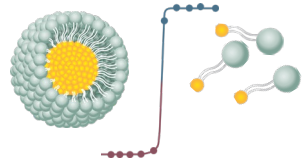
onconano medicine

Company Overview

March 2022

Key Investment Highlights



- Targeted oncology company developing pipeline of assets based on 2 platform technologies – **ON-BOARD™** and **OMNI™** – exploit universal cancer & immune therapeutic targets
  - **ON-BOARD™** is a tumor specific delivery technology with multiple applications
  - **OMNI™** is a polymeric micelle technology for immuno-oncology
- Strategic research collaboration with major pharma to deploy antibodies with OncoNano delivery technology
  - Future capability to monetize the core technology platform with additional strategic collaborations
- Lead internal development program – **pegsitacianine** – currently in Phase 2 with multiple data readouts in ’22
  - Program clinically validates technology platform and manufacture expertise for future therapeutics
- Targeted immune-therapeutics progressing to the clinic
  - **ONM-501**, a dual-activating STING agonist, to enter clinic in 1H’23
  - **ONM-405**, a differentiated IL-2 Fc, on path to enter clinic in 2H‘23
- Multi-year research collaboration with a prominent, world-class UTSW lab to yield future portfolio flow
- $68m+ Series B financing round closed in 2H’21
  - Current cash position finances company into 2H‘24

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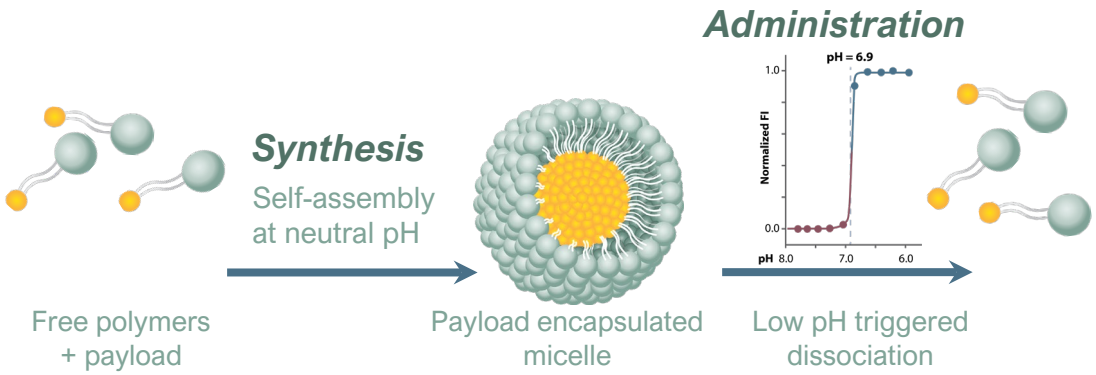
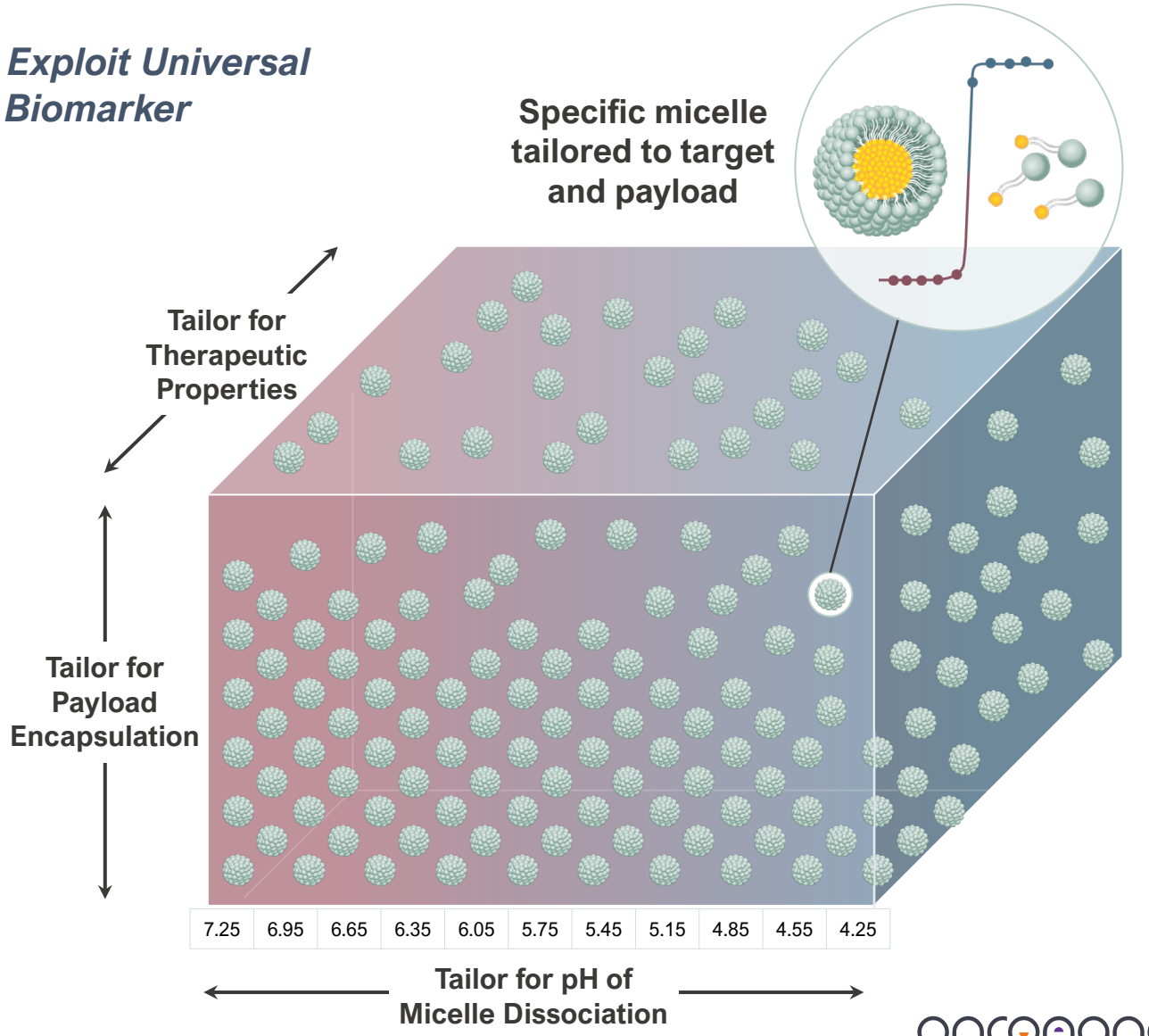
Core Platform Technology – a Library of Differentiated Tunable Polymers

Based on the Principle of Molecular Cooperativity to Exploit Universal Tumor and Immune Targets, including use of pH as a Biomarker

- Polymers form ultra pH-sensitive nanoscale micelles to encapsulate and selectively deliver and release drug payloads
- Payload release follows micelle dissociation in response to pH changes
- Polymers are tailorable to application requirements and target therapeutic properties, including activation of key immune signaling pathways





