



molecule

Fate can be altered

June 9th, 2022

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**Warsaw, June 9, 2022**

# Presenting team



**Marcin Szumowski**

PhD, MBA

Chairman of the Board & CEO

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



molecule



**Sławomir Broniarek**

Board member

CFO

More than 20 years of experience in financial  
markets, including the investment sector



**Zbigniew Zasłona**

PhD,

VP Research Biology

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



# Our vision

To become a leading biotechnology company, globally recognized for discovering and developing breakthrough small molecule drugs acting on novel RNA and unexplored protein targets





# 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

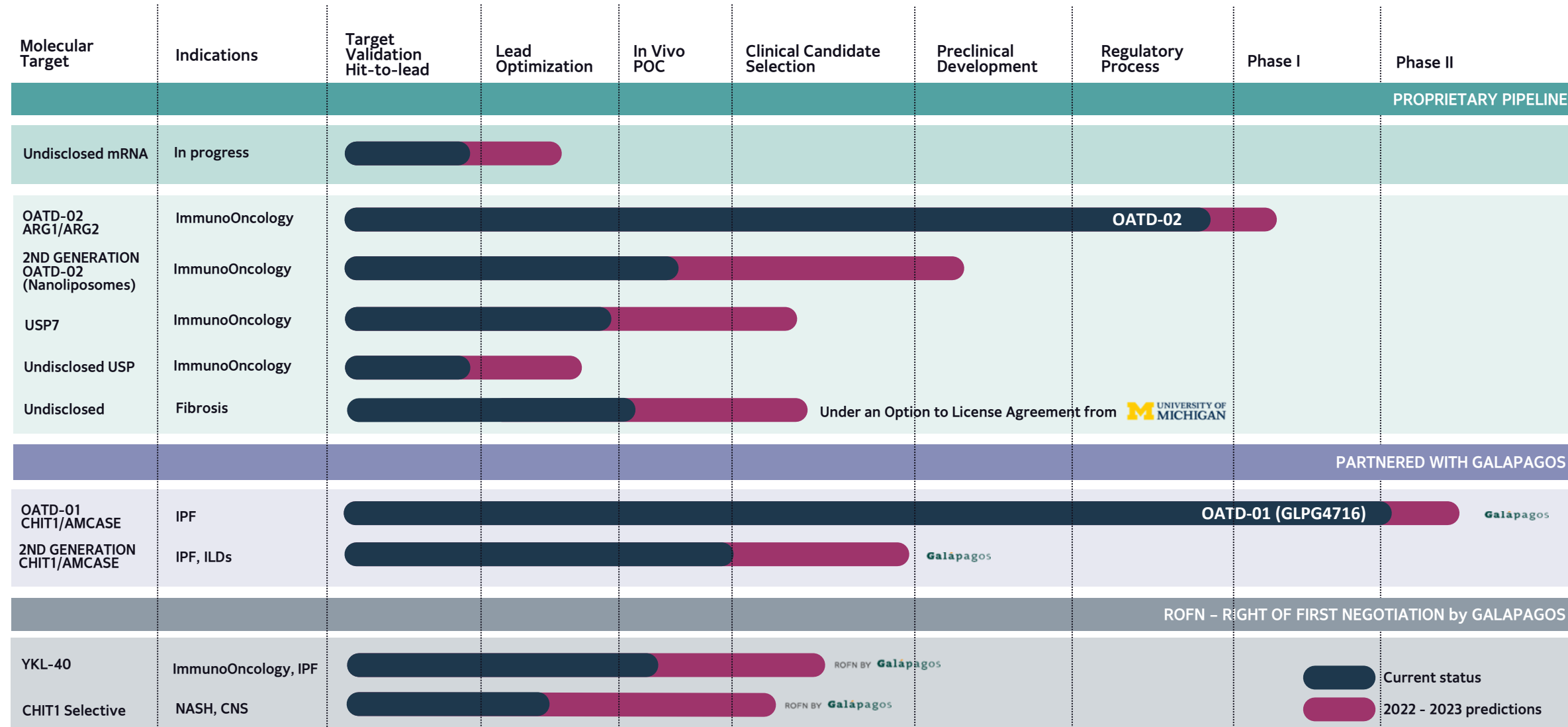
## **Entrepreneurial / risk taking approach**


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)

# Current pipeline



A scientist wearing safety goggles and a lab coat is using a pipette to transfer liquid into a multi-well plate. The background shows various laboratory glassware like beakers and test tubes, all under a blue and purple color scheme.

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

# OATD-01 status of work progress

Molecule out-licensed OATD-01 (currently GLPG4716) to Galapagos in November 2020.

Status of Galapagos progress is presented below:

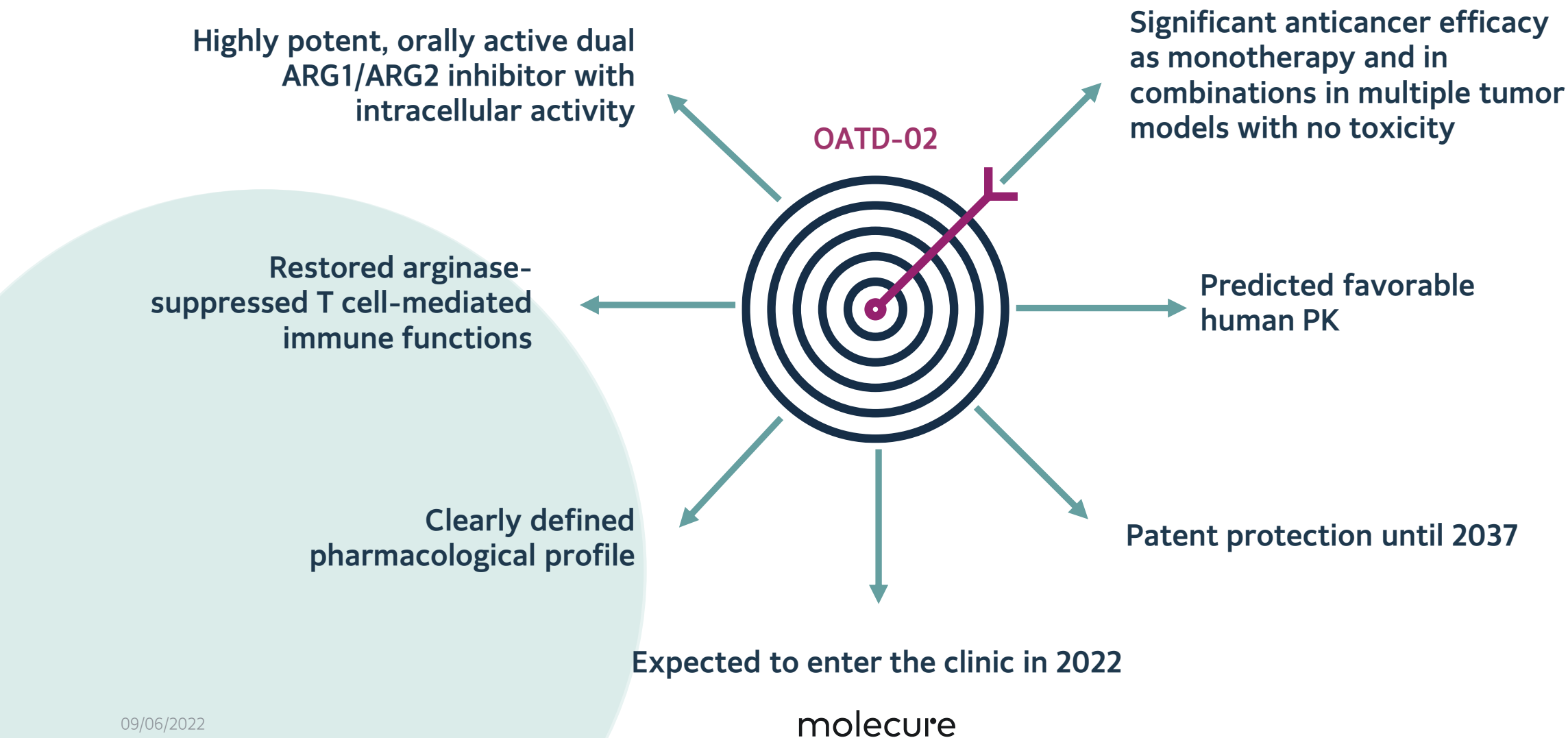
All required preclinical and clinical development studies & analyses have been completed, including:

