LIFE SCIENCES Insight contractions CLS Digital Magazine August 2022

Cancer Moonshot

California Life Sciences' Mission Critical Role in Defeating Cancer











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This issue of CLS' digital magazine, Life Sciences Insights, explores our sector's role in achieving the Biden Administration's Cancer Moonshot initiative. The articles explore the obstacles the life sciences industry faces, what this means for our member companies, and the advancements they are making to end cancer as we know it.

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California Life Sciences Sector Stands United to Achieve the Cancer Moonshot

Submitted by Mike Guerra, president & CEO, California Life Sciences



Pictured (left to right): Peter Kuhn Ph.D. of USC Michelson Center, Dr. Joseph Alvarnas of City of Hope, CLS CEO Mike Guerra, Jonathan Wosen Ph.D. of STAT News, Megan Hall Ph.D. of GRAIL, Stephen Pitt Ph.D. of Johnson & Johnson, Jorge Garces of Exact Sciences

In February, President Joe Biden announced a reignition of the Cancer Moonshot, highlighting two new goals: reduce the death rate from cancer by at least 50 percent over the next 25 years and improve the experience of people and their families living with cancer.

By August, California Life Sciences brought together more than 100 industry leaders to hear from oncology experts at the annual "An Evening with Thought Leaders" in Newport Beach.

We set out to do one thing-explore our sector's essential role in ending cancer as we know it. And the conversation started out with some harsh realities-we've been waging a war on cancer for 50 years, and while we've made significant progress, we're still losing 600,000 people a year. Most of those deaths are from cancers that don't have a recommended screening test at all. And many people receive a diagnosis well after their cancer has progressed.

Knowing these facts, it might surprise you to learn that the tone that night was one of optimism. One of the panelists, Dr. Joseph Alvarnas, vice president of government affairs at City of Hope, said nihilism in the face of cancer is unacceptable.

"Having audacious goals is absolutely defensible," Alvarnas said, reminding those in the audience that cancer deaths have gone down by more than 30 percent since the 1970s.

The panelists agreed that reaching the President's goals will take not only funding for therapeutic research and drug development, but prevention, early detection, and screening. It will also require advocacy and getting



Megan Hall, vice president of medical affairs, GRAIL

involved in legislation both to help patients and to protect the innovation ecosystem. Importantly, there's the essential task of improving profound health disparities and increasing access.

"These technologies are not going to be useful if we can't get them into the hands of the broader population, in particular the underserved, socioeconomically disadvantaged regions," said panelist Megan Hall, Ph.D., vice president of medical affairs at GRAIL. "There's a lot that needs to happen to ensure equitable access for diagnostics and therapeutics across the board."

They explored multi-cancer early detection as an emerging means of screening individuals for cancers that typical screenings might miss, or sending out CT scan

trucks to screen people where detection rates are low. The consensus was that no one technology or effort will detect or treat all cancers.

"If you're looking for sustainable solutions, you need to think about health care delivery in a radically different way," Alvarnas said. "We must serve everyone. We have to really engage communities and community leaders across the country in a much deeper way."

The moderator, STAT News' Jonathan Wosen, admitted he feared the hour-and-a-half time slot would be far too long and that we'd run out of things to say, but we could have talked all night. When the opportunity for questions came, nearly half the ballroom shot their hands up into the air.

And there's more to say. There are more questions to answer, problems to solve, and solutions to discover to achieve the Cancer Moonshot and its worthy goals. As you read this edition of Life Sciences Insights, you'll see the unique ways our member organizations are working in California to end cancer. You'll see how our state's life sciences sector is devoted and essential to achieving these goals that will lead to longer, healthier lives for all.

> For more information about CLS programming or its event portfolio, please contact emorgan@califesciences.org.

