Corporate Presentation

Exploiting molecular cooperativity with a platform technology to deliver novel cancer interventions

July 2021

Investment Highlights

- Targeted oncology company developing pipeline of assets based on 2 platform technologies - **ON-BOARD™** and **OMNI™** - exploits universal cancer & immune therapeutic targets
  - ON-BOARD™ is a tumor specific delivery technology with multiple applications
  - OMNI™ is a polymeric micelle technology with potential in Immuno-oncology
- Lead asset – **Pegsitacianine** - currently in Phase 2, with data anticipated in 4Q'21
- Second asset – **ONM-501** – to enter clinic in 2H'22
- Two meaningful strategic research collaborations already in place, with potential for additional future partnerships
- Recently completed $50m Series B round with key investors
- June cash position of $46.2 million plus additional $23.8 million in undrawn grants support strategic plans through 2023
- Seasoned leadership team with experience leading publicly traded biopharma companies, executing successful M&A transactions, and transforming companies through business development

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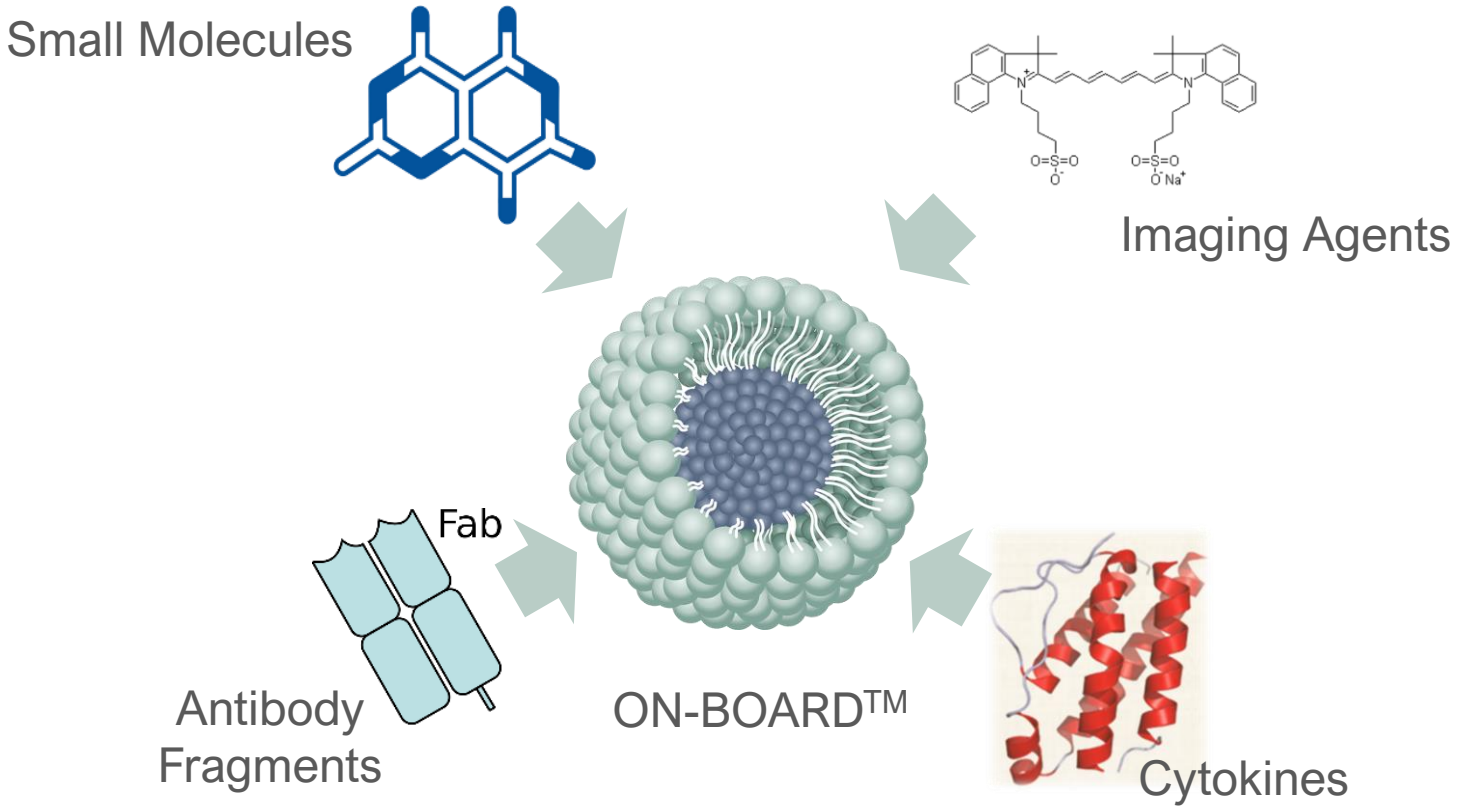
OncoNano Proprietary Delivery Technology