- Drug –drug interaction and Food-effect Study with Midazolam in Healthy volunteers Nov 2021 (completed)
- Drug –drug interaction Study with Nintedanib and Pirfenidone in Healthy volunteers June 2022 (completed)
- GLPG received the Scientific Advice from EMA regarding phase II clinical trial in IPF patients

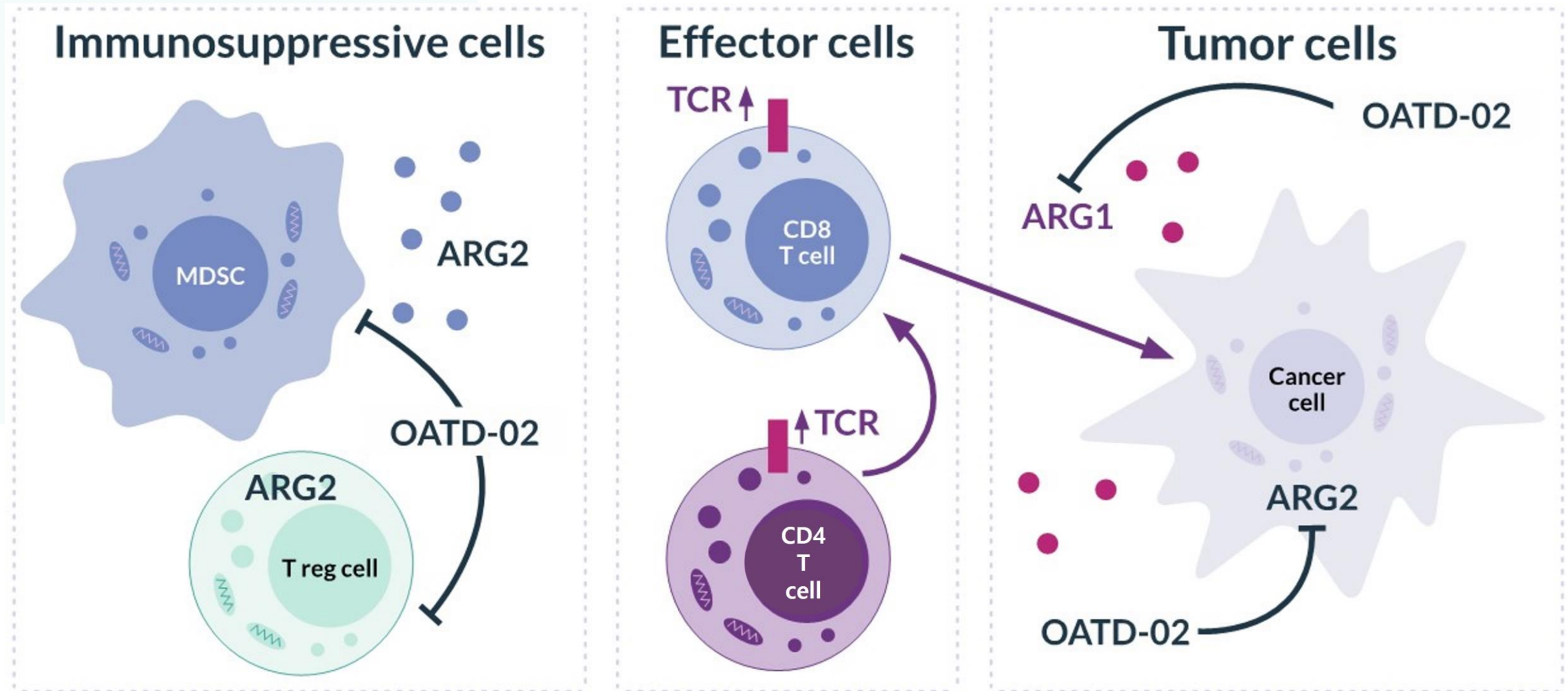


# OATD-02 is a first-in-class dual ARG1-ARG2 inhibitor

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



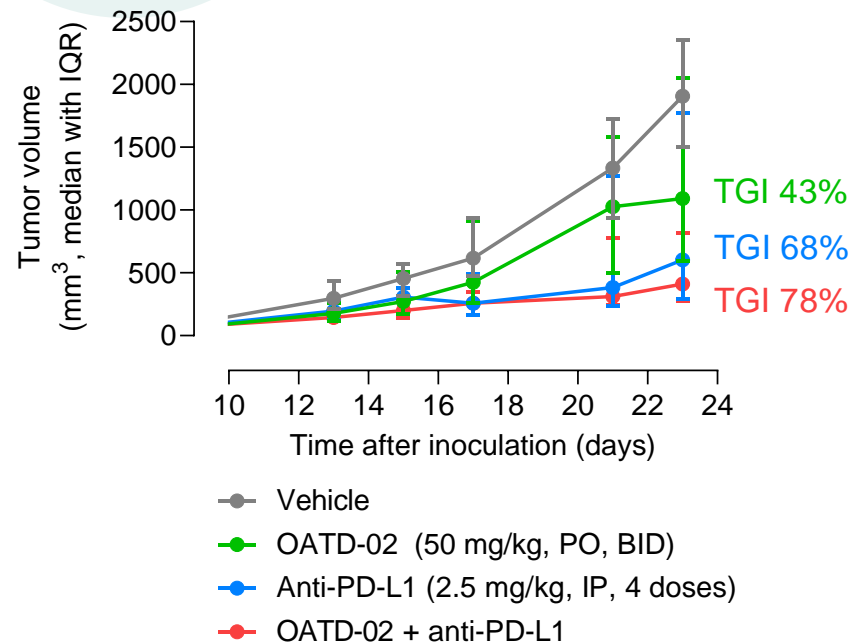
# OATD-02 Restores effective antitumor immune responses



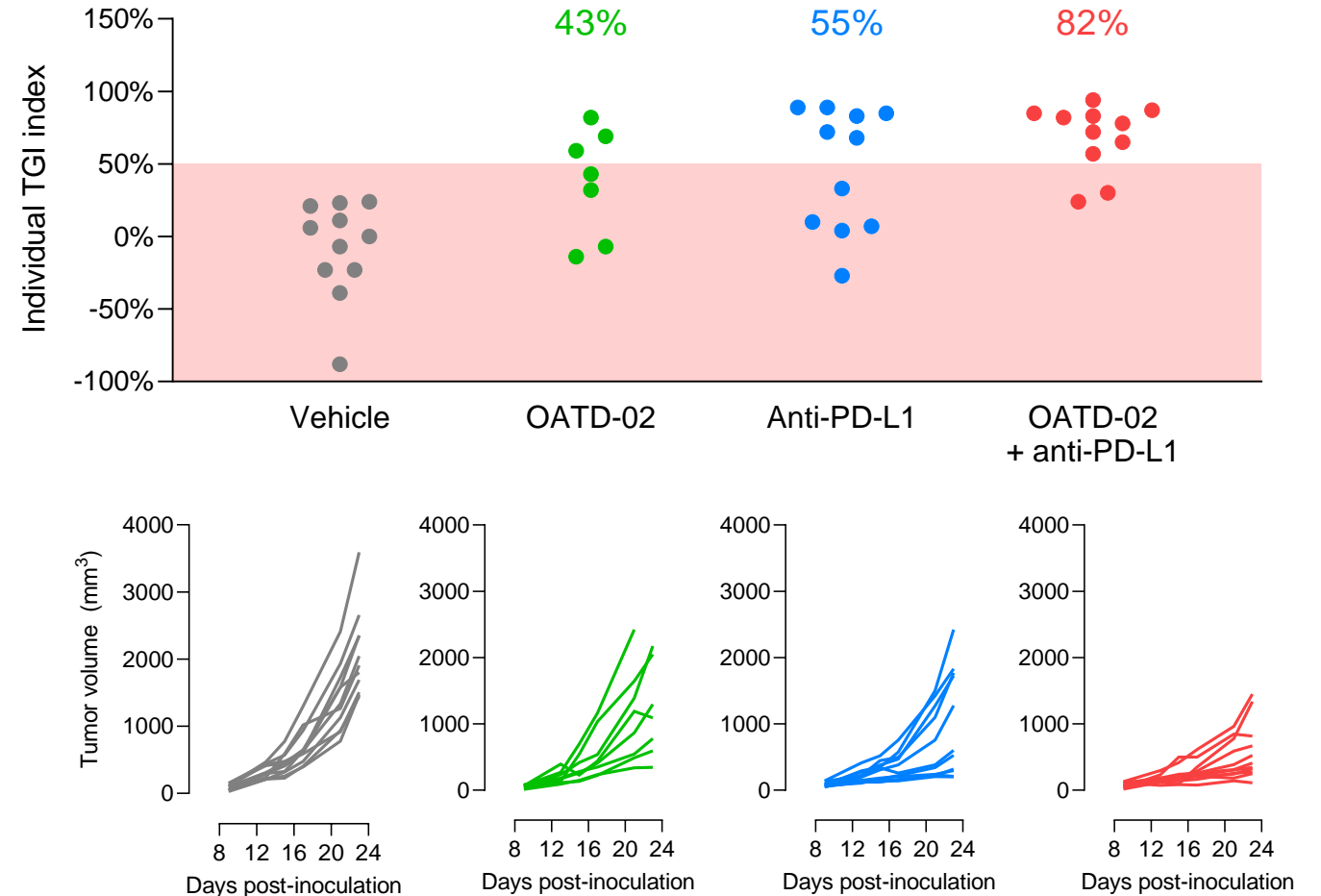
# OATD-02 improved the efficacy of immune checkpoint inhibitors