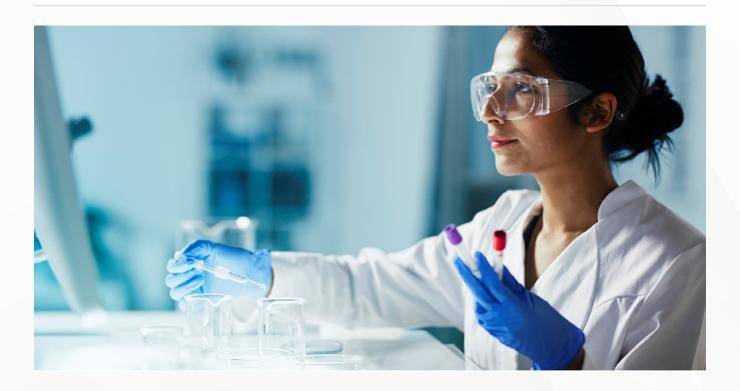


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Keeping Cancer Moonshot Goals in Sight, Guardant Health Continues Its Mission to Conquer Cancer

Submitted by Guardant Health



Guardant Health continues to lead the way in creating blood tests that help patients across all stages of cancer live longer and healthier lives. Our mission aligns with the goals laid out by the Biden-Harris administration in the "Cancer Moonshot." Putting innovative, blood-based technologies into the hands of patients and providers will bring us one step closer to achieving the goal of reducing cancer death rates by at least 50 percent over the next 25 years.

Detecting and diagnosing cancer sooner

Guardant Health believes high-sensitivity multi-cancer screening blood tests will have a significant impact in the reduction of cancer death rates. We've developed the technology to detect early-stage cancers with a simple blood test, and we intend to target cancers for which early detection and intervention can save lives.

Cancer underscreening is an important factor contributing to the high cancer mortality rate in underserved populations. Earlier this year, we launched Shield[™], the company's first blood-based screening test to detect early-stage colorectal cancer (CRC) in average risk adults. Today one in three adults have not completed the recommended screening, even though CRC is curable if caught early.¹ These CRC screening rates are even lower in minority populations—only 59 percent of Hispanics and 65 percent of African Americans are up to date with recommended screenings.² Our technology is also being studied in a <u>large registrational trial</u> to support its use in a test to screen for high-risk lung cancer. Despite clear recommendations, only 14 percent of people eligible for lung cancer screening are up to date with screening recommendations.³ Blood tests have the potential to overcome access barriers and bridge the gaps in screening compliance by incorporating blood-based screening as part of routine medical care with a simple blood draw.

Targeting the right treatments to the right patients

Through a blood test, we can identify cancer patients who have active residual disease after surgery. We can also detect early signs of disease relapse in cancer survivors, a population of nearly 17 million individuals in the United States today.⁴ Tailoring treatment and

interventions in patients with early signs of residual disease can improve cure rates and survivals.

Patients progressing to the advanced cancer stage are already benefiting from the power of groundbreaking blood tests, such as our FDA-approved Guardant360[®] CDx. Through a blood draw, a doctor conducts comprehensive genomic profiling of a patient's tumor at critical time points in their journey, and then matches them with the best available treatment option without the need for an invasive tissue biopsy.

Despite tremendous advancements in cancer care, genomic profiling of cancer is not being performed as frequently as needed. This is a major challenge for advanced cancer patients, especially in the Medicaid population, since genomic profiling can identify appropriately tested life-saving therapies for patients.

We believe simplifying and providing greater access to complete genomic testing throughout the cancer journey will dramatically increase access to important clinical information, lower overall cost and lead to significantly better clinical outcomes as more patients are matched with effective therapies. Legislation under consideration in California, SB 912, would help ensure all patients across the state have access to needed biomarker testing.

Access to innovation can address inequities

Reaching the goals established by the Biden-Harris Administration depends on the ability to ensure widespread adoption of medical breakthroughs like blood-based testing. Federal and state governments must advance legislation to make cancer screening and precision medicine more accessible, including access to new diagnostics and treatment for all patients.

Guardant Health is pioneering innovations in cancer care that have the potential to reach patients where they are and generate significant impact on patient outcomes. But each technical advancement we develop only matters if patients can access it, and that

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access depends on guideline bodies like the U.S. Preventive Services Task Force (USPSTF). The USPSTF issues evidence-based recommendations on which clinical preventive services, including cancer screening, Americans should receive. Health plans must cover preventive services that receive an "A" or "B" grade from the Task Force with \$0 cost-sharing for insured patients. For this reason, USPSTF recommendations are critical drivers of patient access and adoption.

