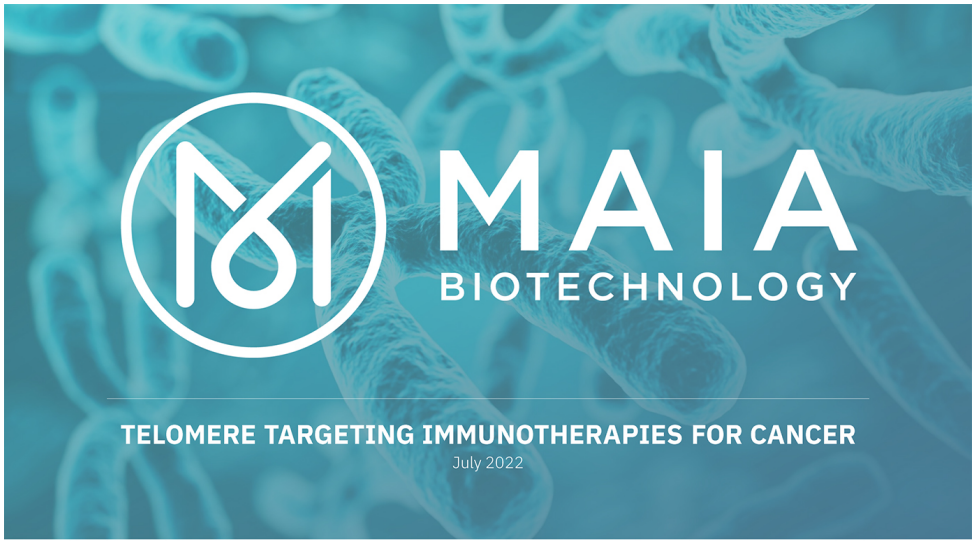
Filed Pursuant to Rule 433 of the Securities Act of 1933
Issuer Free Writing Prospectus dated July 13, 2022
Relating to the Preliminary Prospectus dated July 13, 2022
Registration No. 333-264225



FREE WRITING PROSPECTUS

This free writing prospectus relates to the proposed initial public offering of common stock, par value $0.0001 per share of MAIA Biotechnology, Inc. (the "Company"), which are being registered on a registration statement and should be read together with the preliminary prospectus included in the registration statement filed with the SEC on July 13, 2022, for the offering to which this presentation relates and may be accessed through the following link: https://www.sec.gov/Archives/edgar/data/0001878313/000156459022025709/maia-s1a.htm.

The Company has filed the registration statement (including a preliminary prospectus) with the SEC for the proposed offering to which this communication relates. The registration statement has not yet become effective. Before you invest, you should read the preliminary prospectus in the registration statement (including the risk factors described therein) and other documents we have filed with the SEC in their entirety for more complete information about us and the proposed offering. You may get these documents for free by visiting EDGAR on the SEC website at www.sec.gov. Alternatively, we or the representative of the underwriters will arrange to send you the prospectus if you request it from ThinkEquity, LLC, 17 State Street, 41st Floor, New York, NY 10004, telephone: (877) 436-3673 or e-mail prospectus@think-equity.com.

This Presentation shall not constitute an offer to sell, or the solicitation of an offer to buy, nor will there be any sale of these securities in a jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws jurisdiction. The offering will only be made by means of a preliminary prospectus pursuant to a registration statement that is filed with the SEC after this statement becomes effective.

DISCLOSURE

All statements in this presentation, other than those relating to historical facts, are "forward-looking statements." These forward-looking statements may include, but are not limited to, statements relating to our objectives, plans, and strategies; statements that contain projections of results of operations or of financial condition; statements relating to the industry and government policies and regulations relating to our industry; and all statements (other than statements of historical facts) that address activities, events, or developments that we intend, expect, project, believe, or anticipate will or may occur in the future. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties. We have based these forward-looking statements on assumptions and assessments made by our management in light of their experience and their perception of historical trends, current conditions, expected future developments, and other factors they believe to be appropriate. Important factors that could cause actual results, developments, and business decisions to differ materially from those anticipated in these forward-looking statements include, among other things: the overall global economic environment; general market, political, and economic conditions in the countries in which we operate: projected capital expenditures and liquidity; changes in our strategy; government regulations and approvals; the application of certain service license; and litigation and regulatory proceedings. The Company has filed a registration statement on Form S-1, as amended (Registration No.: 333-264225) (the "Registration Statement") with the Securities and Exchange Commission for the offering to which this presentation relates. Before you invest, you should carefully read the registration statement, including the factors described in the "RISK FACTORS" section of the Registration Statement and other documents that we have filed with the Securities and Exchange Commission to better understand the risks and uncertainties inherent in our business and industry and for more complete information about us and the offering. You may get these documents for free by visiting EDGAR on the Commission's website at www.sec.gov. We caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward looking statements contained in this presentation as a result of, among other factors, the factors referenced in the "Risk Factors" section of the Registration Statement. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this presentation, they may not be predictive of results or developments in future periods. This presentation shall not constitute an offer to sell or the solicitation of an offer to sell or the solicitation of an offer to buy any of our securities nor shall there be any sale of securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction. Any offering of securities can only be made in compliance with applicable securities laws. You should read carefully the factors described in the "Risk Factors" section of the Registration Statement to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements. These statements are only current predictions and are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry's actual results, levels of activity, performance, or achievements to be materially different from those anticipated by the forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance, or achievements. Except as required by law, we are under no duty to update or revise any of the forward-looking statements, whether as a result of new information, future events or otherwise, after the date of this prospectus. These forward-looking statements speak only as of the date of this presentation, and we assume no obligation to update or revise these forward-looking statements for any reason. This presentation is confidential, is intended for the recipient only and thus may not be forwarded, reproduced, redistributed or passed to any other person or published in whole or in part for any purpose. If this document has been received in error, it must be returned immediately to the Company. 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OFFERING SUMMARY