OATD-02 enhanced the efficacy of **anti-PD-L1 antibodies**

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



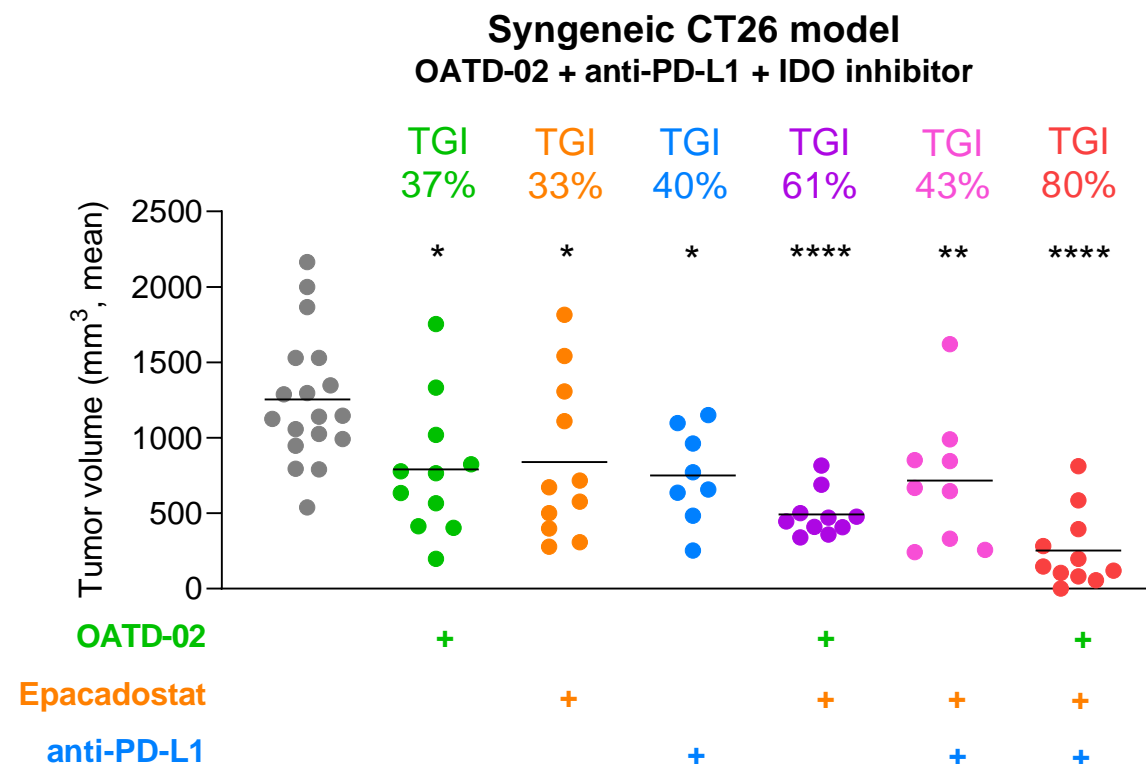
Percentage of small tumors with TGI > 50%



# OATD-02 showed a 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. 40% 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

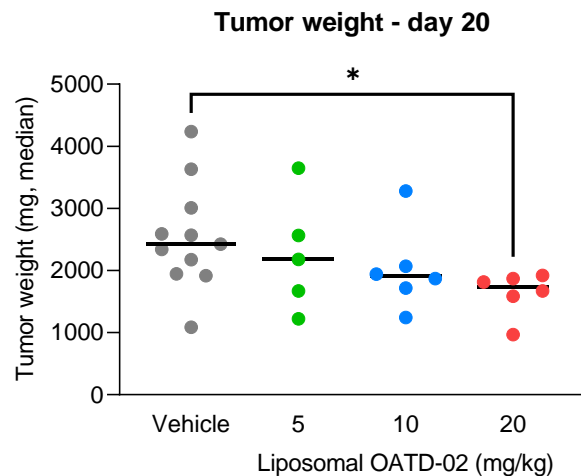
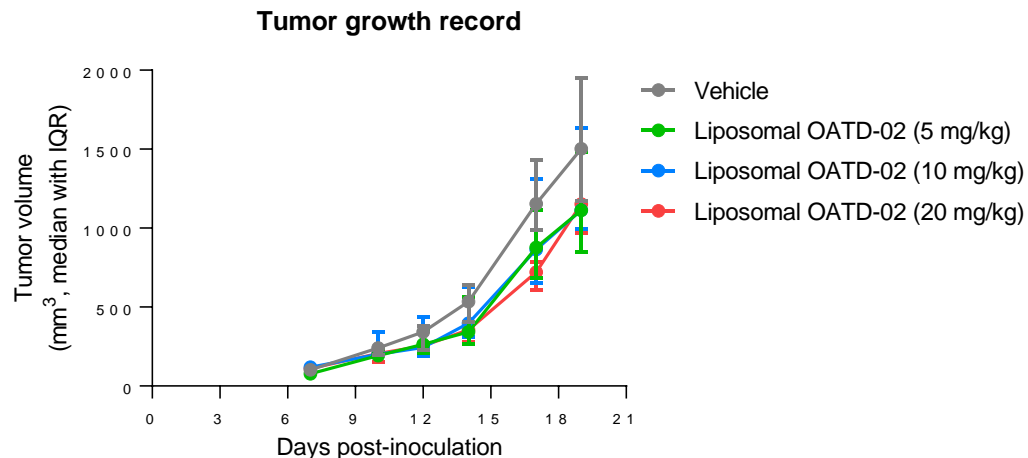


OATD-02 dosed at 50 mg/kg (po, bid from day 1)  
Epacadostat dosed at 30 mg/kg (po, bid from day 1)  
Anti-PD-L1 dosed at 2.5 mg/kg (ip, qd, days 8, 10, 12, 14 & 16)