However, the USPSTF only updates its recommendations every five years, so in the case of blood-based CRC screening, most Americans may not have access to this new technology until the USPSTF next reviews its CRC recommendation in 2026. Aligning USPSTF review cycles with the emergence of new scientific evidence would ensure USPSTF recommendations keep pace with

the speed of medical innovation. Earlier this month, Congresswoman Anna Eshoo (D-CA-18) and Energy and Commerce Chairman Frank Pallone sent <u>a letter to HHS</u> raising important questions on the USPSTF process. We're encouraged to see Congress' interest in this issue and we hope to work with policymakers, HHS, and the White House to ensure timely access to innovative cancer screening technologies for all Americans.

Guardant Health commends the renewed effort on the Cancer Moonshot and the entire healthcare community

for their commitment to the goals the initiative lays out. Mission success depends on patients at all stages of cancer living longer and healthier lives through the power of blood tests and the data they unlock.

Together, we can conquer cancer.

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Cedars-Sinai Cancer: Where Innovation and Diversity Meet

Submitted by Cedars-Sinai

As the nation's Cancer Moonshot initiative works to reduce the cancer death rate and improve the experience of people and their families surviving the effects of cancer, Cedars-Sinai Cancer is running in parallel to meet these same meaningful objectives.

"We integrate community outreach and engagement into our research using principles of convergent science—such as combining wearables, imaging, and organoid and computational models of disease—to develop novel insights into aspects of biology that are specific to race, ethnicity, sex and gender," said Dan Theodorescu, MD, PhD, director of Cedars-Sinai Cancer and the PHASE ONE Foundation Distinguished Chair. "This work is important to Cedars-Sinai Cancer and the patients we treat in our community—who are rich in ethnic and racial diversity—and it is critical to improving the global burden of cancer."

One of the most promising efforts underway at Cedars-Sinai Cancer is the "Molecular Twin" initiative.

This innovative approach harnesses the power of multiomics, big data and artificial intelligence to discover, develop and deliver personalized cancer treatment options. To do so, Cedars-Sinai experts create virtual replicas of patients' DNA, RNA, and other biomarker information to help identify the most effective approach to each patient's disease.

By creating these molecular twins, scientists can decode and classify cancer genes and proteins from tumors donated by thousands of patients. The goal: build a database that will be mined by investigators around the globe to discover novel treatments.



Dan Theodorescu, MD, Ph.D., director of Cedars-Sinai Cancer

"The dream of the 'Molecular Twin' initiative is to identify the best available therapies for a patient, while simultaneously identifying how cancer will affect each individual patient," said Theodorescu, who conceived of, and leads, the initiative.

Realizing this dream requires a concerted effort among Cedars-Sinai investigators, including those who work to develop cutting-edge computer algorithms—collaborators like Jason Moore, PhD, chair of the Department of Computational Biomedicine at Cedars-Sinai.

"These algorithms, developed by teams like those found in our Department of Computational Biomedicine, help us identify patterns across multiple different data types to diagnose, prevent and treat cancer," Theodorescu said.

The Molecular Twin initiative will also advance cancer care and research in underserved populations by enabling investigators to analyze how ethnic and racial disparities affect tumor biology and treatment among diverse populations.

This unique approach is a pillar of Cedars-Sinai's commitment to identify the best intervention for every

individual, taking into consideration ethnic and racial disparities in tumor biology and treatment.

"We have continued to weave a robust and innovative

cancer research enterprise, bringing new hope to the diverse populations we serve," said Robert Haile, DrPH, MPH, director of the Cancer Research Center for Health Equity at Cedars-Sinai Cancer. "Equity and inclusiveness are the keystones of an efficient healthcare system—and keystones of the Cancer Moonshot initiative—and we are proud to prioritize both."

Because of the medical center's location within Southern California, Cedars-Sinai Cancer professionals deliver healthcare to the most diverse population in the country.

