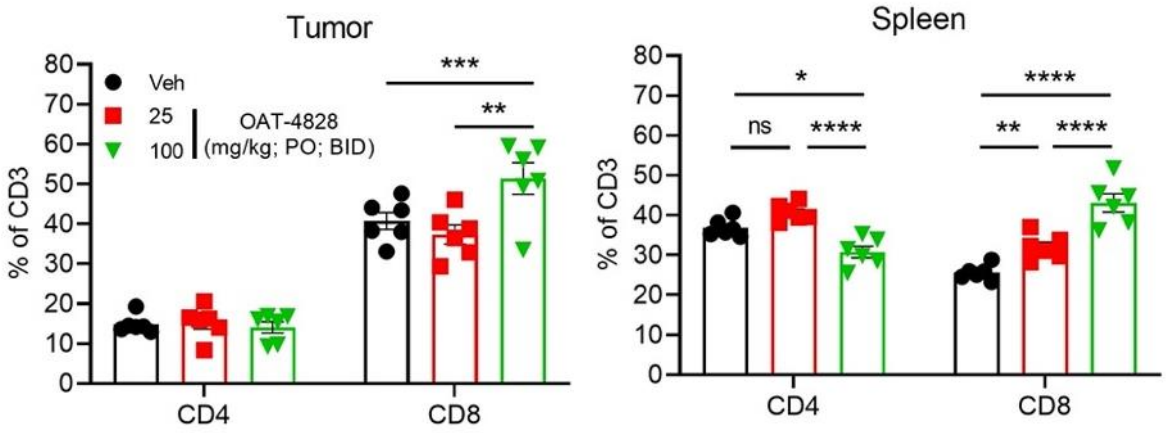
CT26 tumor weight at day 20



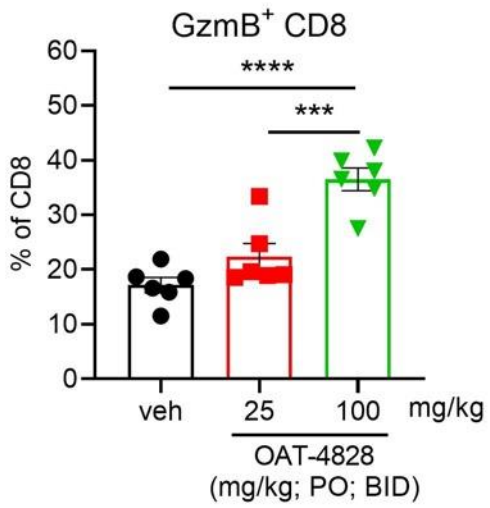
TGI: ■ 38% ▼ 67%

OAT-4828 treatment induces CD8 T cells

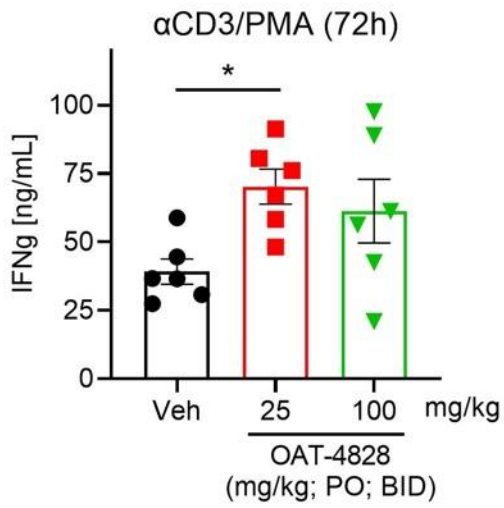
- **OAT-4828 increases cytotoxic CD8+ T cells in tumor and spleen**



- **OAT-4828 increases cytotoxicity of CD8+ T by increasing the expression of Granzyme B and INFg**