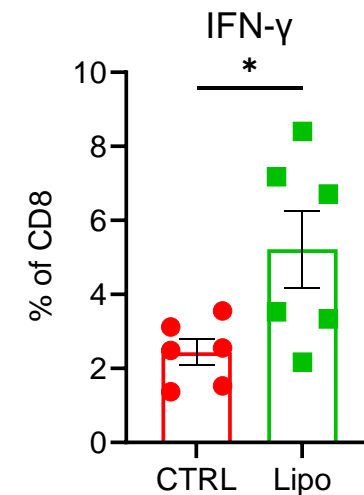
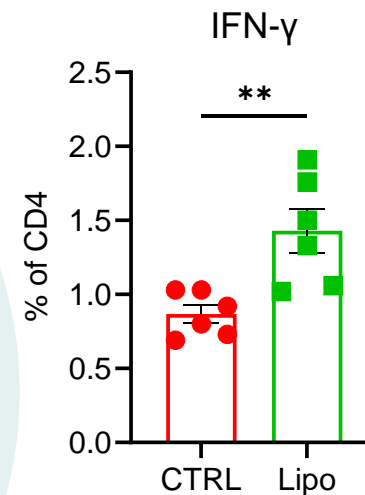
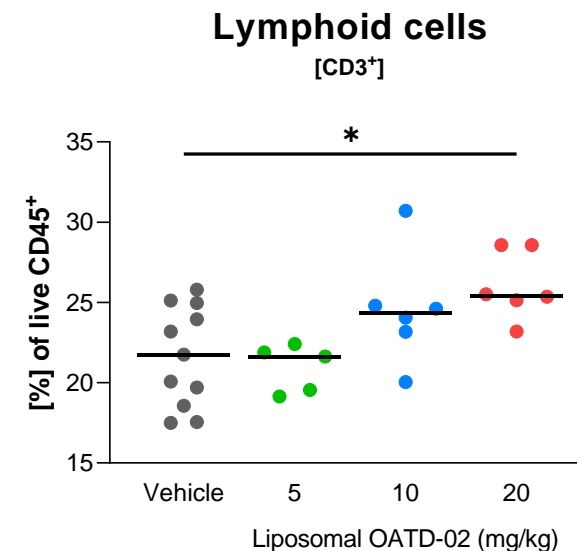


# Liposomal formulation as an effective vehicle for drug administration

Reduced tumor growth



Enhanced immune response against tumor



# OATD-02 on-track to enter the clinic in 2022 – Phase I/II

## Potential best-in-class profile:

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

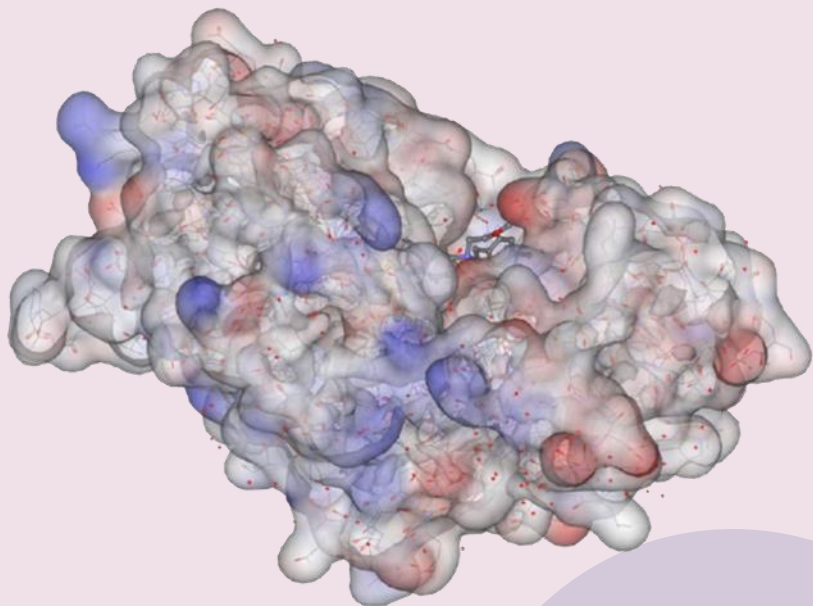
## CTA submission package in finalisation with filing expected Q3 2022

- ADME, Genotoxicity, 14d MTD and 4wk GLP tox in two species
- NOAEL (No-observed-adverse-effect Level) determined
- Efficacy in monotherapy and in combinations validated in multiple tumor models



\*CTA – Clinical Trial Application  
\*FPFV – First Patient First Visit  
\*LPLV – Last Patient Last Visit  
\*CSR – Clinical Study Report

# YKL-40 binders



## Status

- Advanced lead stage
- Selective YKL-40 binder
- Favourable pharmacokinetic profile and positive initial data in a cancer model
- No significant off-target activity

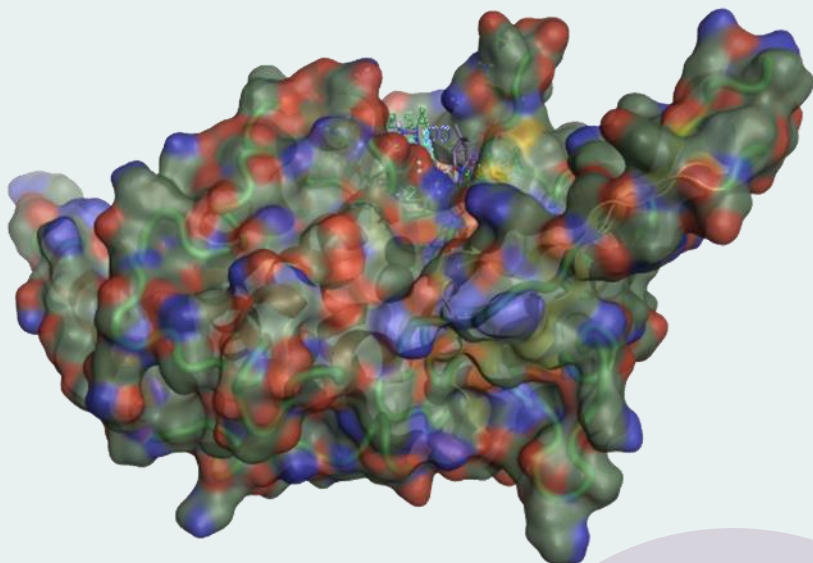
## Research Focus in 2022

- *In vivo* efficacy for the lead YKL-40 binder
- Reveal the mechanism of action of YKL40 and its binder through a number of in vitro studies
- Scientific collaborations with the International Institute of Molecular Mechanisms and Machines (IMOL) and **University Medical Center Hamburg-Eppendorf** to achieve these goals in a timely manner

## Timeline & Milestones

- *In vivo* efficacy confirmation by Q4 2022
- Development candidate nomination by Q1 2023
- IND submission by Q4 2024

# USP-7



## Status

- Lead optimization stage
- Active and selective USP-7 inhibitor OAT-4828
- USP-7 inhibitor shows *in vitro* immunomodulatory properties, specially for lymphocytes

## Research Focus in 2022

- Improvement of the PK profile in order to have predictable level of inhibition of biological target *in vivo*
- Start *in vivo* validation of our lead USP-7 inhibitor as a tool compound

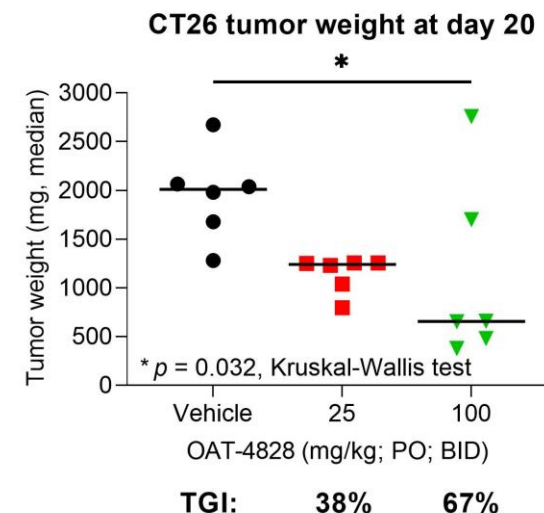
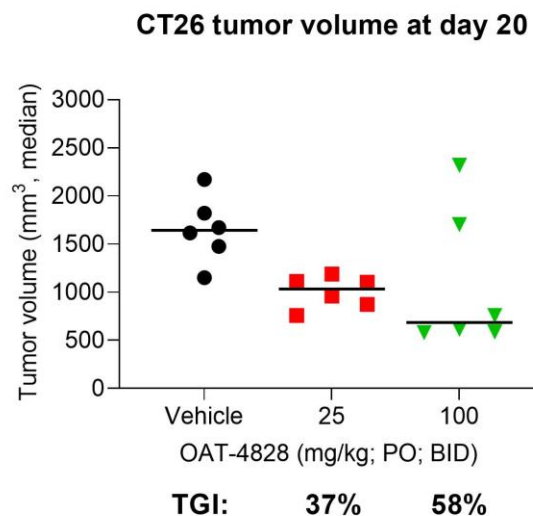
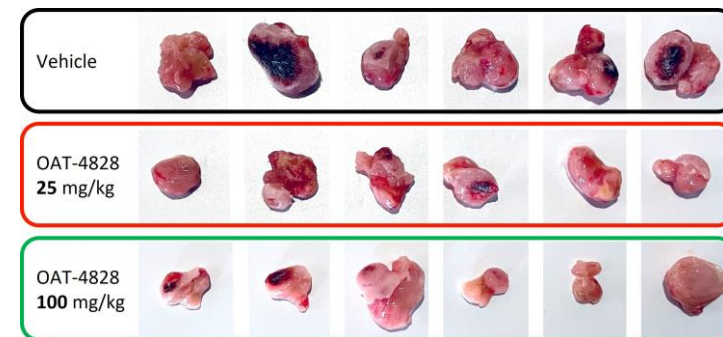
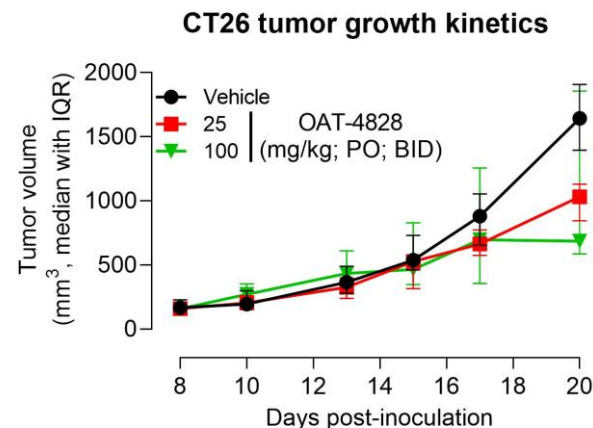
## Timeline & Milestones