In the spring of 2022, Cedars-Sinai Cancer held a first-of-its-kind LGBTQ+ cancer symposium, part of its effort

to equalize healthcare access and treatment for all. The enterprise offers gender-neutral cancer screening guidelines to better serve transgender and gender nonconforming subjects.

Cedars-Sinai Cancer is also taking a comprehensive approach to address the incidence of breast cancer in the Korean community.

"Our programs range from developing Korean-specific breast organoids to better understand the cause of disease, to community educational activities aimed at promoting cancer awareness among young Korean

"These algorithms, developed by teams like those found in our Department of Computational Biomedicine, help us identify patterns across multiple different data types to diagnose, prevent and treat cancer," Theodorescu said.

women," Haile said. "We also aim to address declining participation in cancer clinical trials in racial and ethnic minorities."

This work, done with the help of the Cedars-Sinai Cancer Clinical Trials Office, aims to address disparities within Cedars-Sinai Cancer using multicultural and multilingual enrollment navigators familiar with community and patient barriers that contribute to low enrollment rates.

According to Robert Figlin, MD, deputy director of Cedars-Sinai Cancer, patients have access to approximately 300 cancer clinical trials, many of which are geared toward racial, ethnic and gender minorities.

"To make meaningful change, we must continue to ask ourselves where the disparities are, then identify how best to address them," Figlin said. "While

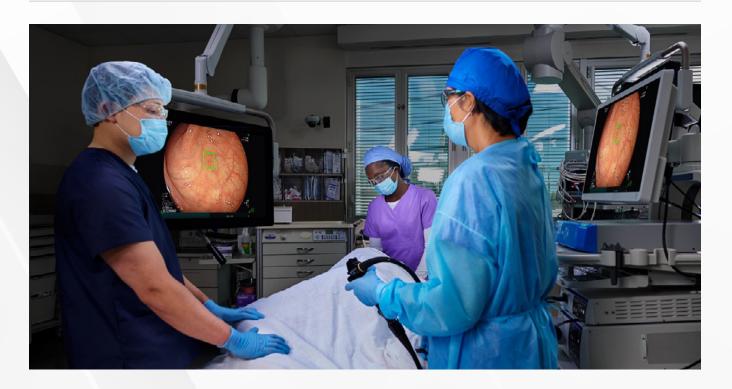
this process can be challenging, recognizing disparities is the first step to repairing them."

Innovation and diversity fuel each other at Cedars-Sinai Cancer.

"Ultimately, big data, machine learning and convergent science lead us to expand and diversify community programs, pursue innovative research, and launch clinical advances that improve and extend the lives of patients," Theodorescu said.

Aiming to Reduce Cancer Deaths, This Program Brings Screening Technologies to Low-Income Communities

Submitted by Medtronic



Medtronic and the American Society for Gastrointestinal Endoscopy (ASGE) are working to provide colorectal cancer screening technologies in low income and underserved communities across the United States through the Medtronic Health Equity Assistance Program for colon cancer screening, with support from Amazon Web Services (AWS). The initiative will include the donation of 133 Medtronic GI Genius[™] intelligent endoscopy modules to 62 facilities across the country that primarily serve communities with low screening rates or where access to the technology is not currently available. Black adults are disproportionately burdened by colon cancer, at greater risk of diagnosis, worse outcome and death.¹

"The crisis of health inequities cannot be solved without expanding access to healthcare technologies that put people first," said Geoff Martha, Medtronic chairman and chief executive officer. "We must begin with local efforts that consider the needs of the community. This program is an important step towards ensuring that our powerful technologies help reduce disparities, improve care and enhance patient outcomes." Certain types of colorectal cancer, when caught early, can have a five-year survival rate of up to 91%²; however, it remains the third most common and third deadliest cancer among adults in the United States. This program

can potentially improve the detection of polyps that can lead to colorectal cancer and could impact more than 500,000 patients over three years.