Issuer	**MAIA Biotechnology, Inc.**
Proposed Symbol	NYSE American: MAIA
Expected Offering Size	$10,000,000
Expected Price Range	$5 - $7 / share
Shares Offered	1,666,667
Over-Allotment	15% (250,000 shares)
Use of Proceeds	– Advance two clinical trials: THIO-101 in NSCLC and THIO-102 in CRC, HCC, and SCLC – Fund IND filing-enabling studies for two second-generation telomere-targeting compounds – General corporate purposes and working capital, as well as other research and development activities
Sole Book Runner	ThinkEquity

COMPANY OVERVIEW

PIPELINE

THIO-101: Phase 2 Trial of THIO + LIBTAYO® (*cemiplimab*) in Non-Small Cell Lung Cancer (NSCLC) enrolling

- Ex-US strategy initially: Australia and Europe
- Evolve into pivotal trial; to include US sites
- Planned second-line therapy
- Regeneron clinical supply agreement for Libtayo
- Plan to readout & file in 2024 for accelerated approval in 2025

THIO-102: Basket/Umbrella Design

- Plan to initiate pivotal Phase 2 trial in CRC, HCC, SCLC in 1H2023
- Sequence with Libtayo (Regeneron), Keytruda (Merck), Tecentriq (Genentech)
- Nine additional market entry strategies

Pre-Clinical Next Generation Telomere Targeting Candidates

- Orphan indication targets for market entry
- Major tumor types for expansion

SCIENCE

THIO (6-thio-dG) Telomere Targeting Agent

- Small molecule eligible for NCE marketing exclusivity
- THIO activity shown to be cancer-specific in tumor types with active telomerase
- Dual mechanism of action
- Complete response with no recurrence during study period
  - *In vivo* in lung, colorectal[1], and liver cancers
- Safety assessment data based on prior human studies:
  - 600+ subjects (adult and pediatric) at significantly higher doses than in THIO-101 trial
- Intellectual Property Portfolio provides protection out to 2041
- FDA Orphan Drug Designations granted for Liver Cancer and Small Cell Lung Cancer

Nobel Prize

- Awarded to scientists who discovered telomeres and telomerase[2]

[1] Published in Cancer Cell, see slides 28-30, below
[2] Nobel Prize awarded in 2009 to Jack Szostak, Elizabeth Blackburn and Carol Greider

Telomerase is an enzyme that is present in a majority of human cancer cells (over 85% in the aggregate), across various tumor types

THIO: DUAL MECHANISM OF ACTION IN VIVO

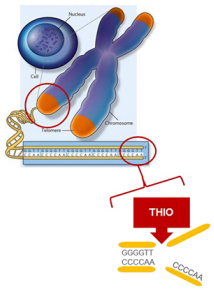
MAIA BIOTECHNOLOGY

Direct Telomere-Targeting:

Lead to Cancer Cell Death[1]

1. THIO metabolized and utilized telomerase in cancer cells
2. THIO metabolite was observed to incorporate into telomeres by telomerase
3. Telomeric structure and function were compromised
4. Followed by fast and efficient cancer cell death.

Basis for New Treatment Approach



Immunogenic Effect:

Anti-Tumor Immune Activation (in vivo[2])

1. Produced micronuclei containing THIO-modified telomeric DNA fragments, which were then observed extracellularly and reached immune cells
2. These neoadjuvant DNA fragments specifically activated cGAS/STING pathway in the cancer and dendritic cells
3. Induced innate & adaptive immune responses that eliminated remaining cancer cells
4. Generated anti-tumor specific immunological memory and prevented tumor recurrence

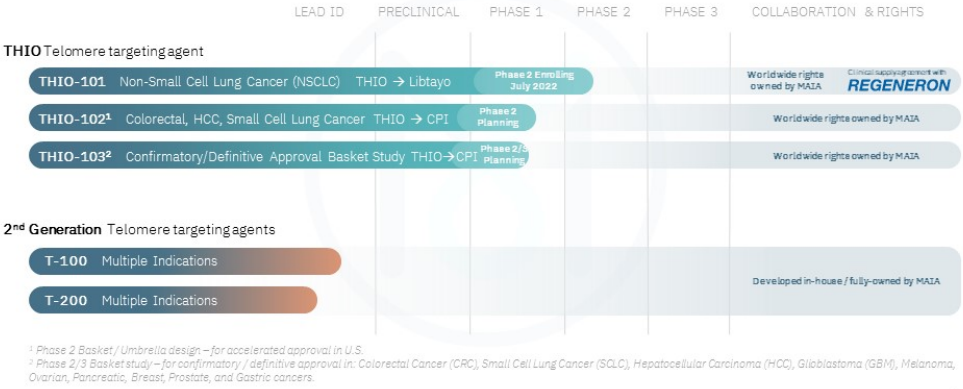
[1] In Preclinical Studies

[2] In Rodent Preclinical Studies

PIPELINE

MAIA BIOTECHNOLOGY

Robust pipeline includes several targeted immuno-oncology therapies for difficult-to-treat cancers



[1] *Phase 2 Basket / Umbrella design – for accelerated approval in U.S.*
[2] *Phase 2/3 Basket study – for confirmatory / definitive approval in: Colorectal Cancer (CRC), Small Cell Lung Cancer (SCLC), Hepatocellular Carcinoma (HCC), Glioblastoma (GBM), Melanoma, Ovarian, Pancreatic, Breast, Prostate, and Gastric cancers.*

REGENERON CLINICAL SUPPLY AGREEMENT - LIBTAYO

Goal of Study:

New Standard of Care for Treatment of NSCLC

Phase 2 dose optimization study, to evolve into a pivotal study for US approval:

- Safety lead-in
- Select optimal dose for planned pivotal study

Contribute Drug Supply

- LIBTAYO® (*cemiplimab*; anti-PD1)
- Development exclusivity only for NSCLC for study period
- All other tumor types remain open

Established Joint Development Collaboration Committee to maximize success

MAIA Biotechnology, Inc. Announces Clinical Supply Agreement with Regeneron for Phase 1/2 Clinical Trial Evaluating THIO in Sequential Administration with Libtayo® (cemiplimab) in Advanced Non-Small Cell Lung Cancer