Xinpeng, Ma.; Zhao, T. et al. J. Am. Chem. Soc., 2014, 136(31), 11085-11092

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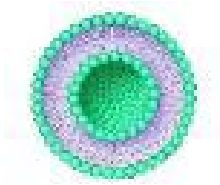
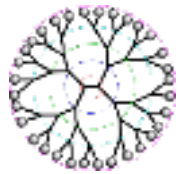
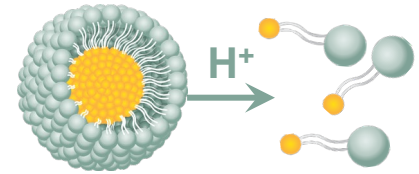
OncoNano's pH-Sensitive Micelle vs. other Nanoparticle Technologies for Oncology Applications



Property	Liposomes	PEG-PLGA/ PEG-PLA	Silica Nanoparticles	Dendrimers	OncoNano's pH-Sensitive Micelle Technology
Tumor Specificity	Low, ligands needed for active targeting	Low, ligands needed for active targeting	Low, ligands needed for active targeting	Low, ligands needed for active targeting	High No ligands needed
Release	Slow	Slow	Structure dependent	Structure dependent	Triggered fast and burst release
Tumor Penetration	Limited	Limited	High dose needed	Size dependent	Rapid micelle dissociation good penetration
Loading/ Payloads	Various	Limited	Limited	Structure dependent	Customizable covalent or noncovalent encapsulation
Clearance/ Toxicity	Liver clearance Acceptable tox	Liver clearance Acceptable tox	Renal clearance Immunotoxicity Possible renal, lung toxicity	Various toxicity	Good safety/tox profile
Manufacturing	Difficult to manufacture uniformly	Difficult to customize	Difficult to customize	Difficult to customize	Highly customizable

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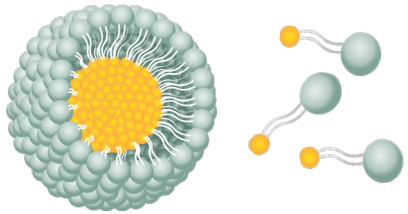
Research & Core Technology Drives Three Pillars of Corporate Strategy



Strategic Opportunities for OncoNano

Therapeutics Pipeline

- **ONM-501**
- **ONM-405**

Research collaborations with Strategic Partners to improve the therapeutic index of oncology payloads

Tumor Imaging

- **Pegsitacianine** – fluorescent nanoprobe for real time surgical imaging
- Targeted investment to validate core technology
- Seek to monetize w/ clinical POC

Pipeline of Differentiated Oncology Assets

Platform	Program	Opportunity	Discovery	Preclinical	Phase 1	Phase 2	Upcoming Milestones
ON-BOARD™ **Tumor specific delivery technology with multiple applications**	Pegsitacianine	Fluorescent nanoprobe for real-time surgical imaging					Phase 2 data readouts expected throughout 2022
	Strategic Research Collaboration	Tumor-specific delivery of antibodies					Non-clinical POC expected 1H'22
	ONM-405	IL-2Fc					IND submission 2H'23
OMNI™ **Polymeric micelles to activate immune response**	ONM-501	Novel dual-activating STING Agonist					IND submission YE'22

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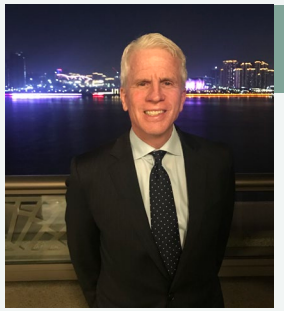
Experienced Private & Public Biopharma Leadership Team



Martin Driscoll
CEO

spring bank pharmaceuticals
Javelin Pharmaceuticals

Matthew Head
CFO

AstraZeneca
ZS Pharma
Alcon
NOVARTIS

Jinming Gao, PhD
CSO, Co-Founder

UTSouthwestern Medical Center

Al Guillem, PhD
Chairman

Rēnibus Therapeutics
Wyeth
ZS Pharma
AstraZeneca
genzyme
Boehringer Ingelheim
Adams Respiratory Therapeutics

Prestigious Scientific Advisory Board

Charles Balch, MD (Chair)

Prof. MD Anderson, Cancer surgery and immunotherapy thought leader, Former CEO ASCO, CEO City of Hope Hospitals, EVP MD Anderson, founding Editor-In-Chief Annals of Surgical Oncology, past President Society of Surgical Oncology

John Niederhuber, MD

Former head, National Cancer Institute; Former head, Department of Surgery at Stanford; Former Director of the Comprehensive Cancer Center at University of Wisconsin

Raphael Pollock, MD, PhD

Director, the Ohio State University Comprehensive Cancer Center; Klotz Chair in Cancer Research; Surgical Oncologist, PhD in immunology

Paul Bunn, MD

James Dudley Chair in Cancer Research at Anschutz Medical Campus at the University of Colorado; Founding Director of the University of Colorado Cancer Center; Previous Chair of the FDA Oncology Drug Advisory Committee

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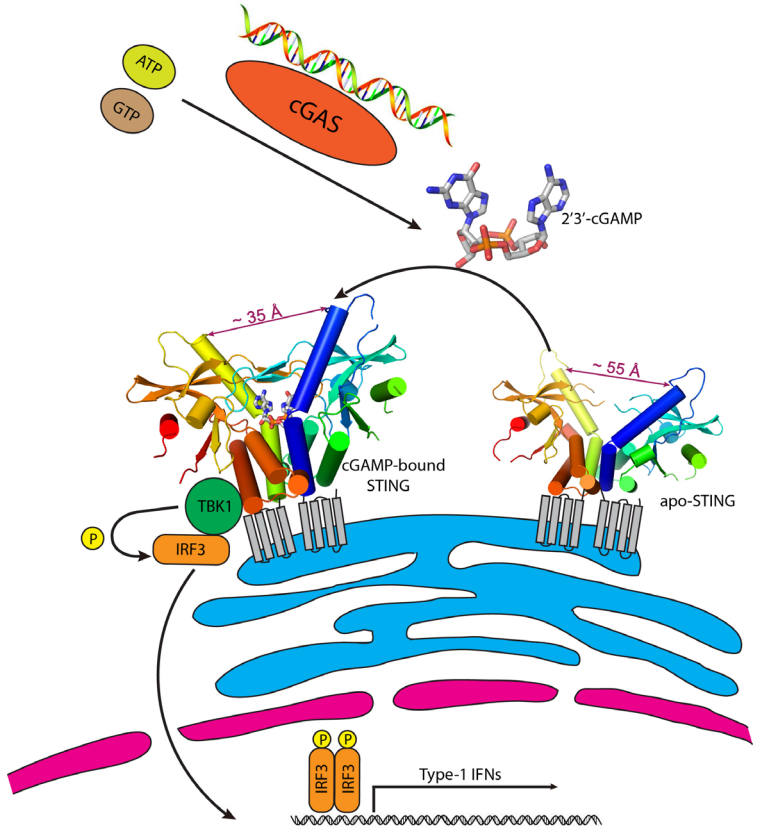
ONMI™: Leveraging STING Pathway for Immune-Oncology Targets

- **Cytosolic DNA is a danger signal**
  - Pathogens or damaged tumor cells shed DNAs into cytoplasm, inducing powerful immune responses
  - Zhijian ‘James’ Chen at UTSW solved the century old mystery
- **Cyclic GMP-AMP synthase (cGAS) is an immune sensor of DNA**
  - cGAS and DNA form polyvalent condensates, facilitating synthesis of cyclic GMP-AMP (cGAMP) as a secondary messenger
  - cGAMP binds and activates STimulator of INterferon Genes (STING), elevating Type I interferons against cancer and infection
- **STING is an essential immune adaptor protein**
  - STING is ubiquitously expressed in most cells including all antigen presenting cells
  - STING activation produces inflammatory agents, turning a tumor from “cold” to “hot” tumor with strong adaptive immune responses
  - STING remains an immuno-oncology target of great interest