Exploiting molecular cooperativity for surgical imaging and cancer immunotherapy

Library of tunable polymeric micelles that encapsulate a payload and deliver to the tumor microenvironment

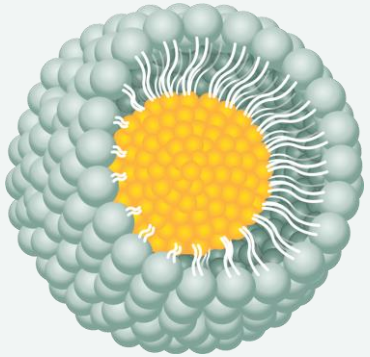


ON-BOARD™ Platform Technology

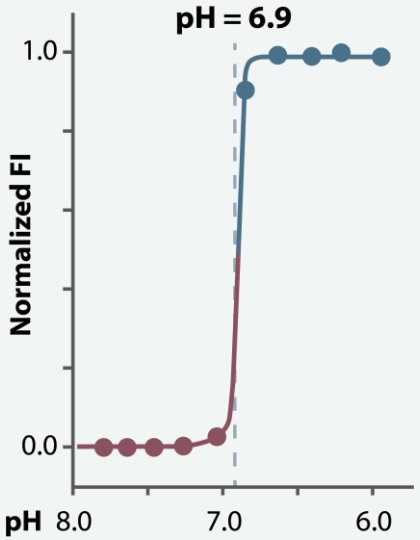
Ultra pH-Sensitive Polymer-Based Micelles Leveraging the Warburg Effect

Micelle intact

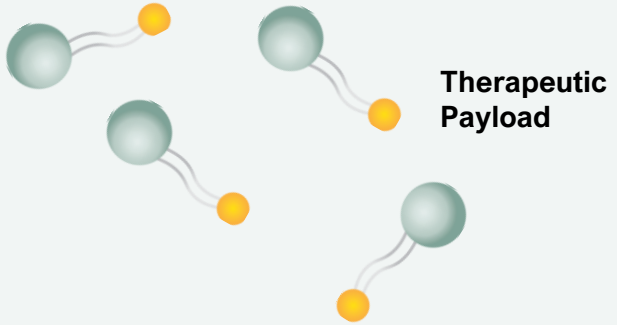
Micelles shield a payload until reaching the tumor microenvironment



Ultra-sharp pH Response



Micelle dissociates



Micelles dissociate in the acidic environment of the tumor and allows for delivery of cancer interventions

Micelles Respond to pH Environment allowing for for use in a broad range of tumors to deliver imaging systems or therapeutic payloads

Zhao, T. et al. Nat Biomed Eng., 2016, 1:0006, 14

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Pipeline of Differentiated 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 Q4 2021 and 1Q 2022
	Research Collaboration 1	Tumor-specific delivery of an antibody					Non-clinical POC data expected Q4 2021
	Research Collaboration 2	Tumor-specific delivery of a small molecule					Non-clinical POC data expected 1Q 2022
	ONM-400	Therapeutic antibody payload for oncology					Payload announced 2H 2021
***OMNI*™** **Polymeric micelles to activate immune response**	ONM-501	Novel dual-activating STING Agonist					IND submission 2H 2022

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Pegsitacianine: Addressing Unmet Needs in Cancer Surgery