February 02, 2021 08:00 AM Eastern Standard Time

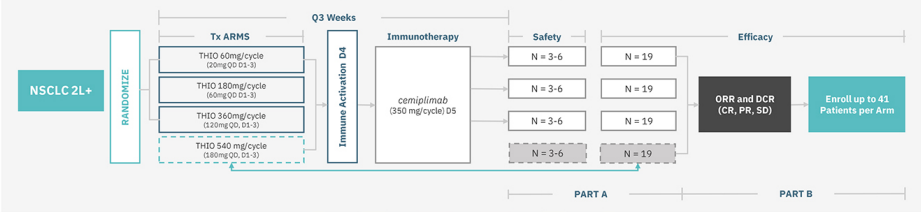
CHICAGO--(BUSINESS WIRE)--MAIA Biotechnology, Inc., a targeted therapy, immuno-oncology company focused on development of first-in-class oncology drugs, today announced a clinical supply agreement with Regeneron Pharmaceuticals, Inc. (REGN) to evaluate THIO (aka 6-thio-dG) followed by the PD-1 inhibitor Libtayo® (cemiplimab), in a Phase 1/2 clinical trial in second-line or later advanced non-small cell lung cancer (NSCLC) patients who have progressed following treatment with standard-of-care regimen that includes a checkpoint inhibitor. This clinical trial will evaluate the safety and efficacy of four dose levels of THIO, the only telomere-by-telomerase targeting agent in development for the treatment of cancer, followed by Libtayo. The lead-in portion of the study will initially assess the safety and immunogenic effects of each of the THIO doses and overall response rate (ORR) as the basis for potentially expanding individual patient cohorts and evaluation in other cancer types. The Phase 1/2 clinical trial is expected to begin enrolling patients in 2021.

"Priming tumors with THIO before Libtayo treatment is a novel approach that may enhance and extend the potential benefits of immunotherapy for patients with advanced non-small cell lung cancer, and we look forward to seeing if the positive pre-clinical results that MAIA has published will translate to the clinic."

Tweet this

"We are excited for the opportunity to partner with Regeneron on our planned clinical trial of THIO and believe this collaboration to be validating of the program's potential to transform both the immuno-oncology landscape and the cancer treatment paradigm," stated Vlad Vitoc, MD, MAIA's Chief Executive Officer and President. "Notably, THIO has a well-demonstrated clinical safety profile at varying dosage levels and in preclinical results, low-dose THIO followed by immunotherapy has shown complete elimination of advanced tumors with no indication of treatment limiting toxicity. The efficacy results of this trial are expected to support the continued development of THIO in NSCLC and potentially its expansion to treat a vast array of other cancers. Based on our extensive preclinical experience, we believe that THIO may transform immunologically 'cold' tumors into 'hot', rendering them responsive to standard-of-care immuno-oncology therapies, and potentially improving their effectiveness."

A Multicenter, Open-Label, Dose-Finding Phase 2 Study Evaluating the Safety and Efficacy of THIO Administered in Sequence with LIBTAYO® (*cemiplimab*)



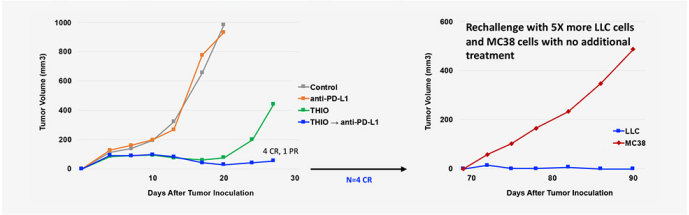
Primary Endpoints	Overall Response Rate (ORR)
Secondary Endpoints	ORR in telomerase positive patients; Complete Response (CR), Partial Response (PR), Stable Disease (SD), Disease Control Rate (DCR), Duration of Response (DoR), Progression-Free Survival (PFS), Overall Survival (OS), Safety
Exploratory Endpoints	Activity of THIO in circulating tumor cells, measured by Telomere-dysfunction Induced Foci (TIFs) and genomic gamma-H2AX; blood biomarkers

ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT05208944?term=05208944&draw=2&rank=1

THIO-101 STUDY IN NSCLC: ANTICIPATED CLINICAL OUTCOMES EXTRAPOLATED FROM PRECLINICAL DATA

Catalyst	Timing	Current SOC (chemo)	THIO → LIBTAYO (expected)
Safety	Q3-Q4 2022	72-79% Grd ≥3	10-20% Grd ≥3
Preliminary Efficacy (ORR in first 30-40 pts)	Q4 2022 – Q1 2023	11-23%	30-60%
PFS	H2 2023	4-4.5 months	6-12 months
OS	H1 2024	8.1-10.5 months	14-20 months

- Demonstrated complete response of tumor with no observed recurrence in Lewis Lung Carcinoma (LLC) in murine models
- Development of immunological tumor-specific directed memory – no tumor development upon rechallenge

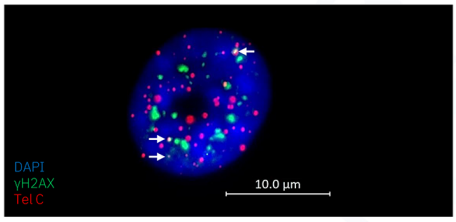


Mender et al, Cancer Cell, 2020

BIOMARKER OF ON-TARGET BIOLOGICAL ACTIVITY: TIFS

THIO induced telomere dysfunction in Lewis Lung Carcinoma (LLC) cells: in vitro NSCLC model

Confocal microscopy image of LLC cell nucleus after treatment with 3 µM of THIO

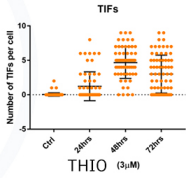


Yellow dots (marked by triangles) indicated telomere damage induced foci (TIFs) by THIO