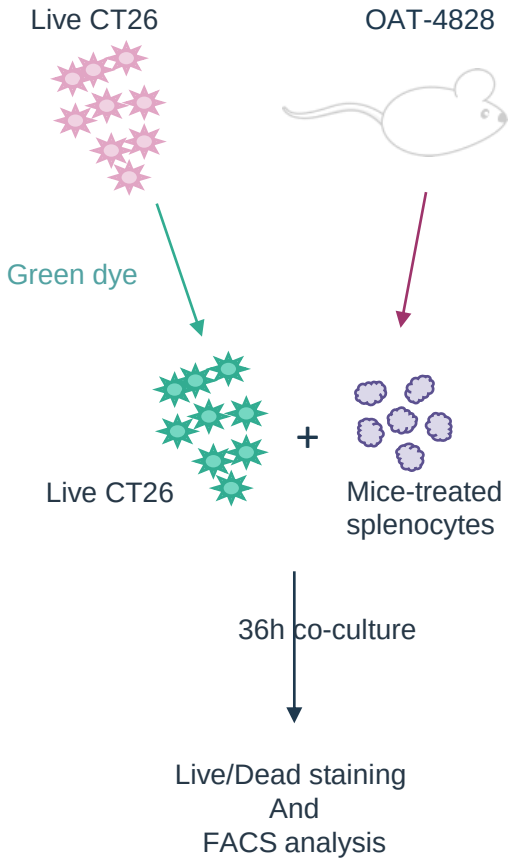


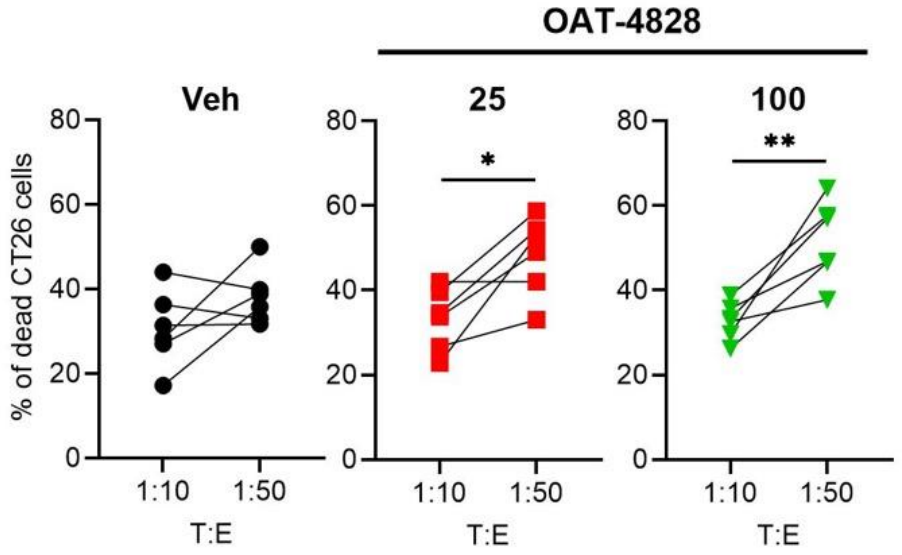
Tumor

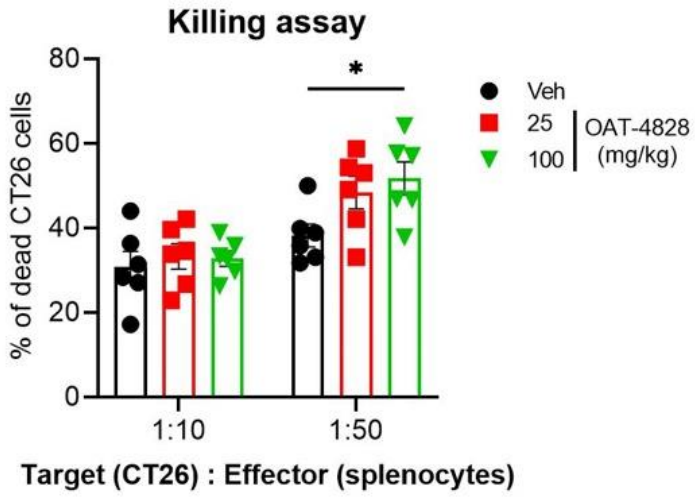


Stimulated splenocytes from OAT-4828 treated mice

Increased killing of CT26 cells by effector cells from OAT-4828 treated mice



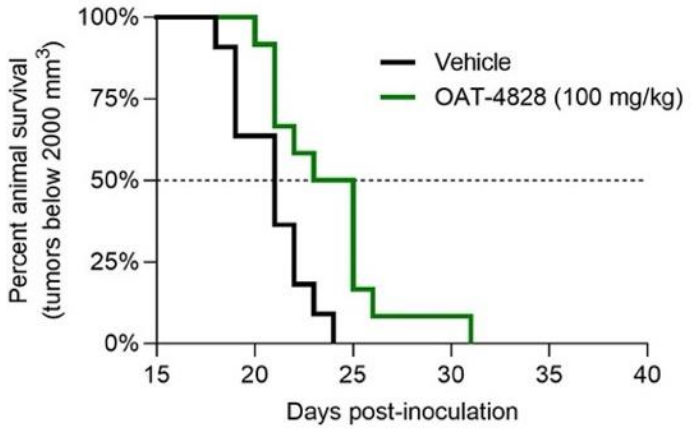




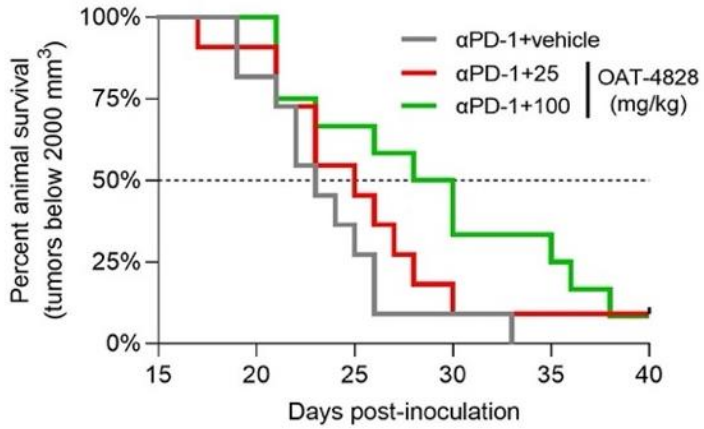
Effector cells isolated from the spleen of mice treated with OAT-4828 for 20 days bear the