Chen et al.
Science, 339, 786 (2013); 339, 826 (2013)

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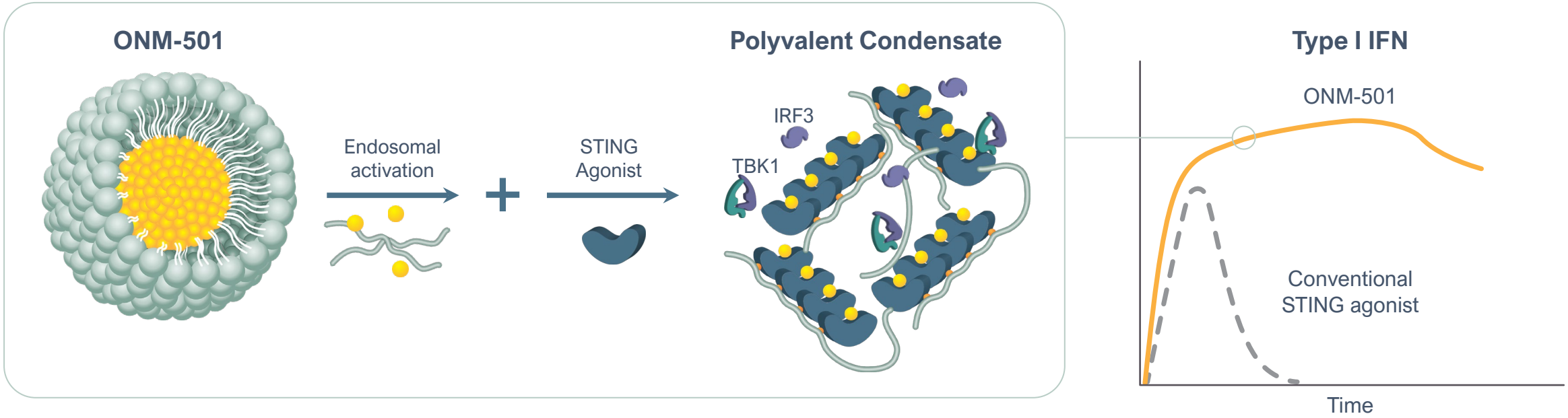
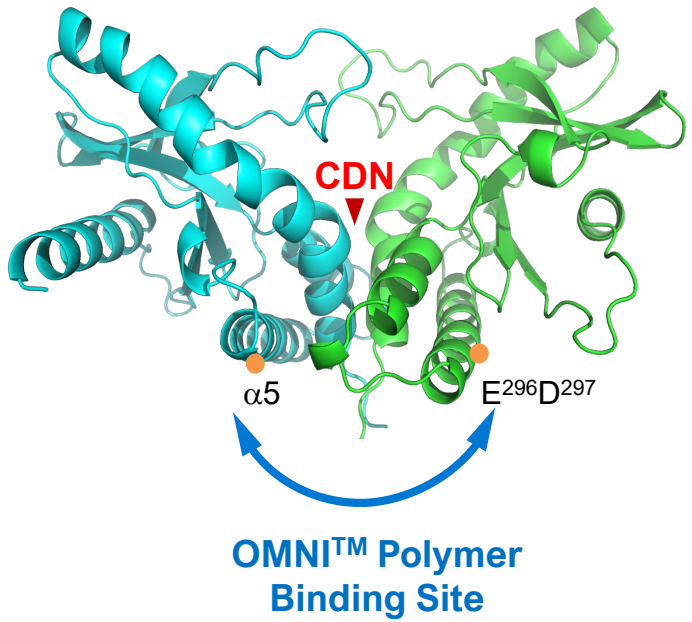
Molecular Cooperativity Enables Tailoring of Polymeric Micelles for Synergistic Activation of STING Leading to T cell Immunity

- Stimulator of Interferon Genes (STING): ubiquitous immune signaling molecule for T cell therapy of solid tumors
- Micelle dissociation releases OMNI™ polymers and endogenous cGAMP
- Non-canonical STING activation via OMNI polyvalency in an unprecedented and advantageous manner synergizes with cGAMP STING activation and leads to Type 1 interferon production and T cell immunity against solid tumors



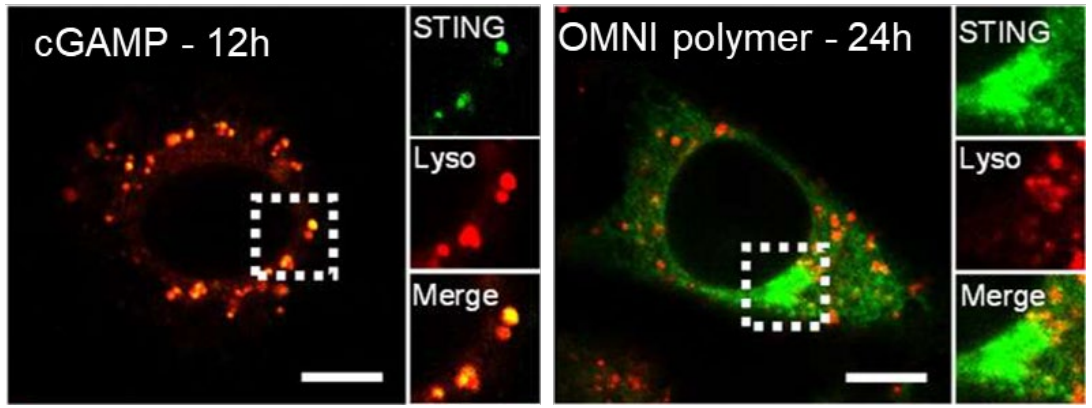
ONM-501 Overcomes the Limitations of Earlier Small Molecule CDN STING Agonists

Challenges w/ Small Molecule STING Agonists	ONM-501 Differentiation
Limited cell entrance to reach cytosolic STING target	**Efficient cytosolic delivery through OMNI™-mediated endosomal disruption**
Lack of cell selectivity – high dose causes T cell ablation	**Selective targeting to antigen presenting cells that activates cDC1 and shifts macrophages toward pro-inflammatory status**
Short-term STING activation with tepid antitumor efficacy	**Dual STING activation with robust antitumor efficacy in a broad set of cancers including immune 'cold' tumors**
Perfusion loss from tumor site results in elevated systemic cytokines and toxicity	**High tumor retention via nanoparticle PK/BD with minimal systemic cytokine elevation**