Green dots - gH2AX

Red dots - telomeres

Quantification of TIFs induced in LLC cell by 3 µM of THIO



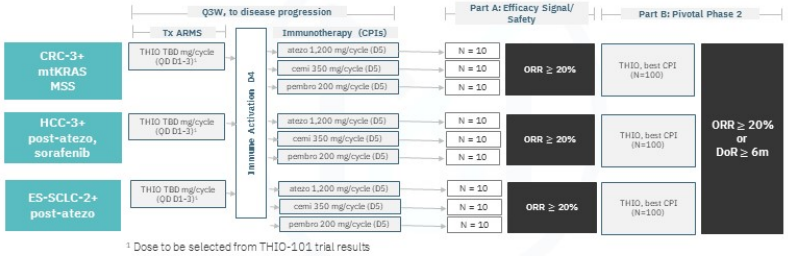
TIFs induction reached maximum after approx. 48 hours of exposure

Formation of TIFs indicated on-target Mechanism of Action (MOA) of THIO

THIO-102 STUDY: PLANNED PHASE 2 STUDY IN THREE CANCER INDICATIONS (MASTER PROTOCOL INCORPORATING DESIGN FEATURES COMMON TO BOTH "BASKET" AND "UMBRELLA" TRIALS)

MAIA BIOTECHNOLOGY

A Multicenter, Open-Label, Phase 2 Study Evaluating the Safety and Efficacy of THIO Administered in Sequence with Anti-PD-1 or Anti-PD-L1 in Patients with Telomerase Positive Cancers



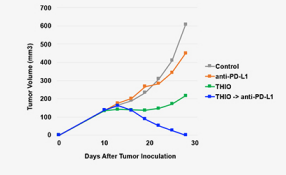
[1] Dose to be selected from THIO-101 trial results

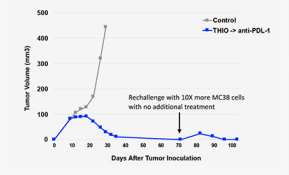
Primary Endpoints	Overall Response Rate (ORR), Duration of Response (DoR)
Secondary Endpoints	Complete Response (CR), Partial Response (PR), Stable Disease (SD), Disease Control Rate (DCR), Progression-Free Survival (PFS), Overall Survival (OS), Safety

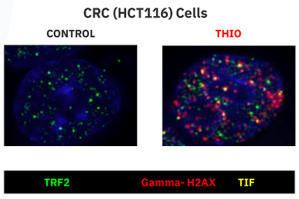
THIO-102 TRIAL: CATALYSTS AND RATIONALE FOR THE CRC ARMS

Catalyst	Timing	Current SOC (chemo)	THIO → CPI (expected)
Safety	Early H1 2023	50-60% Grd ≥3	10-20% Grd ≥3
ORR	Late H1 2023	1-1.6%	10-20%
PFS	H2 2023	1.9-2.0 months	3-6 months
OS	H1 2025	6.4-7.2 months	9-12 months

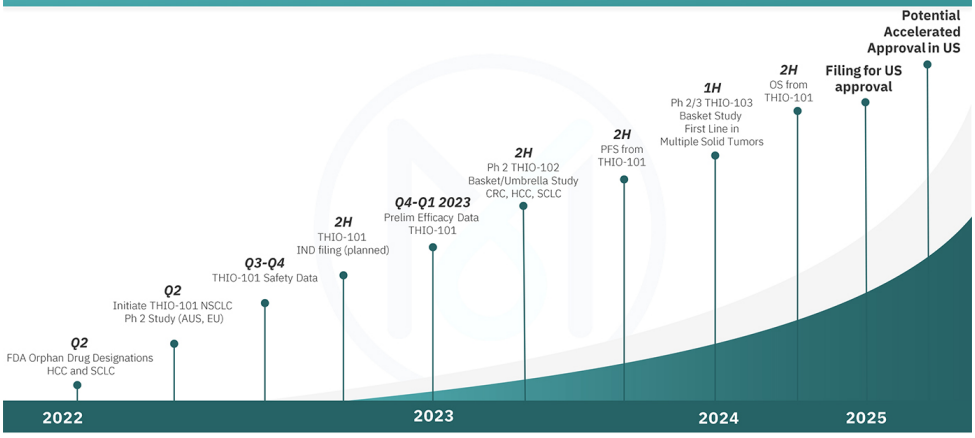
THIO followed by PD-L1 blockade resistance in MC38 cells in murine model turns immunologically cold tumors to hot and results in complete response and no recurrence by the end of study.







MULTIPLE VALUE-DRIVING MILESTONES



SIGNIFICANT MARKET OPPORTUNITY

#1 Worldwide: NSCLC/ #2 Worldwide: CRC

Mortality: 1.6M in 2021
Sales: $23B in 2021

Mortality 943,000 in 2021
Sales $8B in 2021

Checkpoint Inhibitors

Five approved for NSCLC (Keytruda, Opdivo, Tecentriq, Imfinzi, Libtayo)
- $12B of $23B total NSCLC drug sales in 2021
- $12B of $34B total checkpoint inhibitor sales in 2021

Keytruda: $7.5B source of business in NSCLC of $17.2B total (>20 other tumor types)

Libtayo

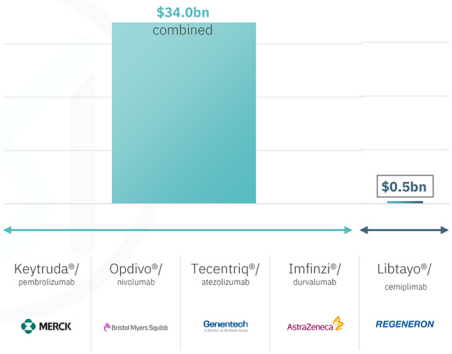
Entrant #5

Needs superior efficacy to Keytruda to take over in first line

Profile similar to Keytruda

Sequential combination with THIO is key

Immune Checkpoint Inhibitors Market



Keytruda®/ pembrolizumab	Opdivo®/ nivolumab	Tecentriq®/ atezolizumab	Imfinzi®/ durvalumab	Libtayo®/ cemiplimab
MERCK	Bristol Myers Squibb	Genentech	AstraZeneca	REGENERON