Current practice today

preoperative scans

visualization during surgery

palpation

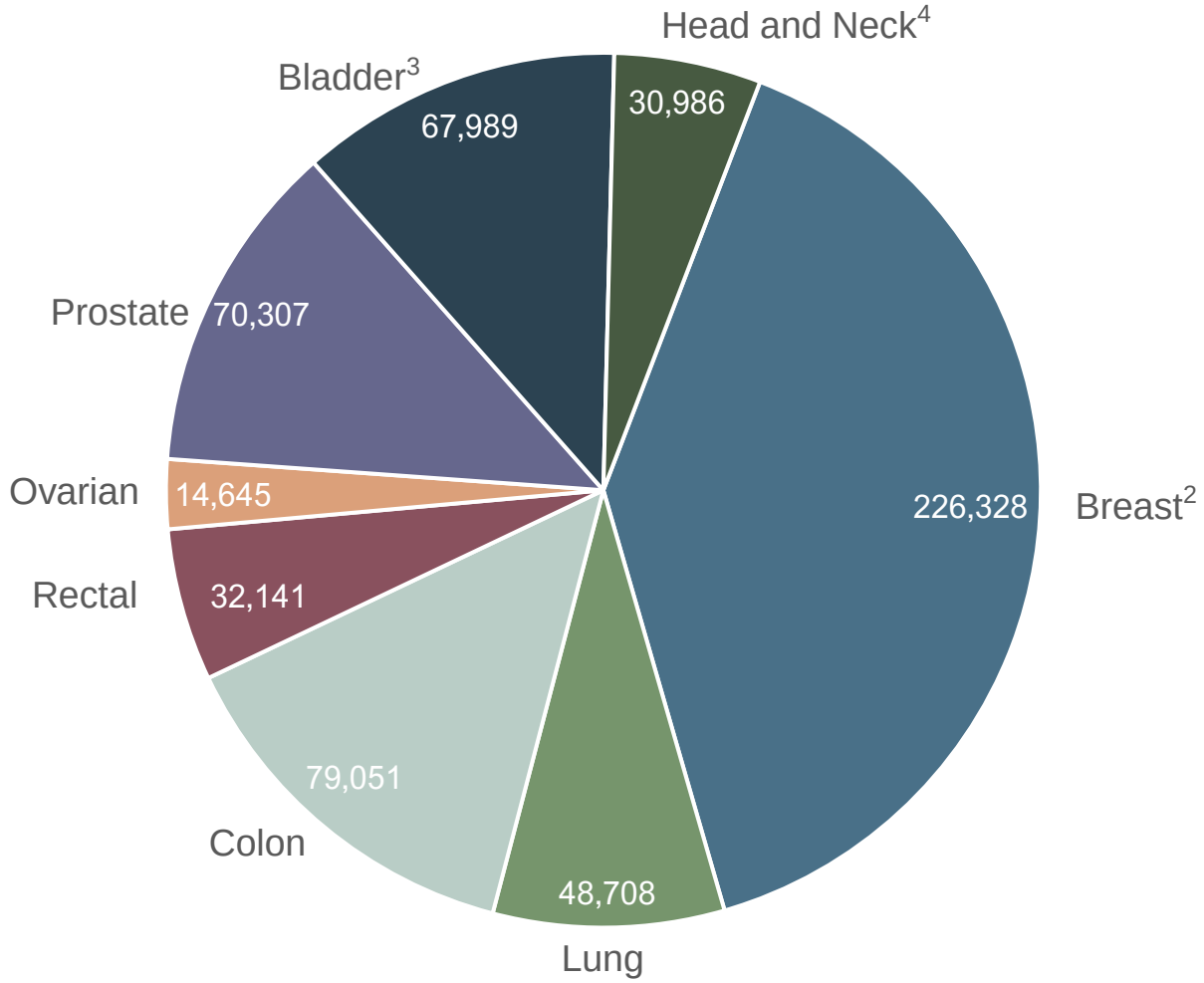
pathology review

Inability to adequately visualize or palpate tumors during surgery risks leaving behind disease

- HNSCC recurrence rates range from 15-50% in published literature
- 20-30% of patients with recurrence are candidates for repeat surgery
- Costs of additional therapy (radiation, chemotherapy, etc.)
- High morbidity with recurrence despite “curative” resection

Image-Guided Surgery: A Significant Market Opportunity

Estimated number of procedures >500K in the US Alone



[1]2016 data published June 2019, Miller et al, (2019); [2]Breast cancer estimate includes breast conserving surgery (n=115,208) and mastectomy (n=111,120) ; [3]Bladder cancer estimate includes cystectomy (n=7,693) and TURBT surgery (n=60.296); [4]Oropharynx and oral cavity cancers only.