potential to induce cell death ex vivo, in fresh CT26 cells in the absence of other treatment

Significant survival increase in CT26 model after OAT-4828 treatment in combination with αPD-1

Survival analysis (mono)



Survival analysis (combo)



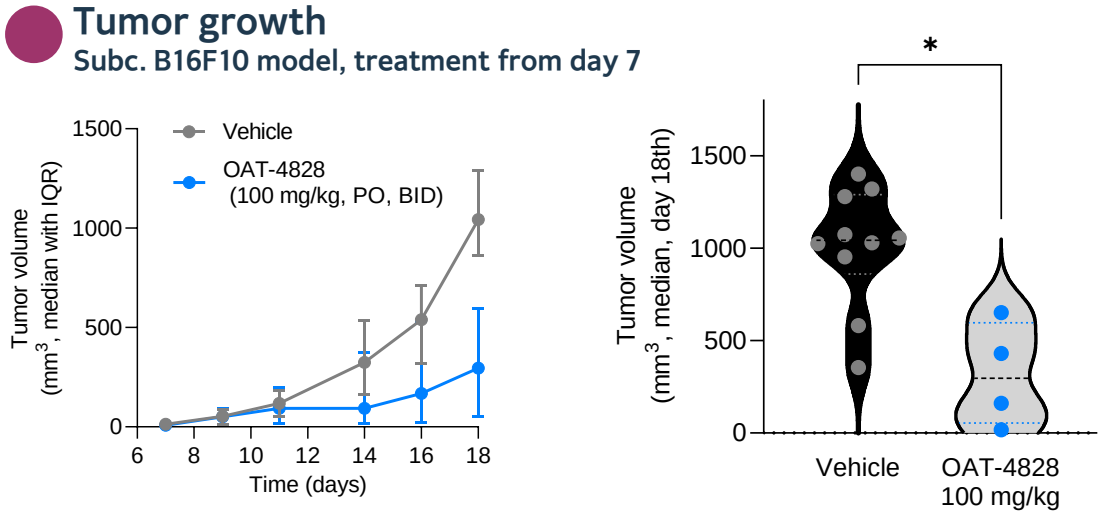
OAT-4828 increases the survival of animals by 14% vs. control (stand alone) and by 26% in combination with an aPD-1 vs. aPD-1 alone at 100 mg/kg PO, BID.