EXCLUSIVITY AND INTELLECTUAL PROPERTY SUMMARY

MAIA BIOTECHNOLOGY

Goal: **NCE Marketing Exclusivity**

- THIO (6-thio-2'-deoxyguanosine) has never been previously approved by the FDA
- NCE exclusivity if granted blocks submission of competing ANDAs and 505(b)(2) NDAs for 5 years

Robust and Growing Patent Portfolio for THIO

1 issued US patent
3 issued foreign patents
4 pending US patent applications
12 pending foreign patent applications

Current patents/provisionals broadly cover the following key areas:

Telomerase mediated telomere altering compounds
THIO's immunogenic treatment strategy: sequential combination with checkpoint inhibitors
Treatment of therapy-resistant cancers

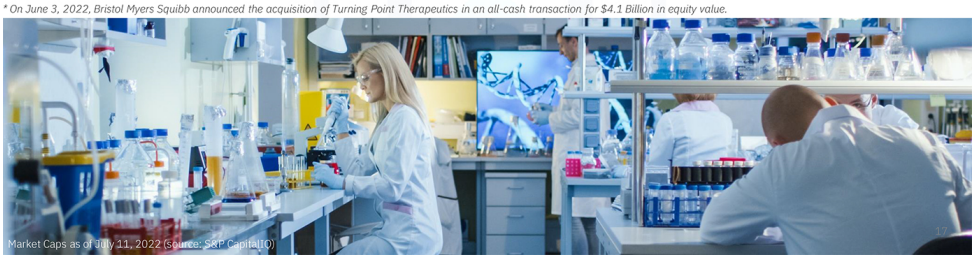
Jurisdiction	Status	Number	Title	Expected Expiration Date	Type of Patent Protection
US	Issued	10,463,685	Telomerase Mediated Telomere Altering Compounds	April 8, 2034	Use of 6-Thio-dG to treat lung cancer or colon cancer
MX	Granted	387008	Telomerase Mediated Telomere Altering Compounds	April 8, 2034	Use of 6-Thio-dG to treat lung cancer or colon cancer
NZ	Granted	73228	Telomerase Mediated Telomere Altering Compounds	April 8, 2034	Use of 6-Thio-dG to reduce the size or a tumor or the growth rate of the tumor
Russia	Granted	2713555	Telomerase Mediated Telomere Altering Compounds	April 8, 2034	Use of 6-Thio-dG to treat lung cancer or colon cancer
US	Pending	16/450,430	Treatment of Drug Resistant Proliferative Diseases with Telomerase Mediated Telomere Altering Compounds	March 23, 2037	A method of treating NSCLC using a 6-mercaptopurine deoxyribonucleoside analogue
US	Pending	16/304,538	6-thio-2'deoxyguanosine (6-thio-dG) results in telomerase dependent telomere dysfunction and cell death in various models of therapy-resistant cancer cells	May 26, 2037	A method of treating a subject with cancer comprising 6-thio-dG) wherein cells of said cancer are telomerase-positive and exhibit enriched telomere transcriptional signature(s), wherein said subject has had disease progression during or after platinum-based therapy, radiotherapy, or immunotherapy
US	Pending	16/982,979	Use of 6-thio-dG to Treat Therapy-Resistant Telomerase Positive Pediatric Brain Tumors	March 22, 2039	A method of treating a brain cancer in a pediatric subject, comprising administering a telomerase substrate precursor analog to a subject in need thereof, thereby treating pediatric brain cancer.
US	Pending	17/200,539	Sequential Treatment of Cancers Using 6-Thio-dG, Checkpoint Inhibitors and Radiation Therapy	March 12, 2041	A method of treating a cancer, in a subject comprising administering to said subject 6-thio-2'-deoxyguanosine (6-thio-dG) followed by treatment with an immune checkpoint inhibitor, wherein the cancer is selected from the group consisting of pancreatic, lung, mesothelioma, stomach, esophagus, liver, biliary tract, bladder, head & neck, oral, nasopharyngeal, adult brain, colon, rectum, colorectal, prostate, ovarian, cervical, uterine, testicular, lymphoma, leukemia, skin, breast, kidney, neuroblastoma, Merkel cell carcinoma, myelodysplastic syndrome, myelofibrosis, and multiple myeloma.

COMPARABLE COMPANIES

MAIA BIOTECHNOLOGY

MIRATI THERAPEUTICS	zentalis	IOVANCE BIOTHERAPEUTICS	veru	Turning Point Therapeutics
$3.48 Billion	**$1.52** Billion	**$1.84** Billion	**$1.26** Billion	**$4.1** Billion*

** On June 3, 2022, Bristol Myers Squibb announced the acquisition of Turning Point Therapeutics in an all-cash transaction for $4.1 Billion in equity value.*



Market Caps as of July 11, 2022 (Source: S&P Capital IQ)

CAPITALIZATION TABLE

Pro Forma Pre-IPO Cap Table *(as of 7/13/2022)*	
Common Stock[1]	8,553,452
Options (WAEP: $2.43)[2]	5,927,523
Warrants (WAEP: $5.97)	702,505
Fully Diluted Shares Outstanding	15,183,480

1) Includes 137,420 restricted shares to be issued to prior round investors, assuming the mid-point of the expected pricing range
2) 5,350,000 options held by directors and officers

*Directors and officers, and their affiliates, own 50% of the 15,183,480 fully diluted shares outstanding

HIGHLY EXPERIENCED MANAGEMENT TEAM

Vlad Vitoc, MD, MBA
Founder, Chairman, and
Chief Executive Officer

22+ yrs. Pharma/Biotech: Commercial, Medical,
12 compounds launched, 20+ tumor types,
8 Oncology companies
Served in Oncology leadership roles at Cephalon (Treanda), Astellas (Tarceva, Xtandi), Bayer (Nexavar), Novartis (Zometa), and Incyte (Jakafi)

Sergei Gryaznov, PhD
Chief Scientific Officer

25+ yrs. Scientist/Expert Drug Discovery and Development, Oncology, 120+ publications and
Head of the J&J Oligonucleotide Center of Excellence Worldwide recognized expert of telomeres and telomerase in cancer
Co-inventor of THIO

Mihail Obrocea, MD
Chief Medical Officer

Hematologist/Oncologist executive with over 21 years of drug development experience: cell therapy, active immunotherapy and cancer vaccines, antibodies, antibody drug conjugates (ADCs), small molecules

Joe McGuire
Chief Financial Officer

30+ yrs. Serving as CFO for privately held and publicly traded companies in the health care, financial services, investment, and manufacturing industries.