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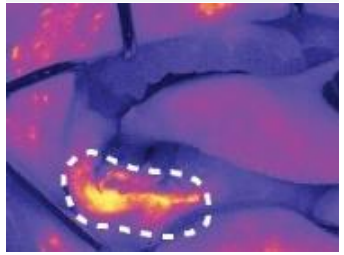
Pegsitacianine – Enhances Tumor Imaging

Intra-operative

White Light

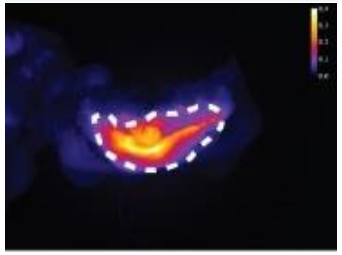
Fluorencence



Ex Vivo

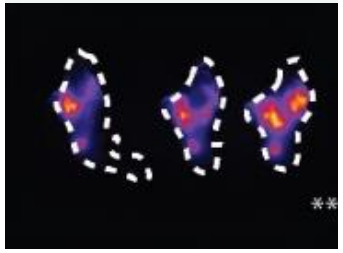
White Light

Fluorencence

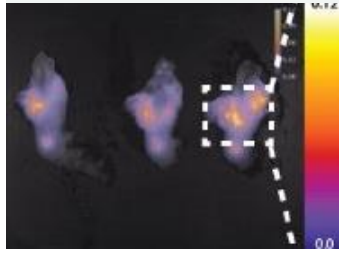


Fresh Tissue Slices

Fluorencence

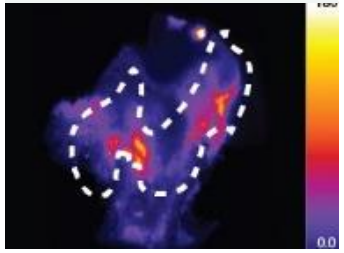


Overlay



FFTPE

Fluorencence



H/E

Imaging Assessments:

Pegsitacianine showed distinct improvements 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.

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Pegsitacianine: 3-Part Phase 2 Trial