OAT-4828 increases the TGI from 46% for the aPD-1 alone, to up to 69% at 100mg/kg BID.

	Vehicle	OAT-4828 100 mg/kg BID
Median survival	21 days	24 days
Statistical significance (Mantel-Cox test)		** p = 0.0059

	αPD-1	αPD-1 + OAT-4828 (25 mg/kg BID)	αPD-1 + OAT-4828 (100 mg/kg BID)
Median survival	23 days	25 days	29 days
Statistical significance (Mantel-Cox test)		ns	* p = 0.0198

OAT-4828 shows efficacy in B16F10 melanoma cancer model



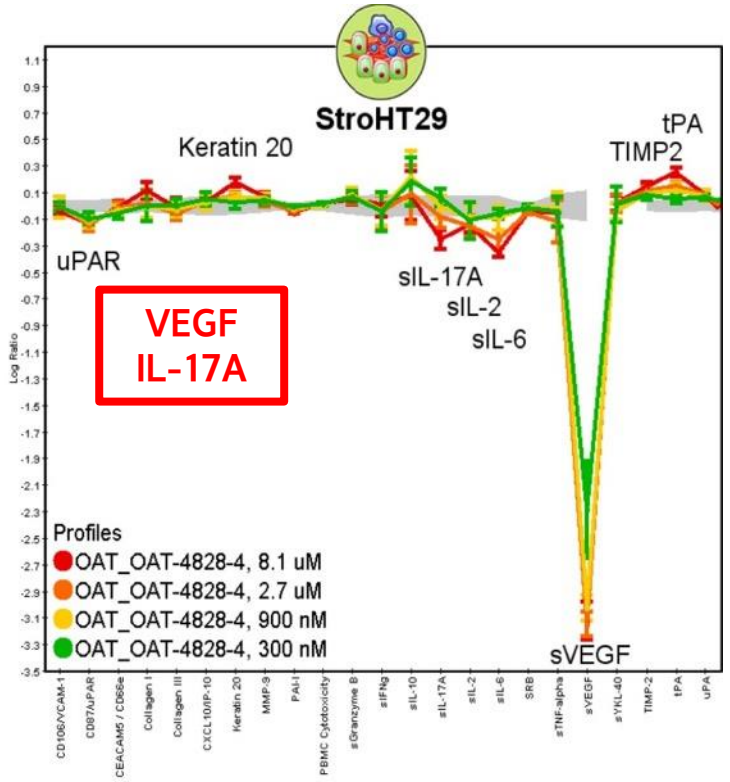
OAT-4828:

- decreases tumor growth in the fast, aggressive, melanoma model
- changes the ratio of T CD8/CD4 cells by increasing the % of CD8
- leads to activation of T CD4 and CD8 lymphocytes (observed in spleens)