- *In vivo* efficacy confirmed in Q2 2022 (6 m ahead of time)
- Development candidate nomination by Q2 2023
- IND submission by end of 2024

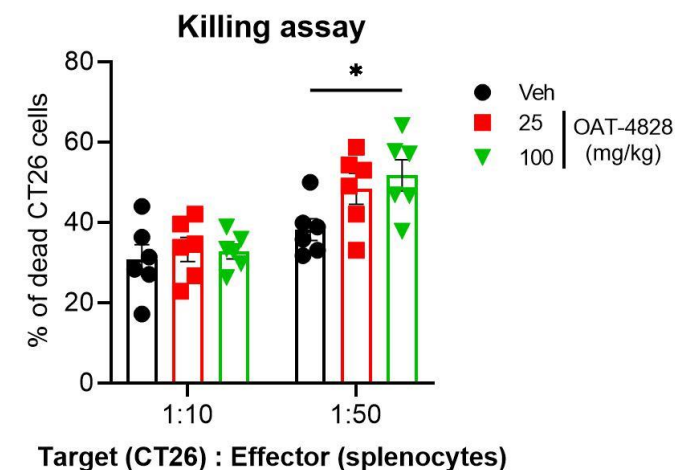
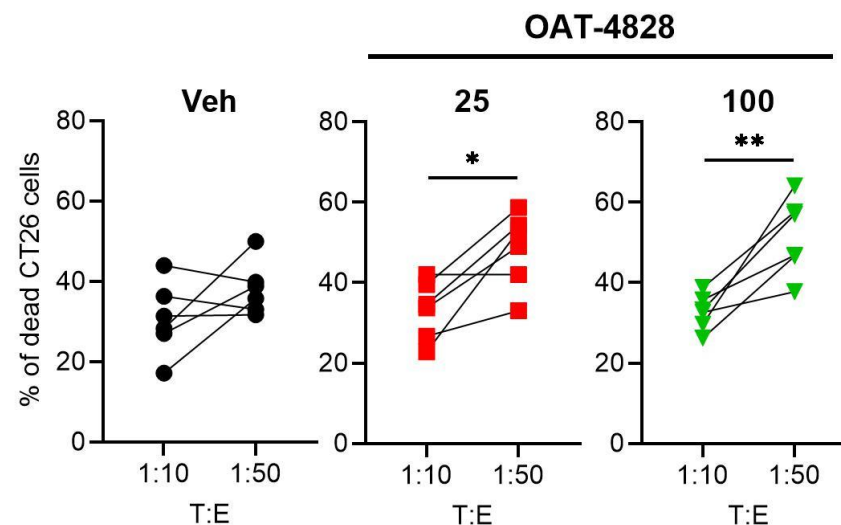
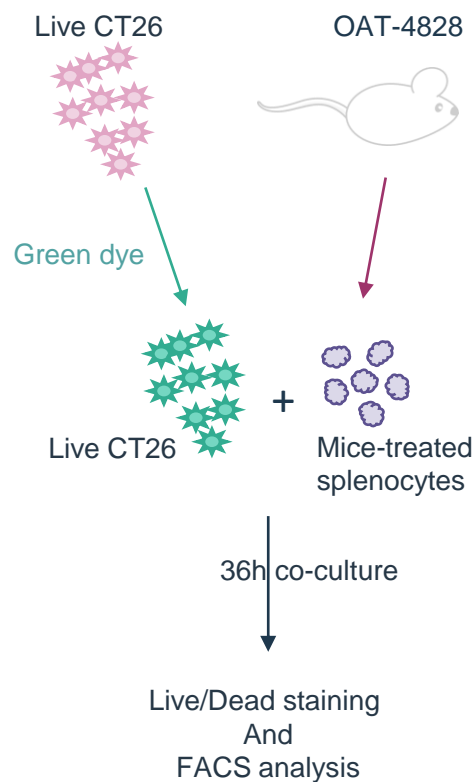


# Significant tumor size reduction in CT26 model after OAT-4828 treatment

When administered in BALB/c mice bearing CT26 tumors, for 20 days at doses of 25 or 100 mg/kg PO, BID, OAT-4828 exerts an anti-tumor effect of up to 67% reduction in weight. Tumors are smaller, lighter and less necrotic

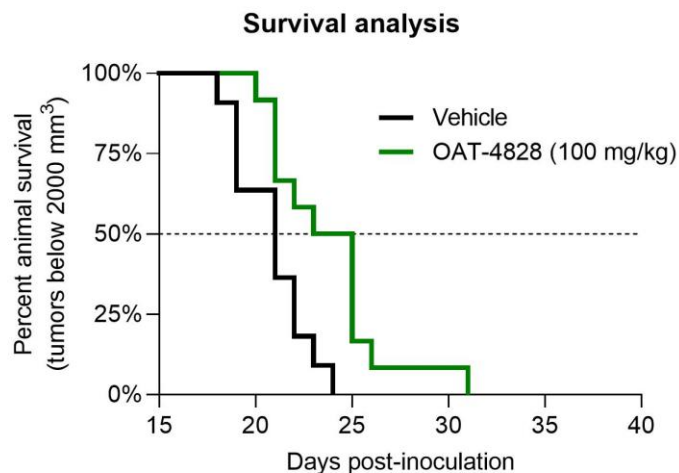


# Increased killing of CT26 cells by effector cells from OAT-4828 treated mice

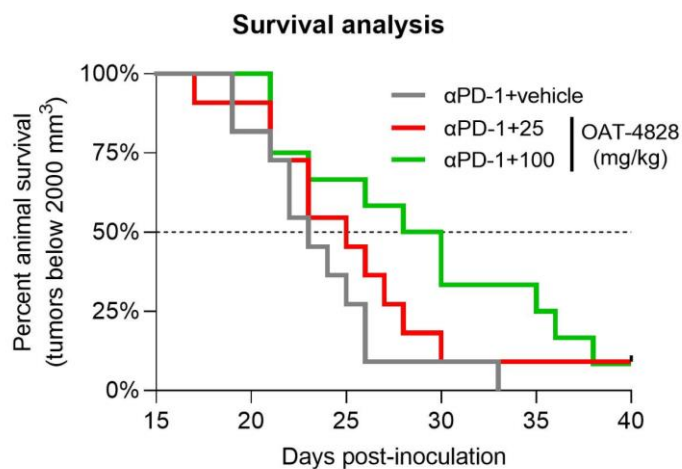
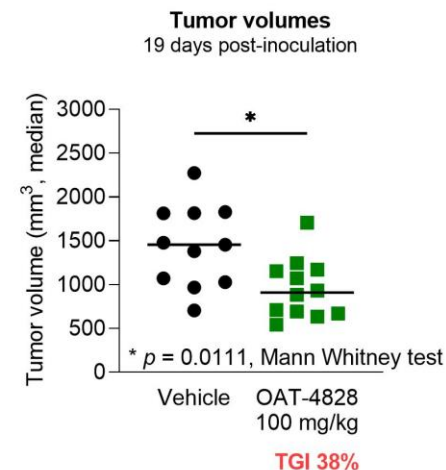