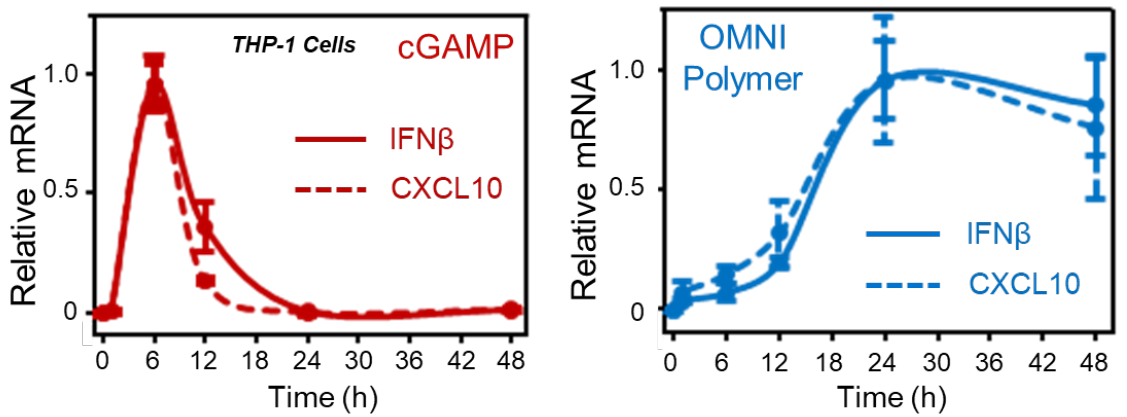


ONM-501: Synergistic Prolonged STING Activation

OMNI™ polymer stabilizes STING protein against degradation



OMNI™ polymer complements cGAMP with prolonged STING activation



- OMNI™ polymer stabilizes STING protein against endosome/lysosome degradation
- cGAMP provides activation for 6-18 hrs; OMNI™ polymers provide activation for 18-48 hrs
- ONM-501 leverages both OMNI™ polymer and cGAMP as STING agonists to provide synergistic prolonged STING activation that facilitates antigen specific T cell generation

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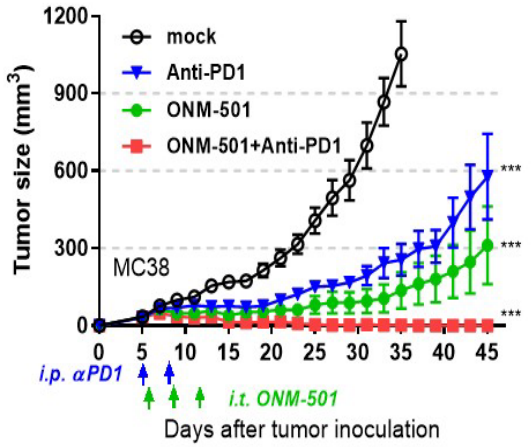
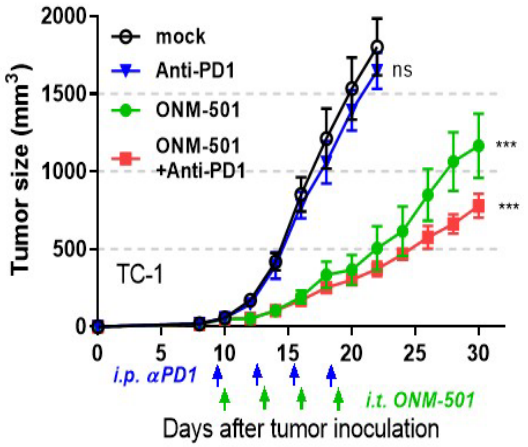
ONM-501 Broad Anti-Tumor Efficacy & Adaptive Immune Trafficking

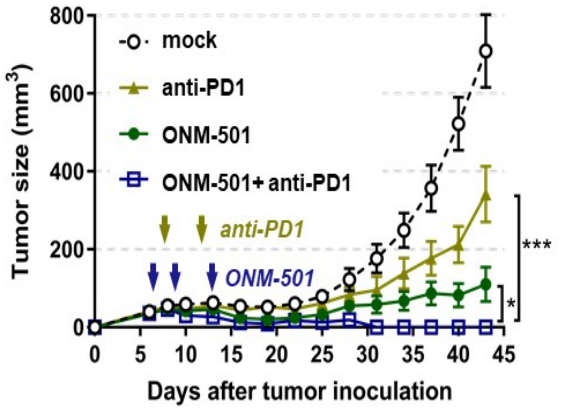
MC-38 Colon

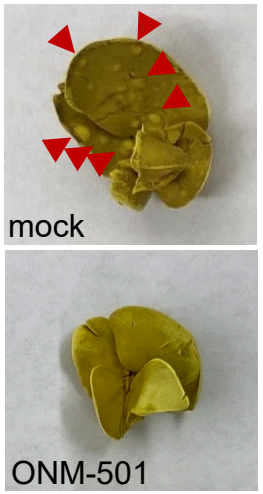


TC-1 Lung



4T1 Breast





ONM-501 + anti-PD1: 100% survival

- ONM-501 – a polyvalent STING agonist differentiated from the earlier CDN STING agonists
  - Dual binding of the target yields an immediate burst & sustained STING activation
  - Maximizes T cell immunity against solid tumors
  - Robust antitumor efficacy in primary, distal and metastatic cancers with long-term memory effect
  - Demonstrated as active against CDN-resistant STING variants

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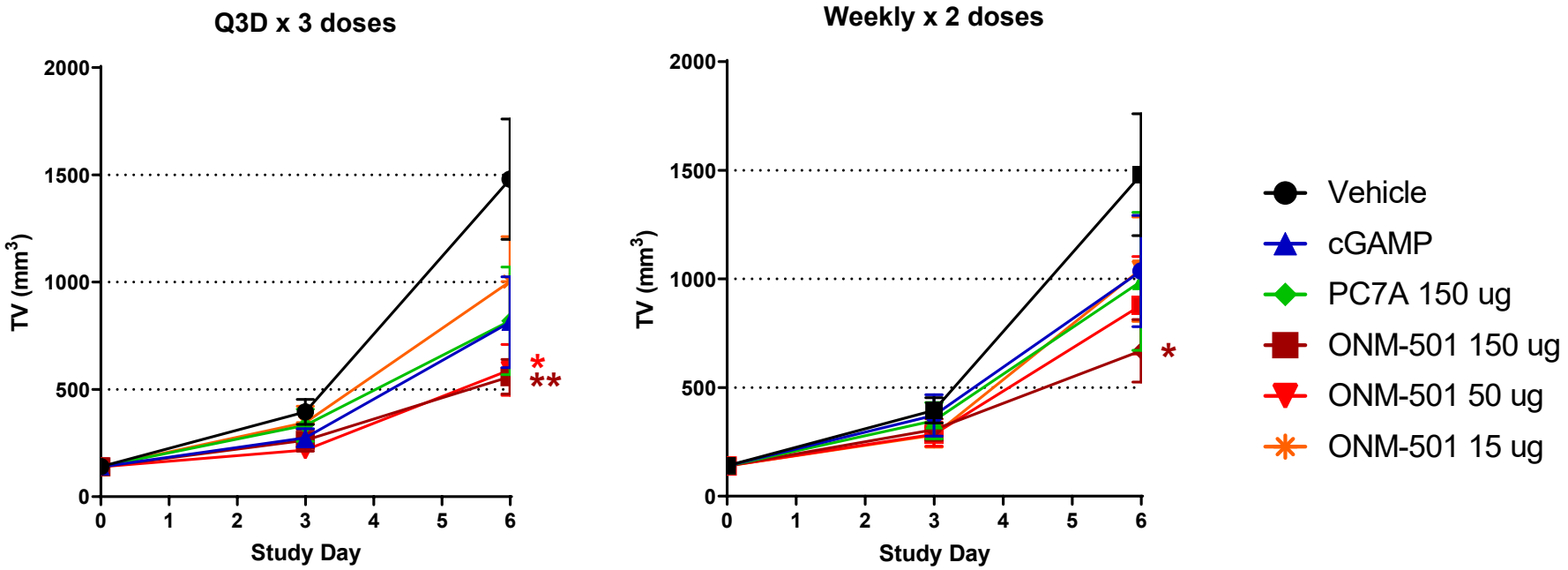
ONM-501 Shows Tumor Growth Inhibition in Large, Aggressive B16F10 Tumor Models