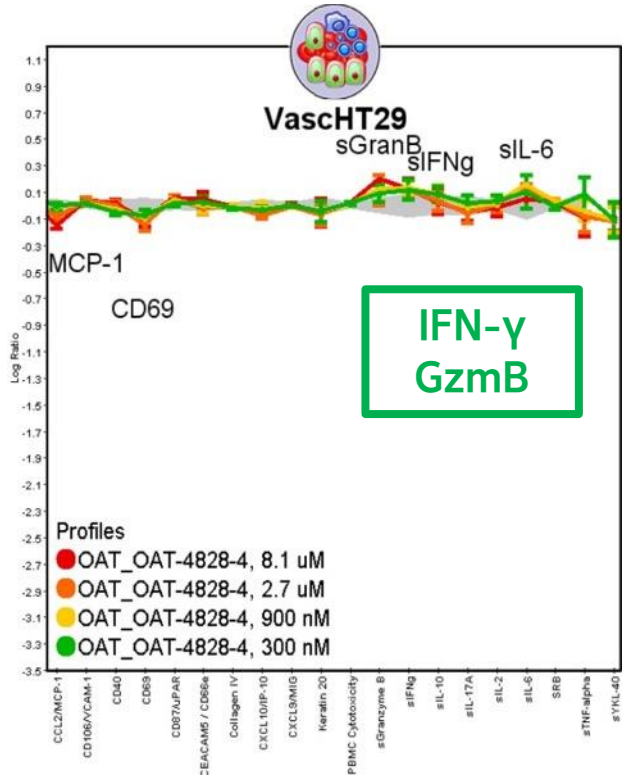
Human primary co-cultures validates anti-tumor and immunomodulatory properties of OAT-4828

In human primary co-culture of fibroblasts (stromal model) or venular endothelial cells (immune model) with PBMC and colorectal cancer cells, upregulation of GzmB and IFNg is observed, as in the animal model as well as an downregulation of IL 2, 6 and 17 and VEGF (ELISA of soluble proteins)

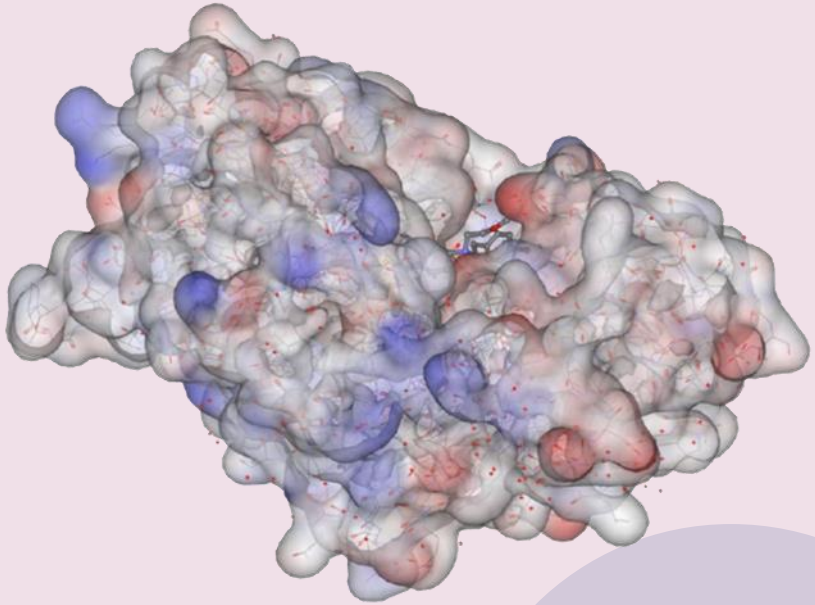
Fibroblasts + PBMCs + HT-29 (CRC)



Venular endothelial cells + PBMCs + HT-29 (CRC)



YKL-40 binders



Status

- Advanced lead stage
- Selective YKL-40 binder
- Favorable pharmacokinetic profile
- No significant off-target activity

Research Focus in 2023

- Reveal the mechanism of action of YKL40 and its binder through scientific collaboration(s)

License option agreement to develop small molecule assets against a novel target for the treatment of fibrotic diseases

Status

- Constant know-how transfer, screening cascade set up and lead optimization
- Verification of the therapeutic efficacy in various fibrosis models
- Aiming for first-in-class status in the program