Adelina Louie Ngar Yee
Board Member

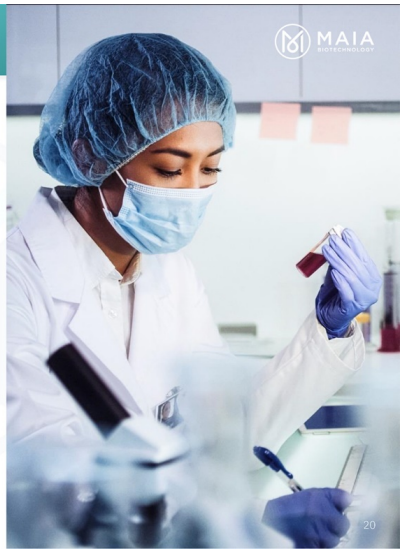
30 years of service with HSBC Group in Global Banking and Markets including investment and securities management, asset management, and global research. Held key leadership positions within Group Internal Audit of HSBC in Latin America, Asia Pacific, and United Kingdom.

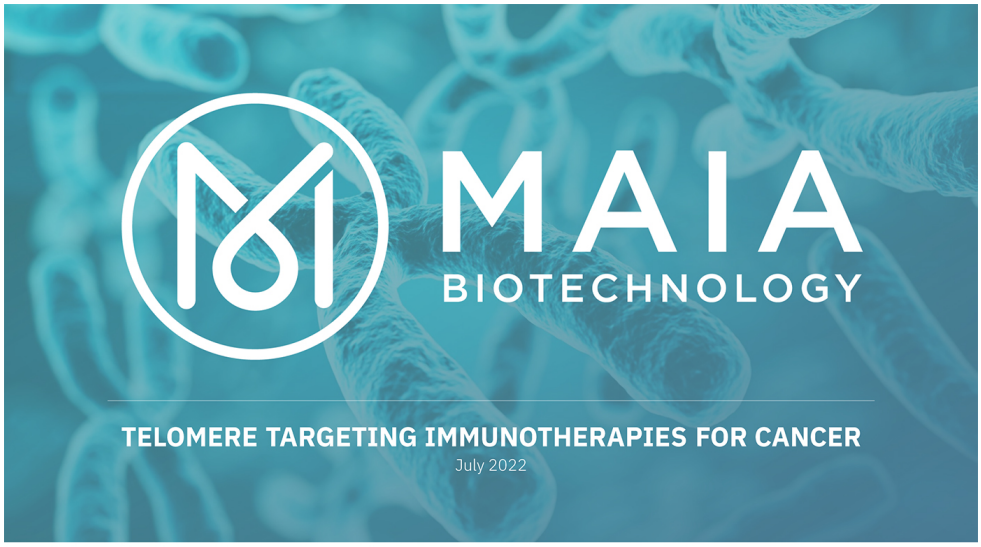
Steven M. Chaouki
Board Member

President, U.S. Markets & Consumer Interactive, overseeing two TransUnion business lines. U.S. Markets provides information and insights to business customers across financial services, insurance, public sector, media and diversified markets.

INVESTMENT HIGHLIGHTS

1. **Two Ex-US Clinical Programs**
   - Ph 2 NSCLC THIO-101 + Libtayo® (cemiplimab) Regeneron; Enrolling
   - Ph 2 CRC, HCC, and SCLC THIO-102; Planned Q1 2023
2. **THIO is a Unique Direct Telomere Targeting Agent**
   - Potential to be used in combination with other anticancer immune therapies
   - Dual, novel mechanism of action
   - Plan to make existing drugs better
3. **Partnership with Major Pharma**
   - Regeneron: relationship started at early stage of THIO development
   - Potentially expand existing relationship and target new companies
4. **Strong and Growing IP Portfolio**
   - Potential for receiving NCE marketing exclusivity
   - 4 patents issued, 16 patents pending
5. **Next Generation Potential Telomere Targeting Therapeutics**
   - Develop two pre-clinical products in new indications
   - Expand beyond immune checkpoint inhibitor combinations
6. **Seasoned Management Team**

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TELOMERE TARGETING IMMUNOTHERAPIES FOR CANCER
July 2022

SCIENTIFIC ADVISORS

David M Ashley, PhD

MBBS (Hon), FRACP, PhD, is Director, The Preston Robert Tisch Brain Tumor Center, Head, Preuss Laboratory, and Director, Pediatrics Neuro-Oncology, Duke University.

Professor David Ashley's career in cancer research dates more than two decades. He is credentialed in both pediatric and adult neuro-oncology practice and this has been the focus of his efforts in translational research and leadership.

Tudor Ciuleanu, MD

Professor of Oncology at UMF Iuliu Hatieganu, and MD at the Oncology Institute "Prof. Dr. Ion Chiricuta," Cluj.

MD Medical Oncology since 1994. PhD at Cluj in 1994 in chemotherapy domain of lung carcinomas. Certified member of ESMO, ASCO member, IASLC, national representative of BUON, RSRMO member, SNOMR.

Z. Gunnur Dikmen, MD, PhD

Professor at Hacettepe University Medical Faculty, Department of Medical Biochemistry

Her research has been focused on the discovery of novel molecules targeting telomeres and telomerase, mainly working on GRN163L (Imetelstat) and 6-thio-2'-deoxyguanosine (6-thio-dG) to show their potent effects on different in vitro and in vivo cancer models.

Thomas F. Gajewski, MD, PhD

Directs the Melanoma Oncology Clinic and leads the Immunology and Cancer Program of the University of Chicago Comprehensive Cancer Center

The focus of Dr. Gajewski's work has been on understanding fundamental aspects of anti-tumor immunity and bringing these concepts forward from the laboratory into clinical trial testing in patients.