TGI (%) on Day 6

Treatment	Q3D	QW
cGAMP	45	30
PC7A 150µg	45	33
ONM-501 15µg	32	29
ONM-501 50µg	60*	41
ONM-501 150µg	62**	55*

Due to rapid tumor growth and large starting tumors, the study had to be terminated earlier than planned

- ONM-501 showed dose-dependent antitumor activity
- Mid-dose (50µg) and Q3D dosing appear to be the optimal dose/schedule
- TGI consistent with previous study in smaller tumors (~35 mm^3) done at UTSW

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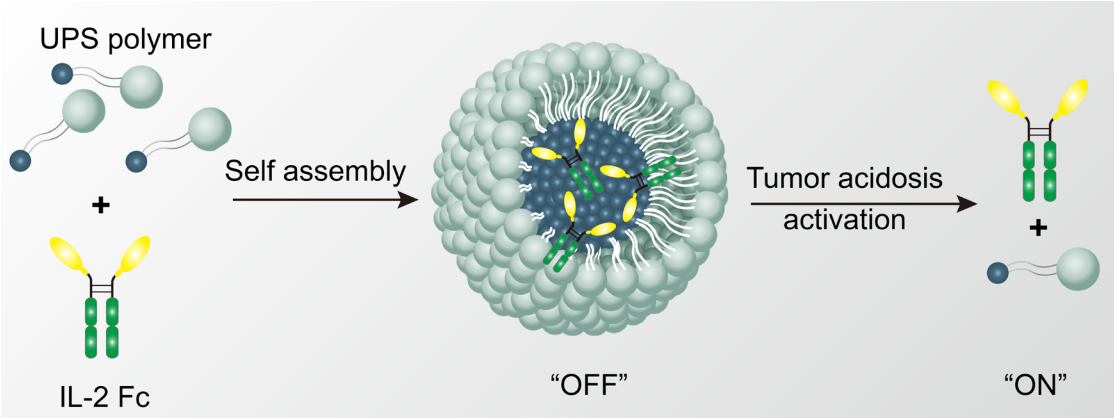
ON-BOARD™ Technology for Increased IL-2Fc Therapeutic Index

- IL-2Fc fusion protein as cytokine payload
- Masked toxicity at neutral pH
- Tumor selective IL-2 activity via pH activation

Key differentiation to other IL-2 programs

- Non-covalent ON/OFF switch
- Increased therapeutic window
- Same polymer as pegsitacianine
  - Already clinical demonstration of tumor activation and safety with pegsitacianine
- Potential for lower COGs as compared to protein engineering approaches



Significant Interest in Novel Technologies to Enhance the IL-2 Therapeutic Index

Merck takes on Lilly/Nektar in IL-2 with $1.85bn Pandion buy

February 25, 2021

Merck & Co/MSD has agreed to buy Pandion for $1.85 billion,

bolting on a pipeline of drugs for autoimmune and other immunological disorders

headed by interleukin-2 (IL-2) based therapy PT-101.

Anaveon to raise CHF 110 million in oversubscribed Series B financing

- Leading international syndicate led by Forbion and corner-stoned by founding investor Syncona
- Confirms depth of support for Anaveon's approach to developing engineered cytokines in multiple indications

Basel, 16 December, 2021 – Anaveon, a clinical-stage immuno-oncology company, today announced that it has agreed a CHF 110 million Series B financing led by incoming investor Forbion, corner-stoned by founding investor Syncona, also joined by existing investor Novartis Venture Fund, as well as new investors, Cowen Healthcare Investments (a division of Cowen Investment Management), Pfizer Ventures and Pontifax. In connection with the Series B financing, Jasper Bos (Forbion), Tim Anderson (Cowen) and Denis Patrick (Pfizer Ventures) will join the Anaveon Board at closing, which is expected before year end.

Anaveon is undertaking a Phase I/II study to evaluate the safety, dosing and clinical activity of its lead program, ANV419, a powerful and selective interleukin-2 (IL-2) agonist in patients with solid tumors. Proceeds from this financing will enable the Company to pursue multiple parallel Phase II programs in order to explore the full therapeutic potential of ANV419. In addition, it will allow Anaveon to continue its work in developing follow-on compounds to expand on the success of ANV419 by delivering the IL-2 agonist to tumor fighting cells and thus expand the therapeutic potential into less immunogenic tumors. Additionally, the Company is building on its cytokine engineering expertise with preclinical-stage programs harnessing the power of cytokines for therapeutic purposes.

Sanofi to acquire Synthorx to bolster its immuno-oncology pipeline for $2.5 Billion

SANOFI

Sanofi to acquire Synthorx to bolster its immuno-oncology pipeline for $2.5 Billion
Proprietary immuno-oncology (IO) platform synergistic with Sanofi's existing therapeutic platforms

- Lead asset THOR-707 ("not-alpha" IL-2) being explored across multiple solid tumor types alone and in combination with immune checkpoint inhibitors and other future IO combinations
- Pre-clinical pipeline for oncology and autoimmune disorders

Asher Bio snags $108M series B for immunotherapy programs, push into the clinic

Asher Biotherapeutics is not the only biotech looking to improve upon the first generation of cytokine immunotherapies hampered by limited efficacy, tolerability and safety issues, but investors have taken note of the selectivity of the startup's cis-targeting platform and are confident enough to dole out **$108 million**.

That series B figure, at an oversubscribed amount, is the same amount hauled in by Synthekine, another company attempting to rewrite the cytokine landscape with an interleukin-2 (IL-2) approach, in June. The two companies have both received cash confidence from Janus Henderson and RA Capital Management.

The proceeds will go toward Asher Bio's three main programs, including lead asset AB248. That lead drug is a cis-targeted IL-2 immunotherapy that activates CD8 effector T cells, which are **critical** to immune defense against intracellular viruses and bacteria and serve a role in surveilling tumors, while not activating regulatory T cells and natural killer cells.