UT Southwestern Medical Center, MD Anderson Cancer Center, & UPenn

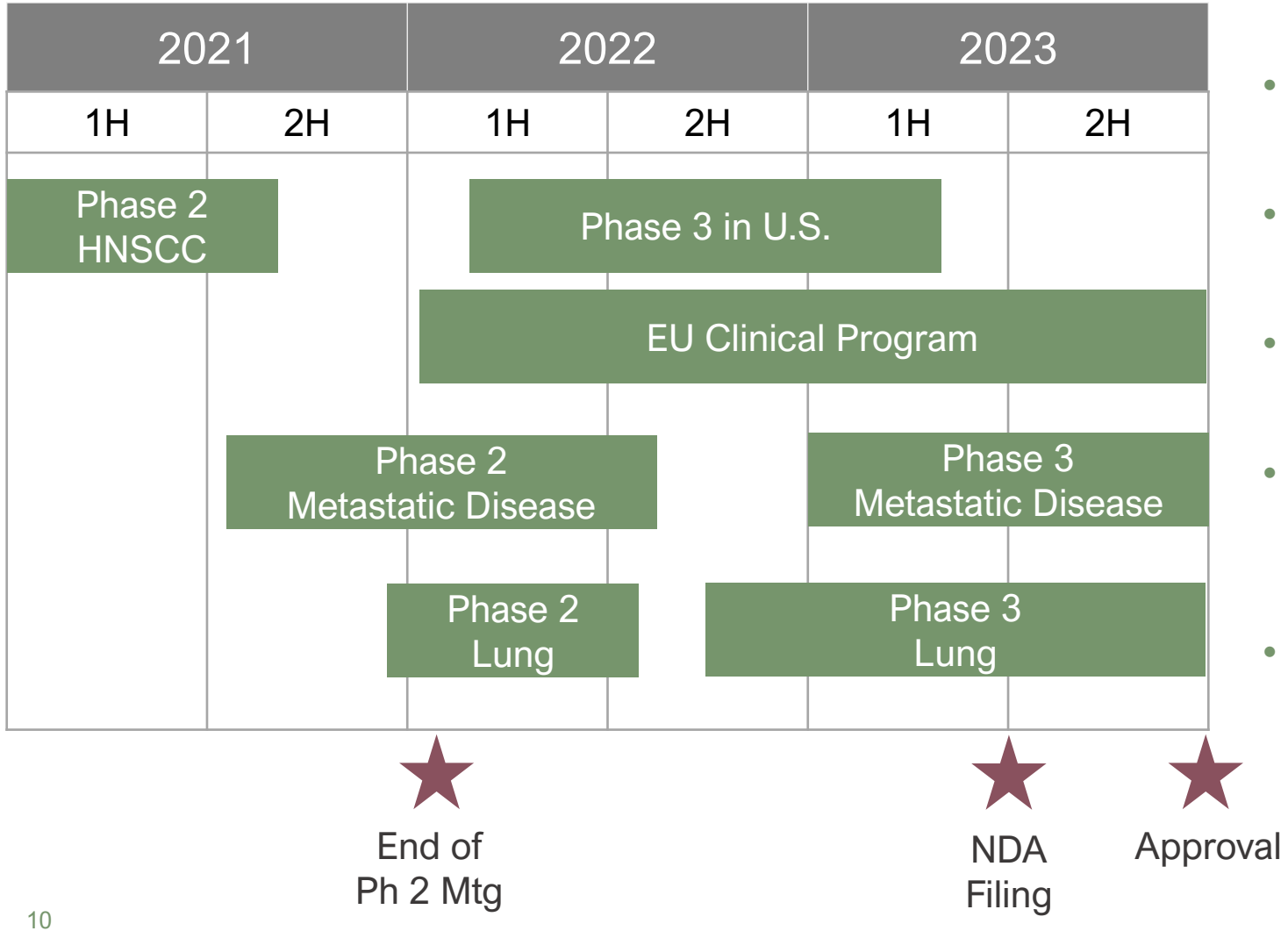
	Disease area	n=	Design
Part 1: Complete	BC & HNSCC	9 Patients	Dose escalation at 6 ± 3 hours prior to surgery
Part 2: Complete	Ovarian & Prostate	10 Patients	1.0 mg/kg, 24 hrs ± 8 hours prior to surgery
Part 3: Recruiting	HNSCC & Lymph Nodes	26 Patients	1.0 mg/kg, 24 hrs ± 8 hours prior to surgery

Primary Endpoints

- Fluorescence correlated to final pathology report
- Sensitivity
- Specificity
- Positive/Negative Predictive Values

Topline data expected Q4 2021 and 1Q 2022
Anticipate FDA End of Phase 2 meeting year end 2021

Pegsitacianine – Potential Revenue Generation in 2024



- Critical milestones coming over the next 2½ years
- Fast Track status granted by FDA in 2019, potential for accelerated NDA review
- Pursuit of EU strategy sequential to US development & commercialization
- Collaborate with regulatory agencies on pathway to label expansion for metastatic disease
- Additional expansion to Rectal, Breast, & Advanced Melanoma