Effector cells isolated from the spleen of mice treated with OAT-4828 for 20 days bear the potential to induce cell death ex vivo, in fresh CT26 cells in the absence of other treatment

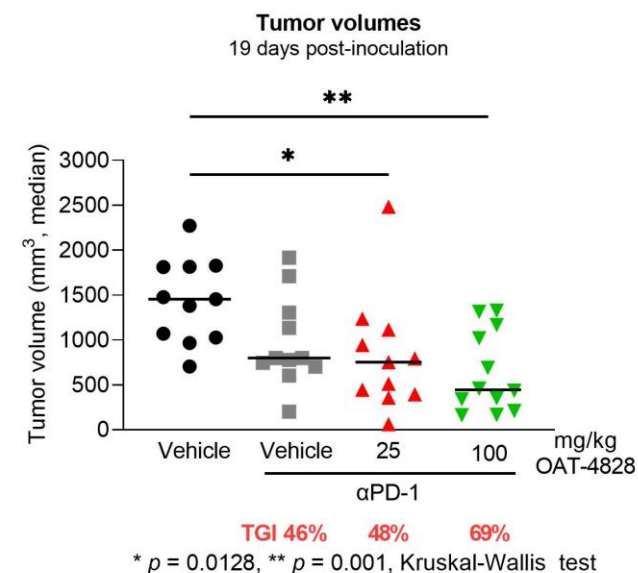
# OAT-4828 increases survival and augments the effects of a mouse anti-PD-1 antibody in a CT26 colorectal carcinoma cancer model



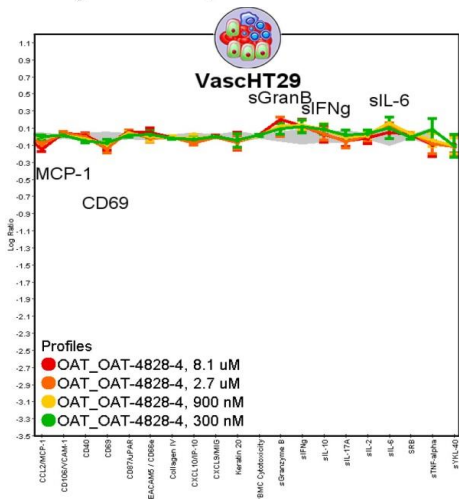
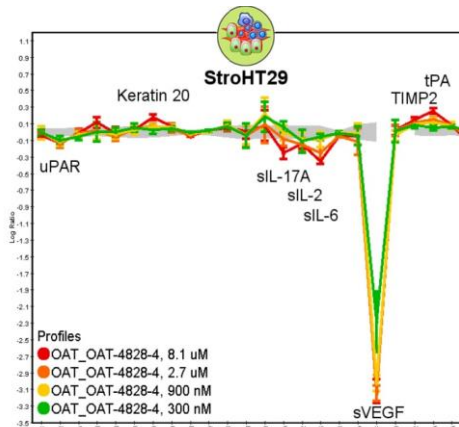
Monotherapy



Combination



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



To validate translational potential of the results we tested OAT-4828 in human co-culture system:

- Human cells (PBMC's, primary fibroblasts or endothelial cells) were cultured with human cancer cell lines representing the tumor microenvironment
- We observed a significant decrease in VEGF. OAT-4828 exerts anti-tumor effect by inhibition of growth of new tumor supplying blood vessels
- We validated an increase in biomarkers such as IFN- $\gamma$  and GzmB demonstrating immunomodulatory properties of OAT-4828 in human systems

IFN-  $\gamma$  – Interferon gamma  
GzmB – Granzym B



# Summary of OAT-4828 anti-tumor effects

Molecure has developed an advanced lead, highly selective small molecule inhibitor of USP7, with drug-like characteristics warranting further development, which:

- Inhibits the growth of CT26 syngeneic colorectal cancer cells in monotherapy and in combination with αPD-1 MAb in a dose dependent fashion.
- Increases number and cytotoxicity of CD8<sup>+</sup> T cells in circulation (spleen) and in tumors
- Increases the secretion of granzyme B and IFN-γ by T cells
- Decreases the TAM-associated markers and increases the pro-inflammatory phenotype of CD4<sup>+</sup> T cells
- Effector cells isolated from OAT-4828-treated animals elicit an effective and direct killing of CT26 cells *ex vivo*

**We have demonstrated OAT-4828 efficacy in colorectal cancer model, elucidated the mechanism of action, which explains in vivo tumor reduction, and we have validated its translational potential.**

# License option agreement



## Status

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

## Research Focus in 2022

- Establishing the screening cascade to identify an advanced lead molecule
- Confirmation of *in vivo* activity of the lead compound
- Improved design of molecules effective *in vivo* within 9-12 months

## Timeline & Milestones

- Decision on option execution expected Sept 2022
- Development candidate nomination by H1 2023
- IND submission by Q4 2024

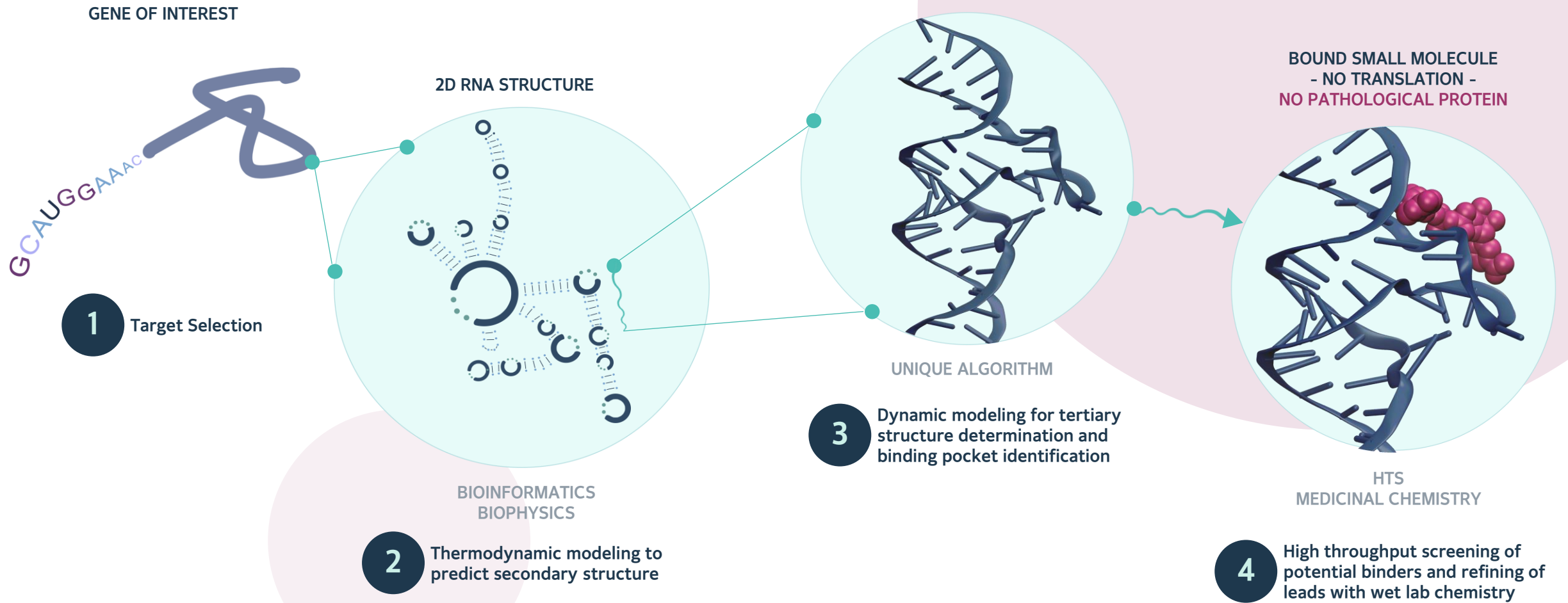
A scientist wearing safety goggles and a lab coat is using a pipette to transfer liquid into a multi-well plate. The background shows various laboratory glassware like beakers and test tubes, all under a blue and purple color scheme.