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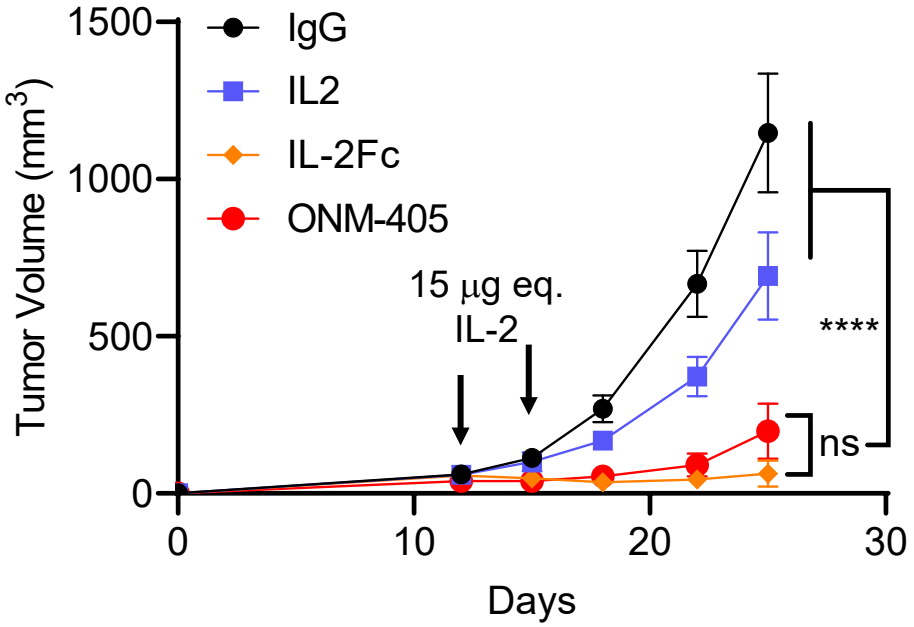
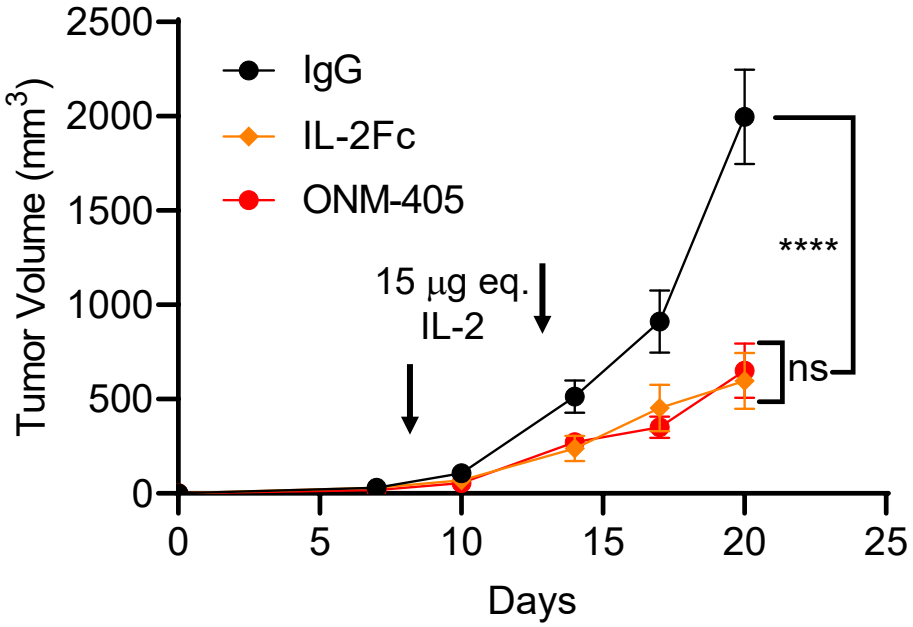
Efficacious Antitumor Immunity in Immune ‘Altered’ and ‘Cold’ Tumors

Immune Altered MC38 tumors



Immune Cold B16F10 tumors



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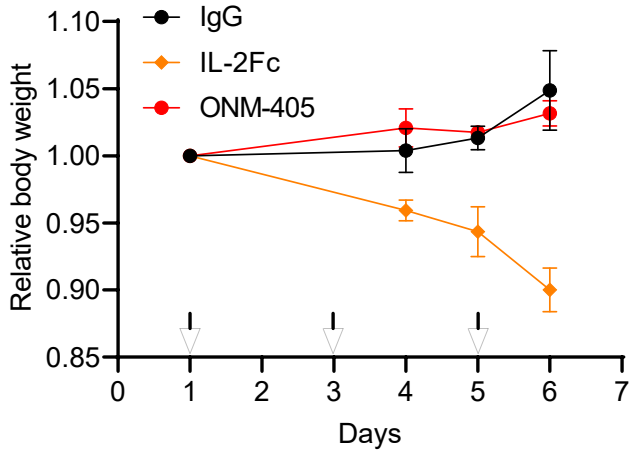
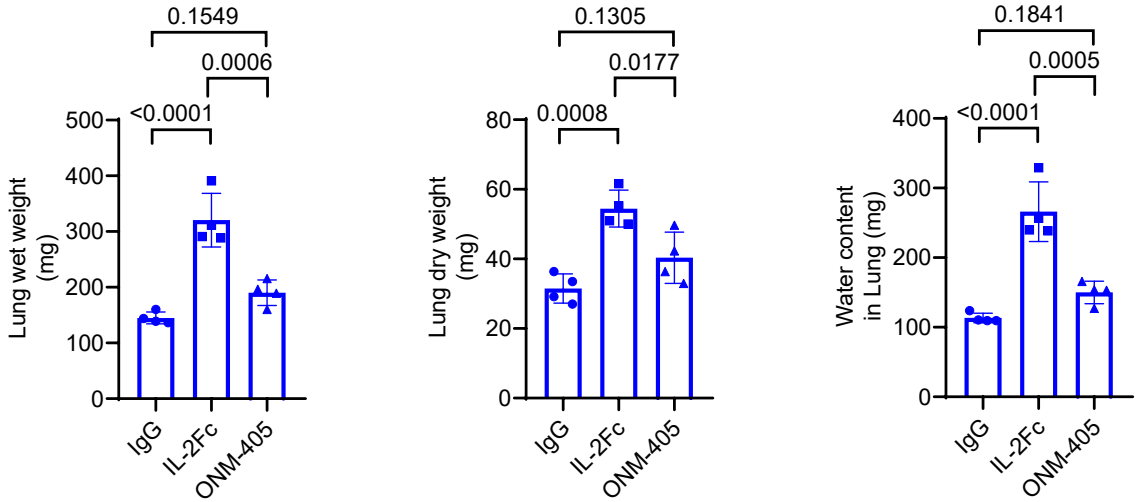
ONM-405 Reduces VLS and Systemic Toxicity over IL-2Fc