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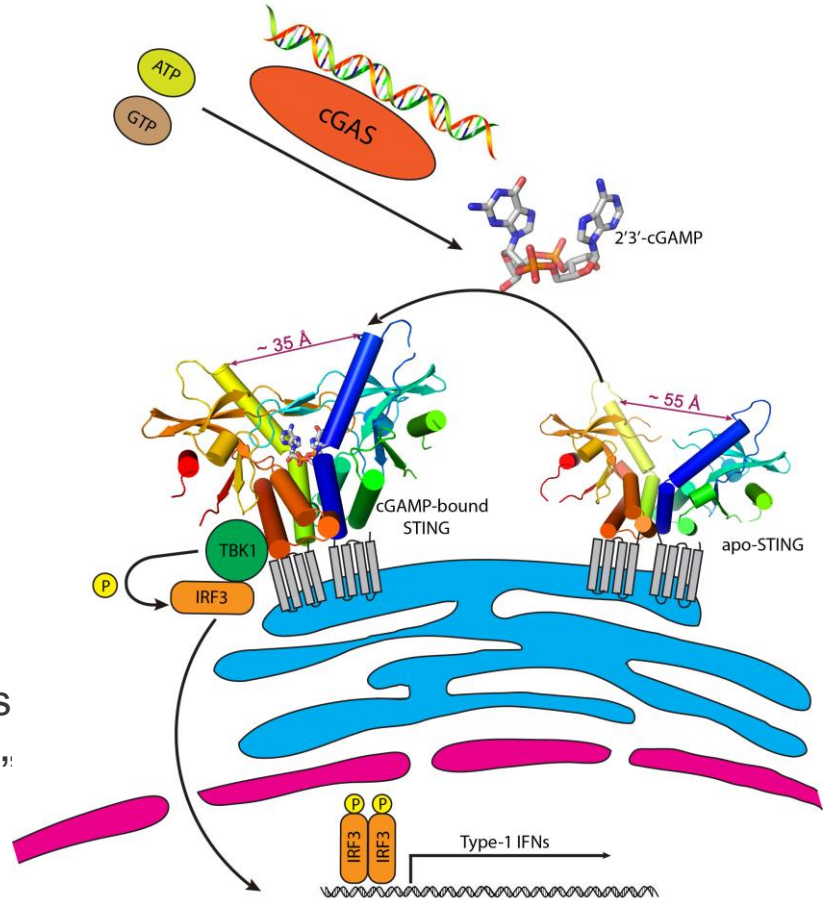
cGAS-STING Pathway: Innate Sensing of Cytosolic DNA

- **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, which facilitates the synthesis of cyclic GMP-AMP (cGAMP) as a secondary messenger
  - cGAMP binds and activates **ST**imulator of **IN**terferon **G**enes (**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 “cold” tumor into a “hot” tumor with strong adaptive immune responses
  - STING remains an immuno-oncology target of great interest

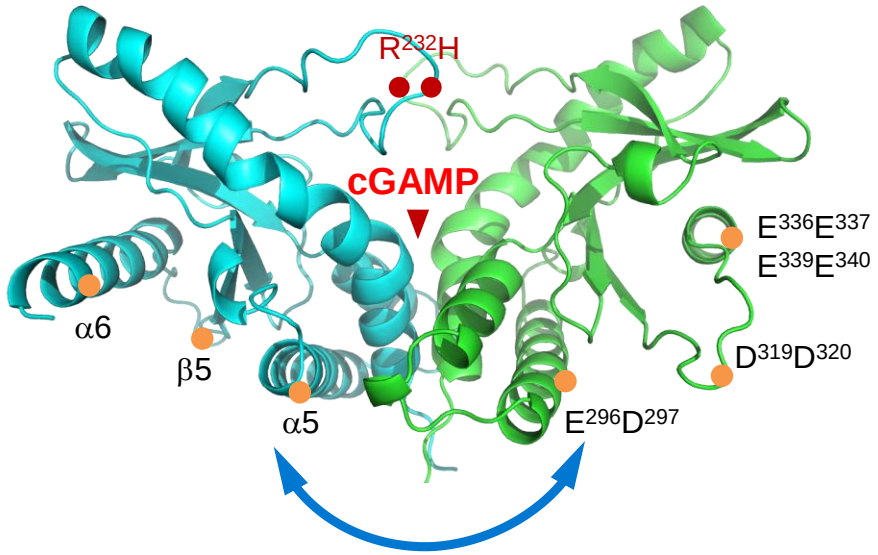


Chen et al.
Science, 339, 786 (2013); 339, 826 (2013)