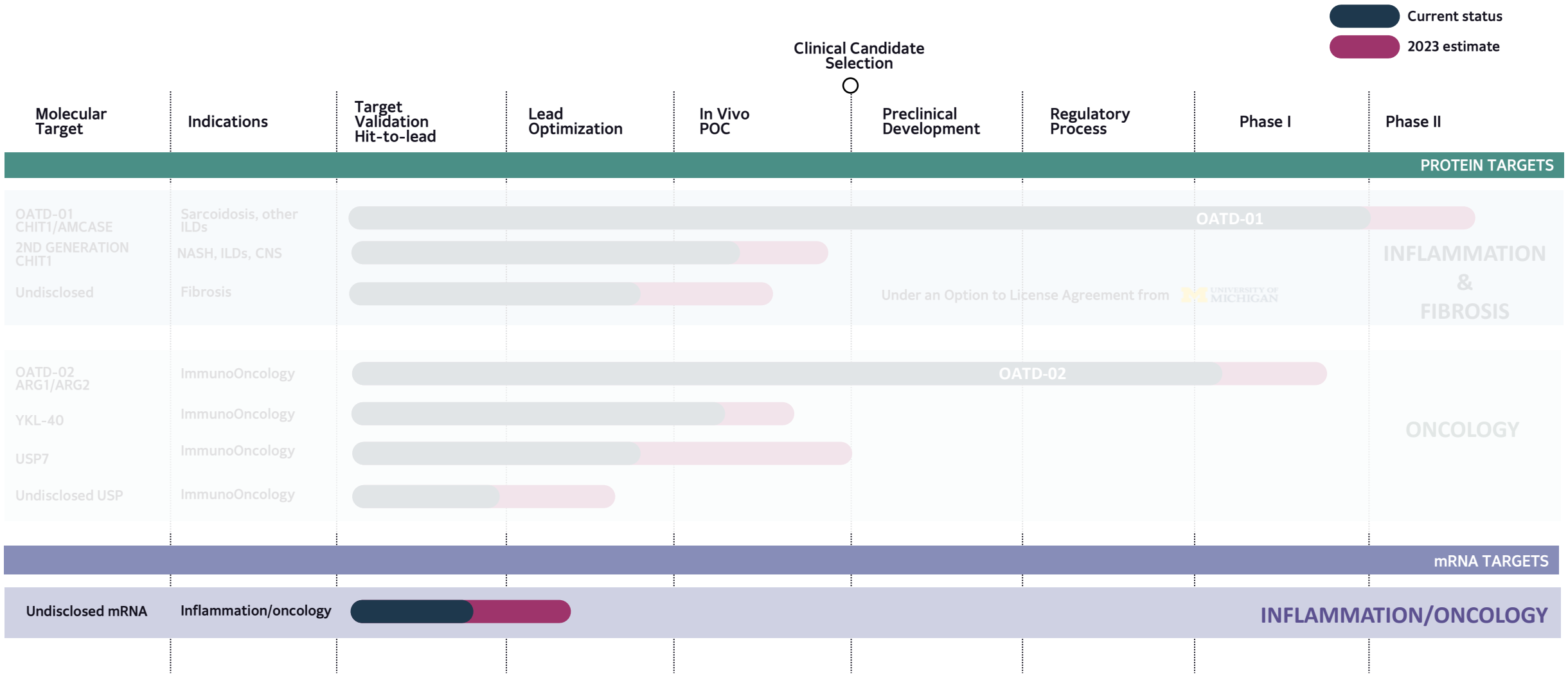
Research Focus in 2023

- Confirmation of *in vivo* activity of the lead compound
- Improved design of molecules effective *in vivo*

Our small molecule mRNA discovery platform

The potential to disrupt mRNA targeting approaches

High Value Pipeline



Discovering medicines of the future

Small molecules targeting RNA to prevent downstream RNA translation

GENE OF INTEREST

GCAUGGAAAc

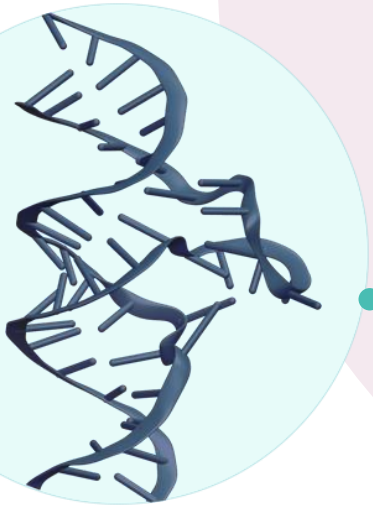
1 Selection of functional targets, with unique properties