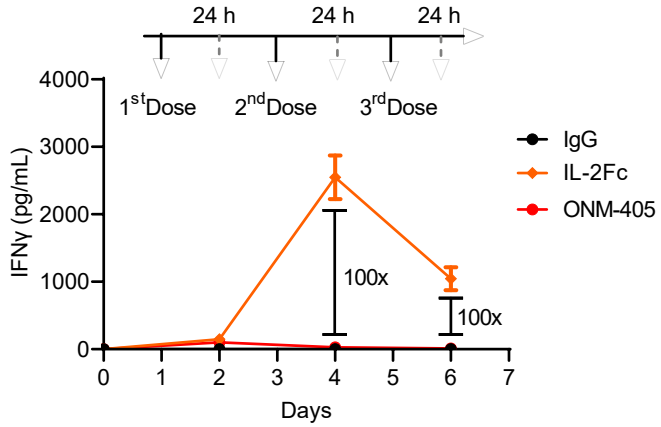
Body weight loss

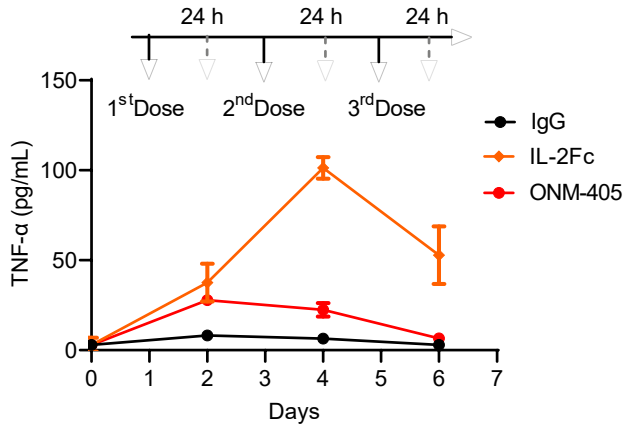


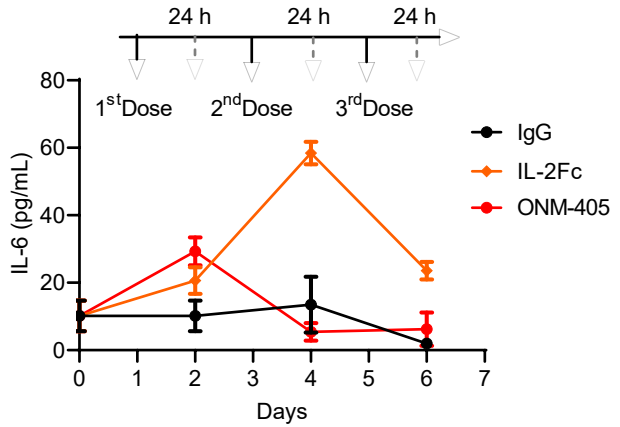
Vascular leakage syndrome (VLS)



Systemic cytokine level



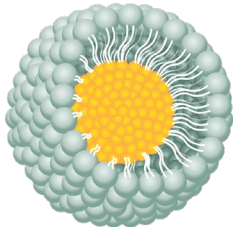


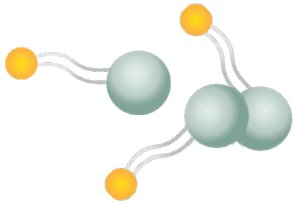


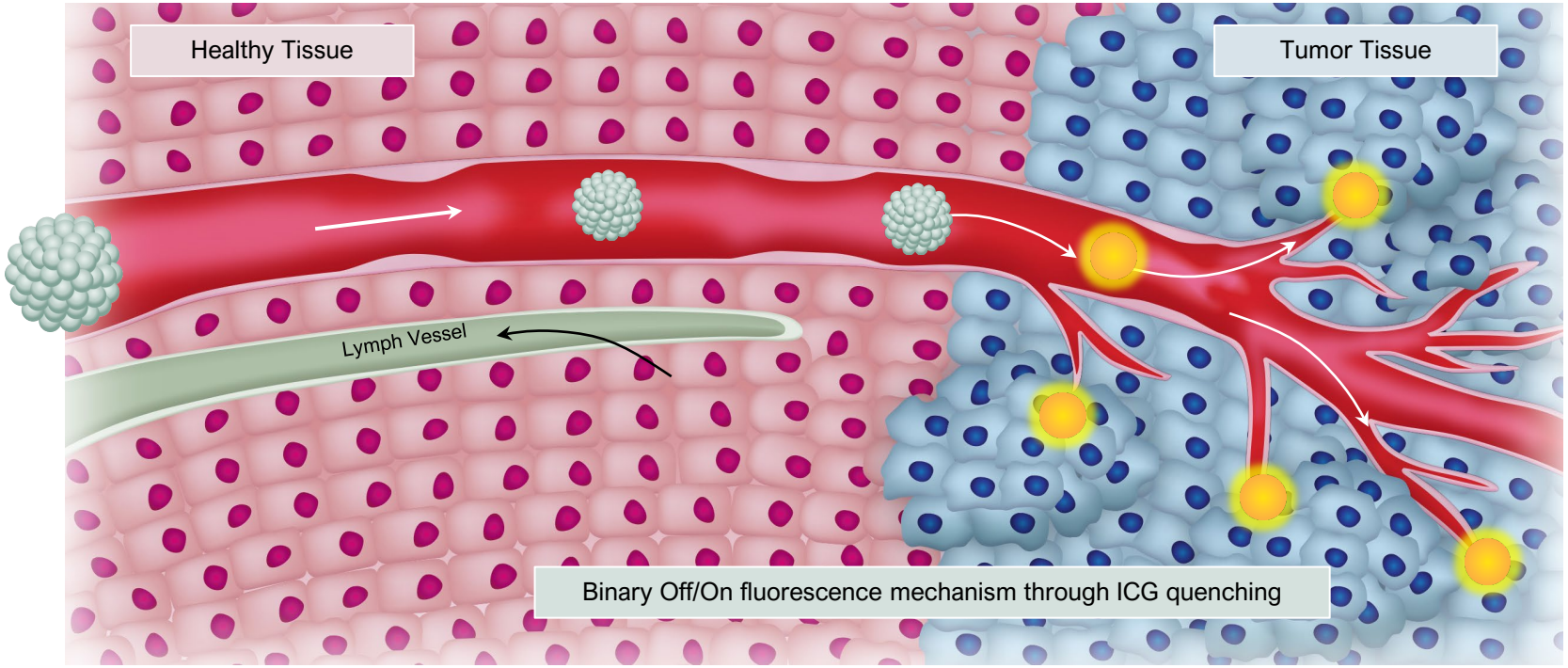
Development of ON-BOARD™ with Fluorophore Payload Validates/De-Risks Mechanism For Tumor Selective Delivery

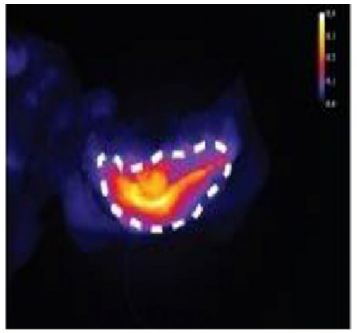
Normal physiological pH | **Acidic Environment**

pH-responsive polymeric micelle encapsulating the fluorophore, indocyanine green (ICG)









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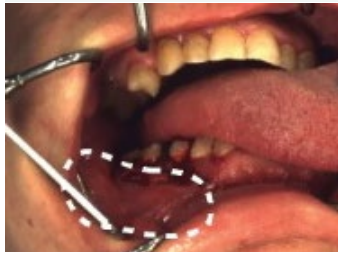
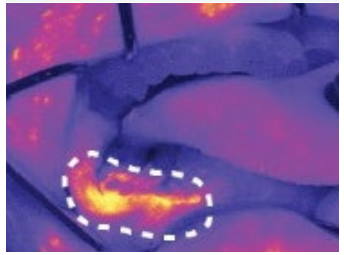
Pegsitacianine – Enhances Tumor Imaging & Provides Technology POC