ONM-501 – A Differentiated Immuno-Oncology Therapeutic

Novel PC7A Polymer + synthetic cGAMP dinucleotide

- **ONM-501 induces dual activation of STING**
  - PC7A polymer binds to $E^{296}D^{297}$ sites on α5 helices, distinctive from cGAMP binding pocket at the STING dimer interface
  - PC7A induces STING condensate formation, prolonging Type I IFN responses over 48 h (vs. 6h for cGAMP)
  - PC7A activates STING haplotypes resistant to CDNs
  - ONM-501 achieves a ***burst*** and ***sustained*** STING activation that maximizes T cell immunity vs. earlier generation CDN STING agonists
- **ONM-501 achieves robust antitumor immunity**
  - Strong abscopal effect from intra-tumoral administration
  - Induces an immune memory effect
  - Antitumor immunity is dependent on cDC1, a subset of dendritic cells responsible for antigen processing and T cell priming



Our partners at the Cancer Prevention & Research Institute of Texas (CPRIT) co-fund ONM-501 Program thru Ph 1a/1b

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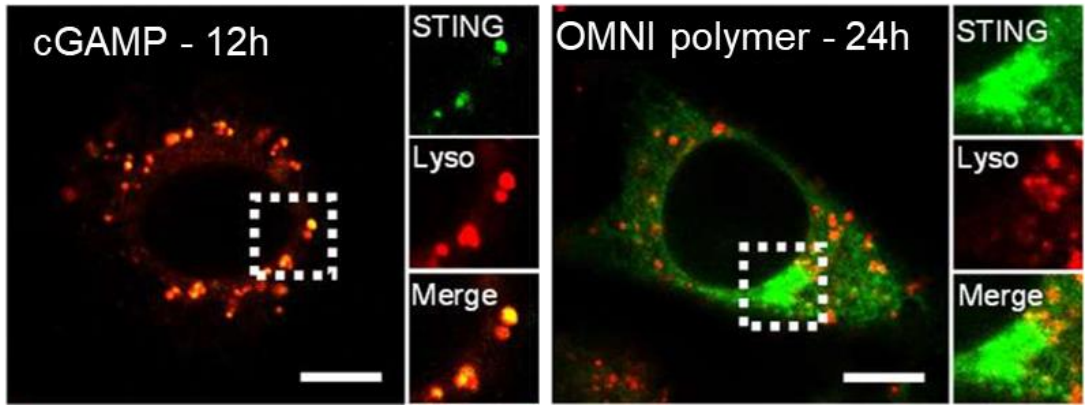
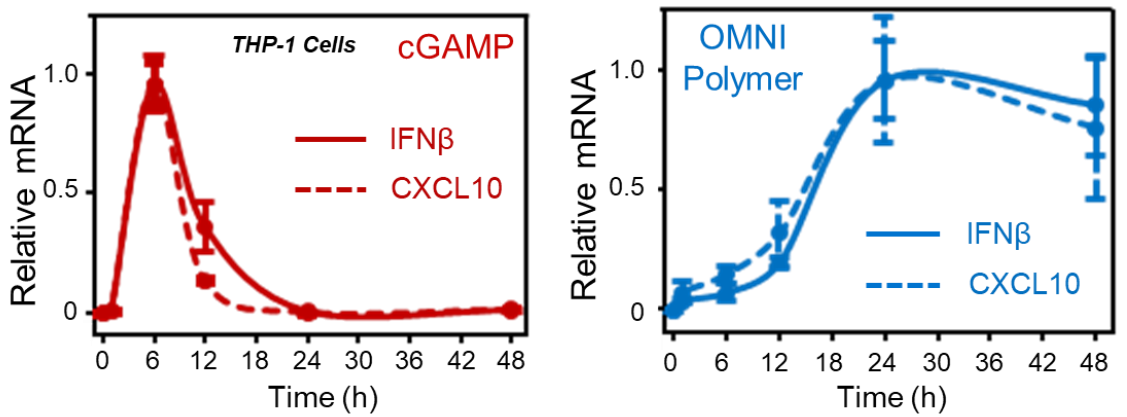
ONM-501: Synergistic Prolonged STING Activation