2D RNA STRUCTURE

BIOINFORMATICS
BIOPHYSICS

2 Thermodynamic modeling to predict secondary structure

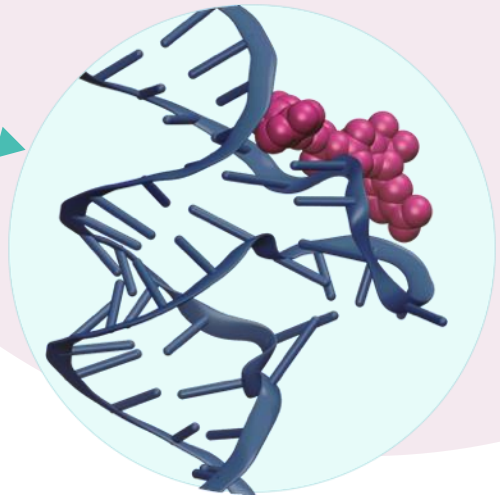
3D CONFORMATION PREDICTION



UNIQUE ALGORITHM

3 Dynamic modeling for tertiary structure determination and binding pocket identification

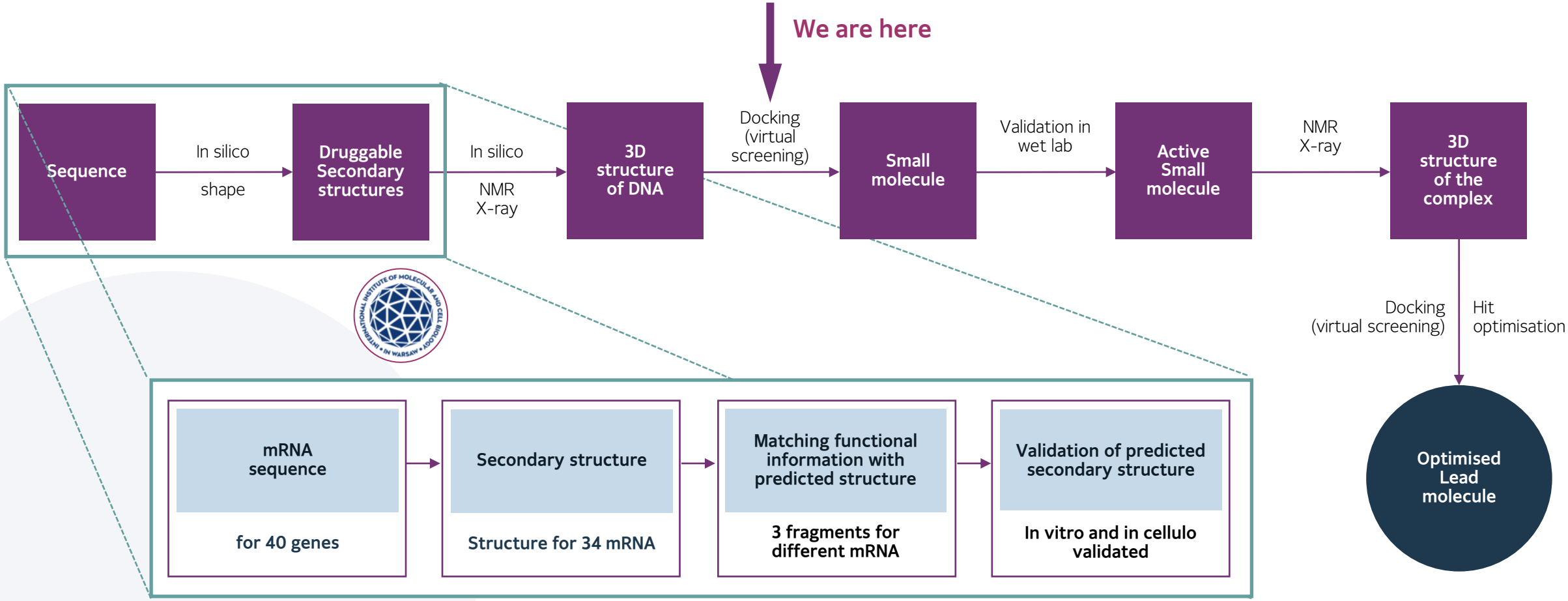
BOUND SMALL MOLECULE
- NO TRANSLATION -
NO PATHOLOGICAL PROTEIN