Intra-operative

White Light



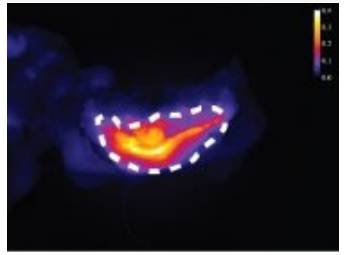
Fluorencence



Ex Vivo

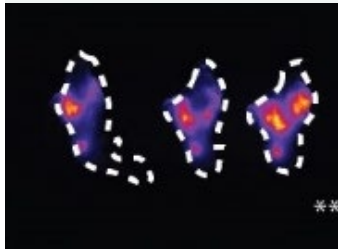
White Light

Fluorescence

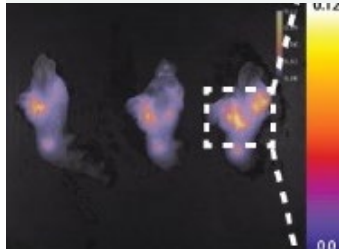


Fresh Tissue Slices

Fluorescence

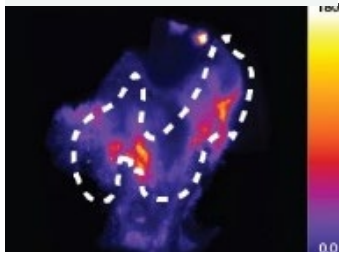


Overlay



FFTPE

Fluorescence



H/E

Imaging Assessments:

Pegsitacianine showed distinct improvements in key measurements of image contrast

- Mean Fluorescence Intensity (MFI)
- Tumor Background Ratio (TBR)

Performance was based on ability to fluoresce primary tumors *in vivo*, determine margin status on the back table, and uncover areas of residual disease within the resection bed.

Pegsitacianine – Phase 2 Results from Head and Neck Cancer

CSE Rate

Number of Patients with a Positive Margin when fluorescence used DURING surgery

0 for 14 (0%) Compared to 17.6% (>28,800 pts)[a]

PPV

Percentage of fluorescing tissue with disease present

63% (83%)

Skewed low: 1 pt with broad dysplasia and inflammation caused 2 false positives

NPV

Percentage of non-fluorescing tissue without disease

100%

Sensitivity

True Positive Rate

100%

Specificity

True Negative Rate

86% (95%)

[a] *JAMA Otolaryngology–Head & Neck Surgery* **2018**, *144*, 1090

N=76 Safety Database across 3 trials

N=44 specimens in Phase 2 study

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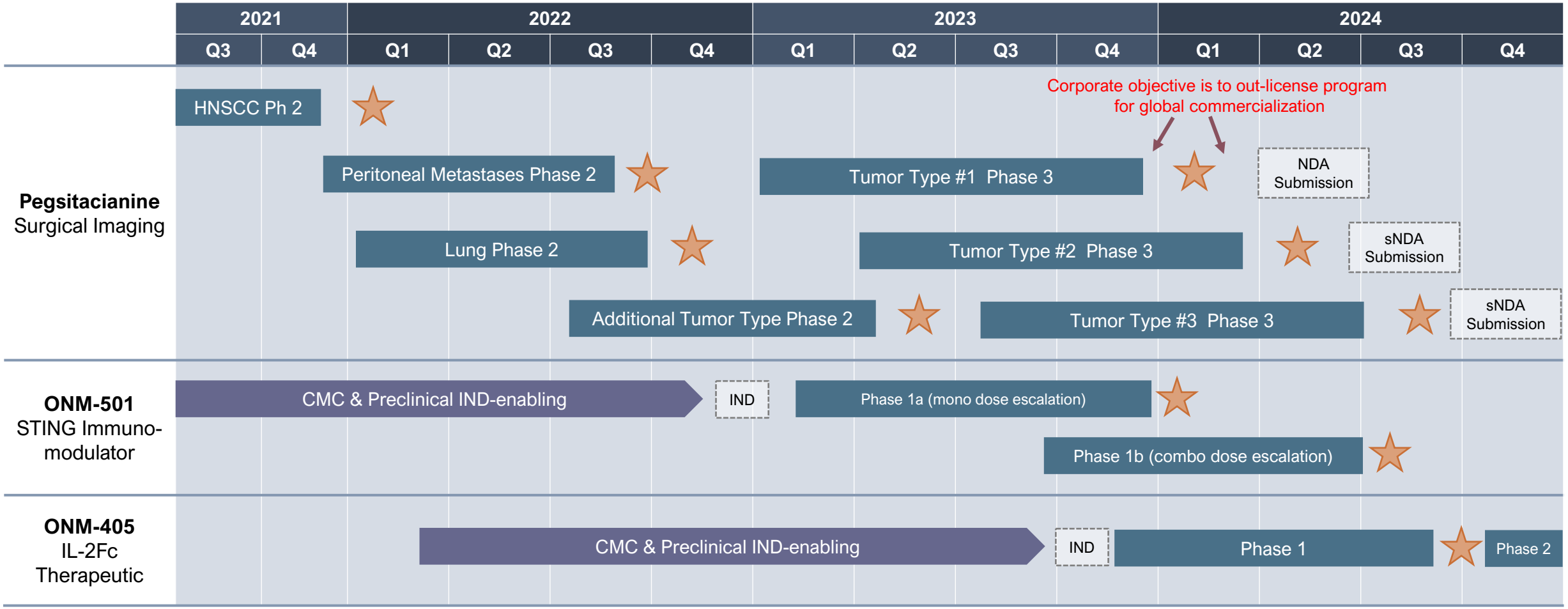
Current Estimates for Key Project Timelines



Clinical data readouts

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Strong Financial Position

- ~$53m Cash Balance
- $68m+ Series B round closed in mid-2021
- Supplemented by ~$7m in available funds from CPRIT grants
- Company currently funded thru 2H'24
- Est. avg. 2022 quarterly burn - ~$3.75m

As of Dec 2021	$ millions
Cash Position	~$53
Undrawn Grants	~$7

Non-Dilutive Funding Awards

Project	CPRIT	SBIR (NIH)
Pegsitacianine	$6.0m (2014) $10.0m (2020)	$1.7m (2017)
OMNI™ ONM-501	$15.4m (2019)	

Lengthy Market Exclusivity with Favorable License Agreements

- Platform technology & first therapeutic program licensed from University of Texas Southwestern Medical Center (UTSW) in Dallas, TX
  - Exclusive global license with full sub-license capability
  - Favorable economic terms with low single-digit royalties
- Multi-year research collaboration with UTSW for future pipeline enrichment

Product/ Platform	IP Coverage Through	Description
Pegsitacianine	2040	• Covers composition, plus use with fluorescent imaging agents • Patents issued in US and OUS, with some jurisdictions pending • Licensed from UTSW
ON-BOARD™	2040	• Covers co-polymer encapsulated therapeutic agents • OncoNano owned IP
ONM-501	2037	• Covers T cell/STING activating cancer therapeutics • Licensed from UTSW

OncoNano Opportunity Summary

- **ON-BOARD™** and **OMNI™** oncology delivery technologies present opportunities for strategic collaborations to monetize the core platform for the company
  - Strategic research collaboration to deploy antibodies expected to yield preclinical POC data in 2022
- Lead development asset – **pegsitacianine** – currently in Phase 2 with multiple data readouts in 2022
  - Anticipated to be “Phase 3 ready” in 2H ‘22
  - Presents clinical validation of core technology platform and demonstration of ability to manufacture future therapeutics
- Two differentiated immune-therapeutics progressing to the clinic
  - **ONM-501,** a differentiated dual-activating STING agonist to enter clinic in 1H’23
  - **ONM-405**, a differentiated IL-2Fc, on path to enter clinic in 2H’23
- Multi-year research collaboration with a prominent, world-class UTSW lab to yield future portfolio flow
- Successful recent financing events provide a solid runway for execution of multiple data generation milestones
  - Current cash position finances company through 2H‘24