# Our small molecule mRNA discovery platform

The potential to disrupt mRNA targeting approaches

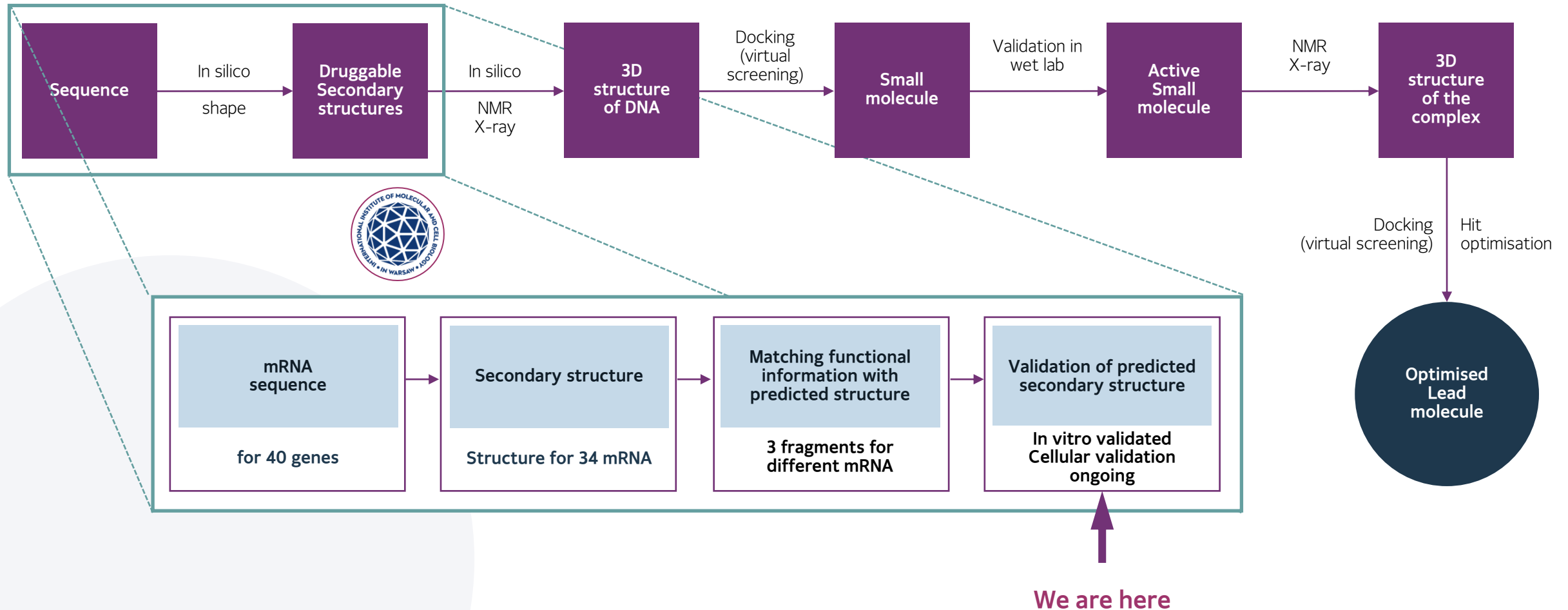
# Molecule - discovering medicines of the future

Small molecules targeting RNA to prevent downstream RNA translation

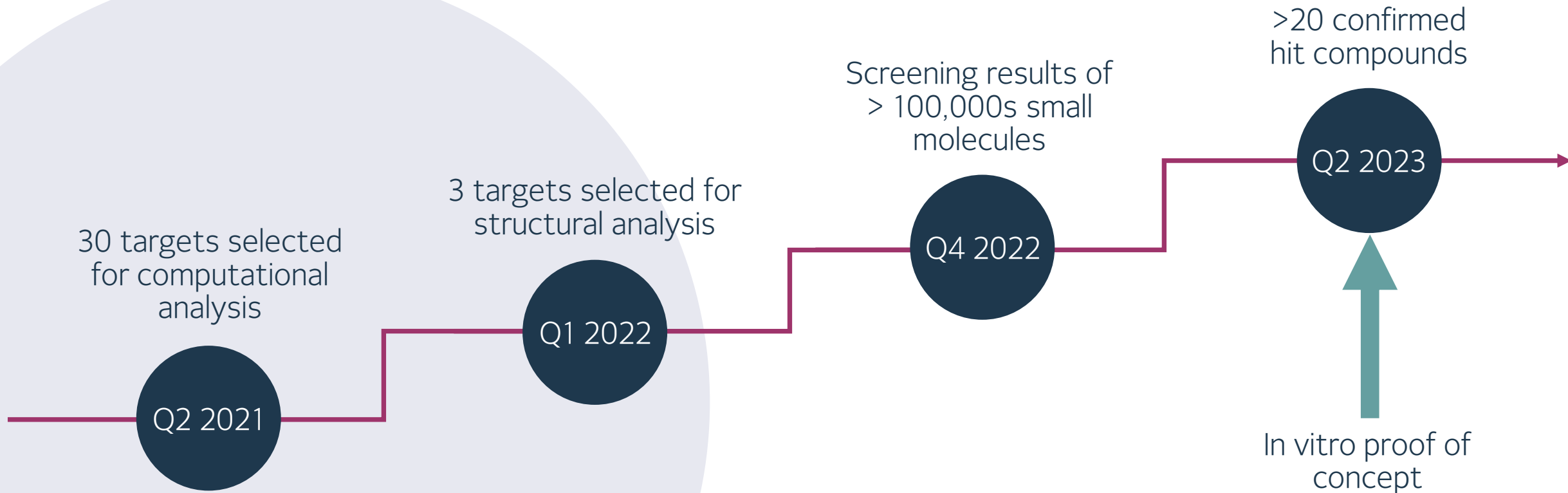




# Our mRNA platform discovery workflow



# Our path to success in discovering RNA targeting small molecules



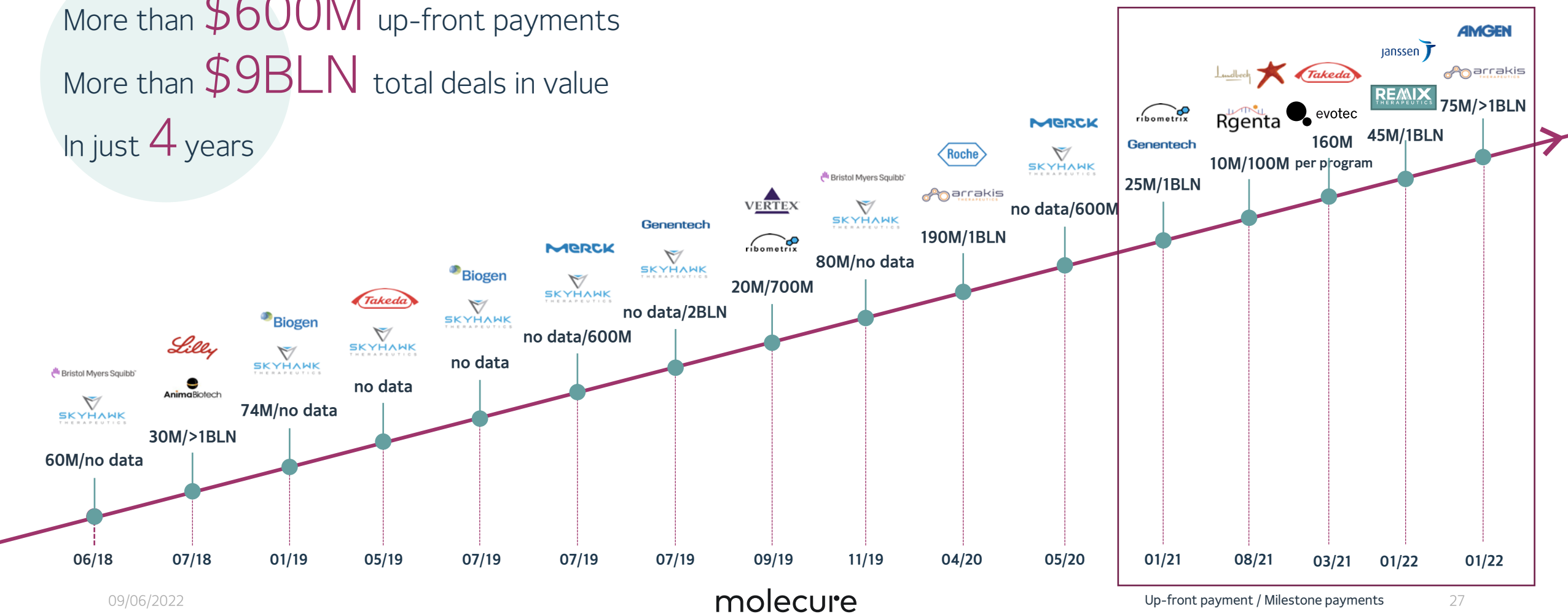
# The RNA space is advancing rapidly

Targeting RNA with small molecules has led to multiple significant biotech / big pharma partnerships