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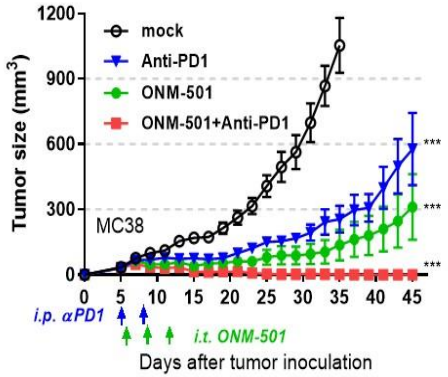
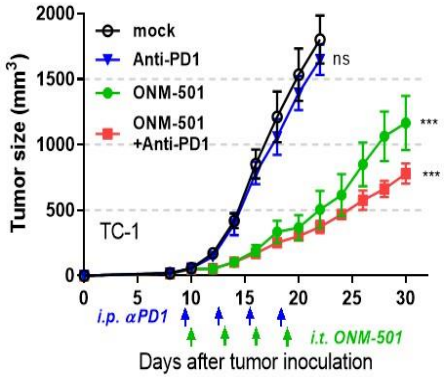
ONM-501
Broad Anti-Tumor Efficacy & Adaptive Immune Trafficking

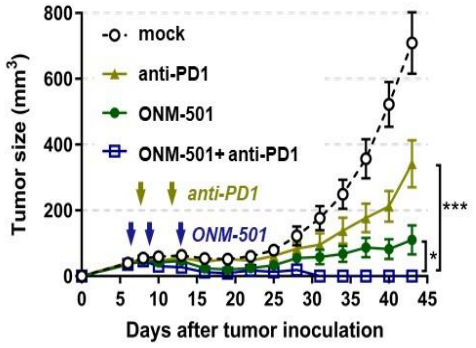
MC-38 Colon



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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Strong Financial Position

- $46.2m Cash Balance as of June 2021
- Recent closing of $50m Series B round
- Supplemented by $23.8m in available funds from CPRIT grants
- Company currently funded thru 1Q'23
- Avg. 2021 quarterly burn - ~$3.75m

As of June 2021	$m
Cash Position	$46.2
Undrawn Grants	$23.8

Non-Dilutive Funding Awards

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

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Key IP Coverage
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

Upcoming Milestones

Pegsitacianine	Ph 2 Results (HNSCC)	Ph 2 Results (Metastatic disease)	Initiate Ph 3 (Metastatic Disease)	Ph 3 Results (Metastatic Disease)	NDA Submission (HNSCC)
	Completion of E of Ph 2 Meeting with FDA in 1H22	Launch US Ph 3 Program (HNSCC)	Ph 3 Data Results Anticipated (HNSCC)		
		Launch EU Clinical Program (HNSCC)	Initial EU Trial Results Anticipated (HNSCC)	Pivotal Program in EU	
Research Partnerships	Non-clinical POC from Research Collaboration with 1st Strategic Partner				
		Non-clinical POC from Research Collaboration with 2nd Strategic Partner			
	2H 2021	**1H 2022**	**2H 2022**	**1H 2023**	**2H 2023**
ONM-501	Initiate IND-Enabling Activities	Complete IND-Enabling Activities	Submit IND & FD/FP Ph 1a/1b		Ph 1a/1b Study Results
ONM-400		Initiate IND-Enabling Activities		Submit IND	Initiate FD/FP Ph 1a/1b

Pegsitacianine Ph 2 data readouts in 4Q'21 & 1Q'22

Pegsitacianine Ph 3 ready in US in 2Q'22 & EU in 2Q'23

Non-clinical POC from ongoing research collaborations 1st strategic in 4Q'21 & 2nd in 1Q'22

ONM-501 enters clinic in 2H'22

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Investment Summary

- Targeted oncology company developing pipeline of assets based on 2 platform technologies - ON-BOARD™ and OMNI™
  - ON-BOARD™ is a tumor specific delivery technology with multiple applications
  - OMNI™ is a polymeric micelle technology with potential in Immuno-oncology
- Lead asset – **pegsitacianine** - currently in Phase 2, with data anticipated in 4Q'21
- Second asset – **ONM 501** – to enter clinic in 2H'22
- Two meaningful strategic research collaborations already in place
  - Future potential to monetize the core delivery technology platform
- Cash position of $46.2 million plus additional $23.8 million in undrawn grants support strategic plans through 2023
- Leadership team with experience leading publicly traded biopharma companies, executing successful M&A transactions, and transforming companies through business development

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