David E. Gerber, MD

Professor of Internal Medicine and Population & Data Sciences at UT Southwestern Medical Center

He is an active clinical investigator with more than 180 publications and continuous federal and foundation research funding for more than 10 years

Jerry W. Shay, PhD

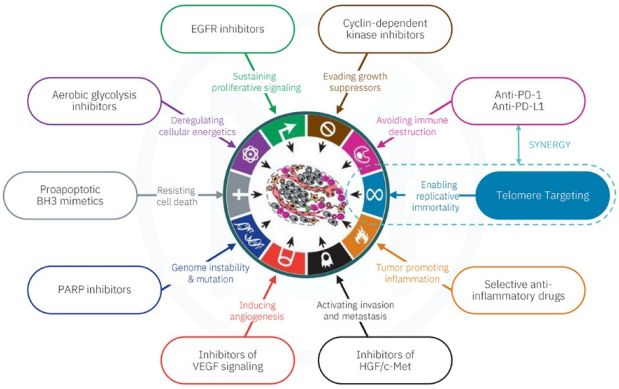
THIO Expert

Dr. Shay has been noted as a highly influential biomedical researcher as noted by the Institute for Scientific Research and Science Watch, with over 30 issued patents, >500 peer reviewed publications and a citation h-index of 112.

Adam Yopp, MD

Occidental Chemical Chair of Cancer Research and an Associate Professor and Division Chief of Surgical Oncology and Colorectal Surgery, at Harold C. Simmons NCI-designated Comprehensive Cancer Center at UT Southwestern Medical Center in Dallas

TELOMERES: KEY THERAPEUTIC TARGETS FOR CANCER



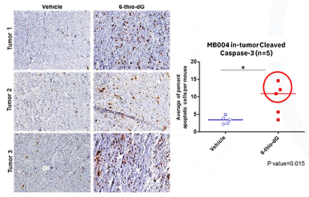
* Source: Adapted from Cell , Volume 144, Issue 5, Pages 646-674 (DOI:10.1016/j.cell.2011.02.013)

THIO PREPARING FOR CLINICAL TRIALS IN PEDIATRIC BRAIN TUMORS

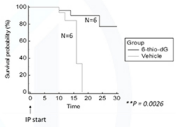
THIO demonstrated penetration of BBB and inhibited tumor growth in in vivo models, inducing in-tumor Telomere dysfunction and cancer cell death in difficult to treat cancer where no therapy exists

Evidence of THIO's Primary Mechanism

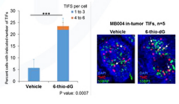
In-tumor Cleaved Caspase-3



Based on these promising preclinical findings, Principal Investigator Dr. Maryam Fouladi, a Pediatric Brain Tumor Consortium (PBTC) member, has submitted Letter of Intent (LOI) to NCI to conduct Phase 1/2 clinical studies with THIO in pediatric brain tumors



Demonstrated Increased Survival in Brain Cancer Mouse Model



Observed Evidence of Telomere Dysfunction

PRECLINICAL RESULTS SHOW THAT THIO TREATMENT LED TO TIFS

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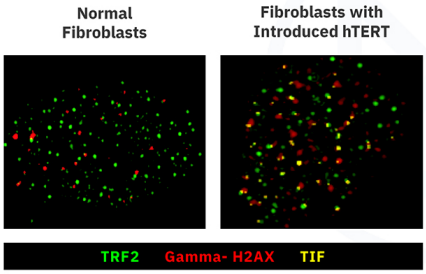
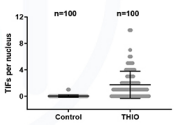
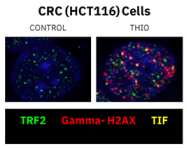
THIO led to telomere dysfunction-induced foci (TIFs) in telomerase-positive cancer cells, but not in normal, telomerase-negative cells (in vitro)



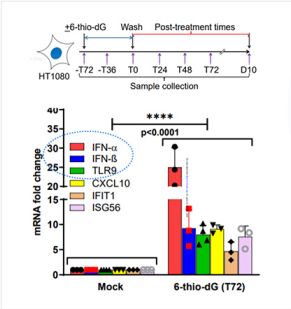
Telomeric DNA is ~1/6000 of total genomic DNA; thus, any telomeric co-localization with DNA damage is highly significant.

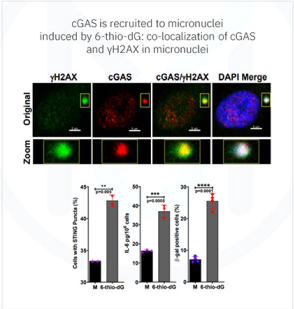


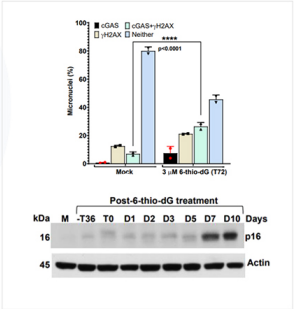


MOA BIOMARKERS OF THIO'S IMMUNOLOGICAL ACTIVITY IN VITRO

Micronuclei generated in response to THIO-induced telomeric DNA modification, replication stress, recruit and activate of cGAS, which leads to cellular senescence in cancer cells







NEW RESULTS ABOUT IMMUNOGENIC EFFECTS OF THIO PUBLISHED IN CANCER CELL

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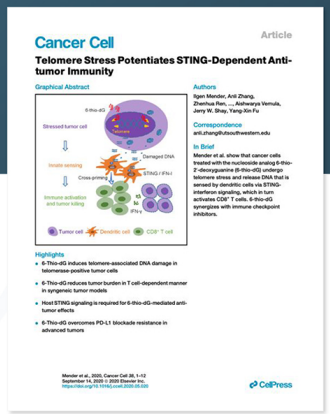
A key peer-reviewed publication released online in the renowned journal Cancer Cell on July 2, 2020.

"Telomere Stress Potentiates STING-Dependent Anti-tumor Immunity," was authored by researchers at the University of Texas Southwestern.