More than **\$600M** up-front payments

More than **\$9BLN** total deals in value

In just **4** years



A background image of a scientist in a white lab coat and safety goggles, using a pipette to transfer liquid into a test tube. The image is overlaid with a semi-transparent blue circle. In the foreground, there are various laboratory glassware including a graduated cylinder, an Erlenmeyer flask, and a rack of test tubes.

# Financials

# Financials update

PLNm	Q1 2021	Q1 2022
Revenue	0.20	0.99
Costs	2.56	4.25
Partnered project costs	1.13	0.48
New started projects	0.00	0.91
EBITDA	-2.41	-3.62
CAPEX	0.03	0.88

R&D spending end of Q1 2022

PLN 6,61M (\$1,5M)\*

of which grants end of Q1 2022

PLN 2,5M (\$0,6M)

Cash position May 2021

>PLN 86M (\$20M)

Financing available until end 2023

## 2021

- 1 clinical program
- 1 preclinical program
- 4 early pipeline programs

## 2022 R&D plans

- Expenditures >PLN 40M
- Including Grants >PLN 16M out of granted 35M

## Next 12 months

- 1 Ph1 (OATD-02) + 1 Ph2 (GLPG4716)
- 1-3 preclinical programs
- 5-7 early pipeline programs

\* Exchange rate based on USD/PLN = 4,29



# ESOP (long-term incentive program) proposal

**The ESOP program is dedicated to:**

- All employees and members of the Management Board of Molecure for the years 2022-2024

**The criteria for awarding Molecure shares are the following:**

- Employment and/or management board membership for at least 6 months
- Achievement of individual KPIs (as in MBO or equivalent) in line with the Company's strategic goals
- Loss of shares in the event of termination of employment and/or function
- New shares will be issued only if MOC stock price increases from baseline

**Principles of acquiring MOC shares in exchange for phantom shares.**

- MOC shares within ESOP are issued after the end of the last incentive period (beginning of 2025)
- Maximum number of ESOP shares to be issued: 400 000
- Shares awarded at the end of the program will be released for trading in portions of 1/3 each year with two year lock-up agreement (each portion of 1/3 shares will be released for trading in 2025, 2026 and 2027).

# Authorized Capital proposal

- Two components of the authorised capital:
  - [i] ESOP authorised capital and
  - [ii] INVESTMENT authorised capital;
- ESOP authorised capital is connected directly to the maximum amount of MOC new shares issued within the ESOP program and will not be available to other shareholders/investors.
- shares issued within INVESTMENT authorized capital will be available to investors (preferably biotech specialist international investors with a long-term perspective).
- This preference is aligned with the Company's long-term strategy of gaining international recognition & exposure.
- The Management Board will have the right to issue shares under the authorised capital under market conditions after the approval of the Supervisory Board.
- Details of the subscription are provided in the published projects of Shareholder's Assembly resolutions.

A background image of a scientist in a white lab coat and safety goggles, using a pipette to transfer liquid into a test tube. The image is overlaid with a semi-transparent blue circle. The text 'Business Development' is written in white, sans-serif font over the left side of the image.

# Business Development

# Business Development at BIO International Convention



The BIO International Convention attracts 10,000+ biotechnology and pharma leaders who come together for one week of intensive networking to discover new opportunities and promising partnerships.

After 3 years, we are back in person for the 2022 International Convention happening in San Diego, CA June 13-16.

Our Focus this year will be on

- Continuing discussions with existing prospects on OATD-02 as well as newly identified prospects in the US and China
- Introducing, for the first time, OAT-4828, our lead asset in the fast-progressing USP7 program
- Raising awareness about our small molecule targeting mRNA platform and demonstrating the uniqueness of our approach

With one week to go before the start, we already have **27 one-on-one meetings** confirmed including some of the top 20 pharma companies as well as specialist biotechs, with more pending confirmation.

Of the prospects we are going to meet, the most well known are the likes of



# DUBs inhibitors development landscape

- Inhibition of deubiquitinases as a therapeutic modality is a relatively recent approach, with the first collaborations dating from 10 years ago.
- The main therapeutic areas of DUB inhibition are **oncology**, **neurology** and **fibrosis**
- Until March this year, there were no relevant inhibitors targeting DUBs that entered clinical trial.
- **Mission Therapeutic** (UK) is the leader in the field, with 3 programs at preclinical stage, and 1 USP30 inhibitor program, MTX652, approved by the US FDA to enter phase I in acute kidney injury.
- Mission Therapeutics also concluded 2 deals at preclinical stage, with Abbvie (2018) and Pfizer (2020)
- **Ubiquigent** (UK) proposes as a fee-for-service or through collaborations, access to DUB profiler, their screening platform with the likes of BMS, LEO Pharma, Dorian therapeutics, FORMA and KSQ therapeutics



# Competitive landscape-USP7 specific

**No USP7 inhibitor has entered clinical development stage yet**

The main, active competitors based on patent searches are:

- **RAPT Therapeutics** – pipeline molecule
- Ubiquigent (in-licensed from Medivir AB)
- Forma Therapeutics
- Servier
- **Hybrigenics** – pipeline molecule
- Almac Discovery
- Shouyao Holdings
- Schrödinger, Inc

# Molecule 3-year goals

## Potential milestones targeted by end of 2024

### RNA Platform

#### 2023

- In vitro PoC reached for at least three high value mRNA targets

#### 2024

- Drug-like molecules (leads) in 2 or more RNA-targeting small molecule programs
- First high-value collaboration / partnership
- Expansion in new therapeutic areas and modalities

### Protein Targets

#### 2023

- Two clinical stage assets administered to patients
- 2-3 candidates in formal preclinical development (internal pipeline + in-licensing)
- Early tolerability and safety data, possible efficacy signals, MTD established for OATD-02

#### 2024

- Preliminary results from the completed phase I study
- New IND preparation and filing

### Financial/Operational

#### 2023

- Significant value assigned to the mRNA-targeting discovery platform

#### 2024

- Significant cumulative revenue from partnering & collaboration agreements
- Dynamic growth: +50% human resources
- Increased international presence and recognition

A background image of a scientist in a white lab coat and safety goggles, using a pipette to transfer liquid into a test tube. The image is overlaid with a semi-transparent blue circle. The text 'Questions & answers' is written in white on the left side of the image.

# Questions & answers

# Glossary

**CTA – Clinical Trial Application**

**FPFV – First Patient First Visit**

**LPLV – Last Patient Last Visit**

**ARG - Arginase**

**MTD – Maximum Tolerated Dose**

**GLP – Good Laboratory Practice**

**IND – Investigational New Drug**

**PBMCs - Peripheral Blood Mononuclear Cells**

**VEGF - Vascular Endothelial Growth Factor**

**IFN $\gamma$  – Interferon gamma**

**GzmB – Granzyme B**

**Anti-PD-L1 - A monoclonal antibody directed against  
programmed cell death-1 ligand 1**

**IPF - Idiopathic Pulmonary Fibrosis**

**NASH - Non-alcoholic steatohepatitis**

**ILDs - Interstitial Lung Diseases**

**CHIT1 – Chitotriosidase**

**DUBs - Deubiquitinases**

**ESOP - Employee Stock Option Plan**

**KPI - Key Performance Indicators**

**MBO - Management by Objectives**

**TGI -Tumor Growth Inhibition**