HTS
MEDICINAL CHEMISTRY

4 High throughput screening of potential binders and refining of leads with wet lab chemistry

Our mRNA platform discovery workflow




Q&A

Molecure 3-year goals

Potential milestones targeted by 2025

Protein Targets

2023-2024

- Two clinical assets in PhI/II multi center clinical trials in patients
- Two candidates in formal preclinical development (internal pipeline + in-licensing)
- Three new discovery programs in lead-op

2025

- Final reports from OATD-01/02
- Indication expansion for OATD-01
- One new clinical stage program in (immuno)oncology

BD/Financial/Operational

2023-2024

- At least one clinical stage program partnered in a high-value deal
- High value assigned to pre-translational & post-translational discovery platform

2025

- Significant cumulative revenue from partnering & collaboration agreements
- Dynamic growth: >50% human resources

RNA Platform

2023-2024

- In vitro PoC reached for 2-3 high value mRNA targets
- Drug-like molecules (leads) in 2 or more RNA-targeting small molecule programs

2025

- High-value collaboration / partnership agreements
- Expansion into new therapeutic areas and modalities

Value creation potential based on our key strengths

World class medicinal chemistry and biology expertise
Validated discovery & development capabilities through major out-licensing deal with Galapagos

Bold & smart target selection – both mRNA and proteins
Undrugged, limited competition, attractive commercial potential, unmet medical needs

Multiple academic partnerships to access the target biology
Allows us to generate first/best in class drug candidates from our medicinal chemistry expertise

Entrepreneurial / risk taking approach
Belief in our medicinal chemistry expertise and expanding biology capabilities allow us to work on challenging, high reward targets

Preferential access to the highly regarded and rapidly growing Polish life science talent pool
Significantly higher cost efficiency & potential ROI compared to international competition (USA)

Fully integrated biotechnology company with two first-in-class clinical stage assets as well as pre-translational (mRNA) and post-translational protein modification discovery engine


Thank you
molecure

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
- dMMR+: Deficient Mismatch Repair
- ELISA: Enzyme-linked Immunosorbent Assay
- EMA: European Medicine Agency
- ESAT: Early Secreted Antigenic Target
- FDA: Food And Drug Administration
- FIH: First-in Human
- FVC: Forced Vital Capacity
- FPFV: First Patient First Visit
- GLP: Good Laboratory Practices
- GzmB: Granzyme B
- ICI: Immune Check Point
- IFNg: Interferon gamma
- IND: Investigational New Drug
- IPF: Idiopathic Pulmonary Fibrosis
- KOL: Key Opinion Leader
- LPLV: Last Patient Last Visit
- MAb: Monoclonal Antibody
- MSI: Micro Satellite Instability
- MTD: Maximum Tolerated Dose
- NASH: Non-alcoholic Steatohepatitis
- nM: Nanomolar
- NOAEL: No-observed-adverse-effect Level
- ODD: Orphan Drug Designation
- PBMC: Peripheral Blood Mononuclear Cells
- PK/PD: Pharmacokinetics / Pharmacodynamics
- PO: Per Os - Orally
- PoC: Proof Of Concept
- QoL: Quality of Life
- VEGF: Vascular Endothelial Growth Factor