Article

Cancer Cell

Telomere Stress Potentiates STING-Dependent Anti-tumor Immunity

Graphical Abstract

Authors
Ilgen Mender, Anli Zhang, Zhenhua Ren, ..., Aishwarya Vemula, Jerry W. Shay, Yang-Xin Fu

Correspondence
anli.zhang@utsouthwestern.edu

In Brief

Mender et al. show that cancer cells treated with the nucleoside analog 6-thio-2′-deoxyguanine (6-thio-dG) undergo telomere stress and release DNA that is sensed by dendritic cells via STING-interferon signaling, which in turn activates CD8+ T cells. 6-thio-dG synergizes with immune checkpoint inhibitors.

Highlights

- 6-Thio-dG induces telomere-associated DNA damage in telomerase-positive tumor cells
- 6-Thio-dG reduces tumor burden in T cell-dependent manner in syngeneic tumor models
- Host STING signaling is required for 6-thio-dG-mediated anti-tumor effects
- 6-Thio-dG overcomes PD-L1 blockade resistance in advanced tumors

Mender et al., 2020, Cancer Cell 38, 1–12
September 14, 2020 © 2020 Elsevier Inc.
https://doi.org/10.1016/j.ccell.2020.08.020

CellPress

Key Takeaways

Researchers concluded that THIO-targeted telomeres via telomerase and selectively killed cancer cells, without impacting normal cells *in vivo*

When used in sequence with standard-of-care immunotherapy, THIO eliminated tumors in advanced lung and colorectal preclinical models

THIO was shown in *in vivo* mouse models to trigger immunogenic effects which produced immune memory that deterred cancer from returning

* THIO is an investigational agent under development

THIO INDUCTION OF SYSTEMIC ANTI-TUMOR IMMUNITY IN COLORECTAL CANCER (CRC) IN VIVO

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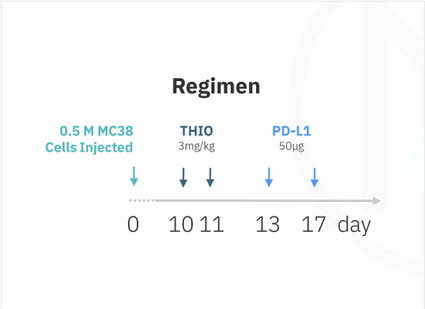
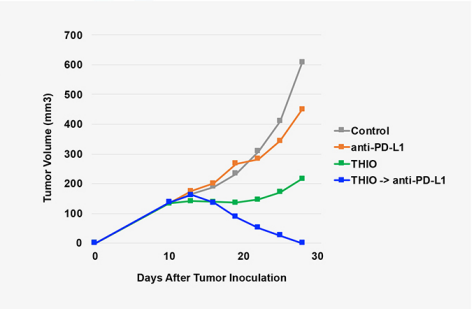
THIO followed by PD-L1 blockade resistance in MC38 cells in murine model turns immunologically cold tumors to hot and was curative





THIO INDUCTION OF SYSTEMIC ANTI-TUMOR IMMUNITY IN COLORECTAL CANCER (CRC) IN VIVO

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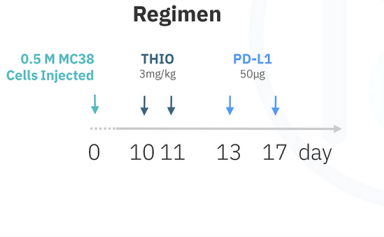
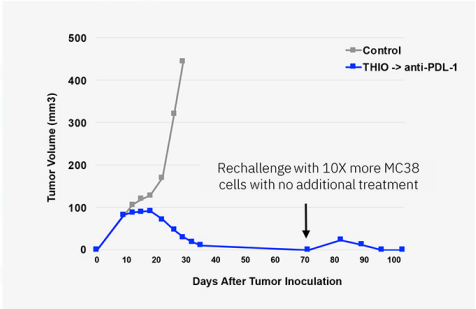
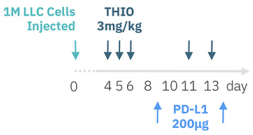
THIO followed by PD-L1 blockade in MC38 cells in murine model was curative, accompanied by generation of immune memory

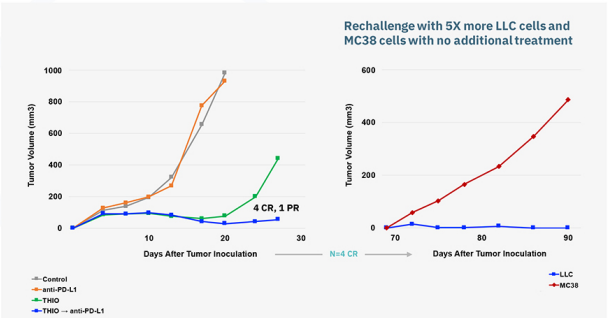




THIO SEQUENTIAL WITH PD-L1 ANTIBODY IN LUNG CANCER IN VIVO

- Anti-tumor in Lewis Lung Carcinoma (LLC) model: 80% complete response, 20% partial response
- Development of immunological tumor-specific directed memory





EXTENSIVE STUDIES WITH ESTABLISHED ACTIVITY AND SAFETY PROFILE

- THIO has been shown to be synergistic *in vivo* with immune checkpoint inhibitors (standard-of-care immuno-therapy agents in oncology)
- THIO was active in cancer cells that are resistant to tyrosine kinase inhibitors (TKIs), checkpoint inhibitors, IL-2, IFNα, YERVOY® (ipilimumab) and chemotherapy
- THIO has shown eradication of tumor when administered in sequential combination with checkpoint inhibitors in *in vivo* syngeneic tumor models of lung, colorectal, and liver cancers

- THIO has been evaluated and shown high complete response rates and no recurrence in multiple tumor types:

IN VITRO:

Lung	Brain
Colorectal	Melanoma
Prostate	Liver
Breast	Neuroblastoma
Ovarian	Pancreatic
Head and Neck	

IN VIVO:

*Detailed data sets for in vivo/in vivo studies are available for further reviews