The GI Genius[™] intelligent endoscopy module, authorized by the FDA in April 2021, can visualize colorectal polyps of varying shapes and sizes in real time. It's the first-to-market, computer-aided polyp detection system powered by artificial intelligence (AI) that offers physicians a powerful screening and

detection tool in the fight to prevent colorectal cancer. In the first U.S. trial using GI Genius, <u>results published</u> <u>this spring</u> showed a 50% reduction in missed colorectal polyps with AI technology versus standard colonoscopy.³

"This initiative is so important because we know that almost half of all cases of post-colonoscopy colon cancer may be attributed to not catching polyps during the index colonoscopy,"⁴⁵ said Dr. Austin Chiang, M.D., M.P.H., chief medical officer of the Gastrointestinal

"The crisis of health inequities cannot be solved without expanding access to healthcare technologies that put people first."

business, which is part of the Medical Surgical Portfolio at Medtronic. "We have seen the impact that Al-assisted colonoscopies can have, and this study unequivocally demonstrates that this technology

> helps physicians better detect polyps during colonoscopies. The impact of missed polyps could ultimately be the difference between life and death when we consider that 90% of patients with colon cancer can beat it when it's caught early."⁶

> The American Society for Gastrointestinal Endoscopy, who led the submission and selection process for this program, <u>recently released</u> <u>their full list of recipients for donated GI</u>

<u>Genius</u> units.

The following facilities in California will be receiving GI Genius[™] modules:

- Adventist Health Sonora, Sonora
- Enloe Medical Center, Chico
- Harbor UCLA Medical Center, Torrance
- Los Angeles County University of Southern California, Los Angeles
- Riverside University Health System, Moreno Valley

2. https://www.cancer.net/cancer-types/colorectal-cancer/statistics

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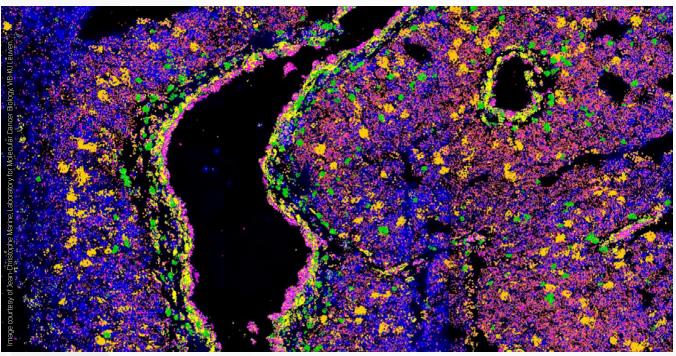
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Spatial Biology Can Help Beat Cancer, Here's How

Submitted by Jason Gammack, CEO, Resolve Biosciences



This Molecular Cartography™ image spatially resolves the distinct cell populations by using specific gene markers in the perivascular niche microenvironment in a mouse primary melanoma tumor.

In the last decade, advances from next-generation sequencing and single-cell analysis have transformed the cancer research and oncology treatment landscape. Targeted therapies are now frequently prescribed based on the genetic signatures of each patient's specific cancer, offering better outcomes than ever.

But even amid this surge of new molecular information about cancer, there has been one critical piece missing: the context of location. The biological neighborhood where a tumor lives is a unique place with unusual behavior and cellular interactions that must be thoroughly characterized in order to make the next big leap in progress against cancer. We cannot hope to truly defeat cancer until we understand the tumor microenvironment.

That's where spatial biology comes in. A new generation of technologies has finally made it possible to detect large numbers of genes and proteins in a sample *and* map them to their precise location in a biological microenvironment. Already, scientists are pursuing tantalizing new clues about how the proximity of certain cell types to each other or the physical interactions of expressed genes may help explain why a treatment works well for one patient's cancer but not another. Spatial biology offers a remarkable opportunity to identify new biomarkers, understand the interplay between tumor and immune cells, predict cancer progression, and analyze the effects of therapies based on spatially resolved molecular data. Despite this promise, spatial biology tools are still in their infancy. Much improvement is needed to map sufficient numbers of genes or proteins, to increase resolution for accurate detection of subcellular

structures and signals, to analyze more samples at a time, and to interrogate multiple elements (such as genes, proteins, and metabolites) with a single platform.

One of the newest commercial platforms in the spatial biology field comes from Resolve Biosciences, which offers a technology designed to detect as many as 100 genes even rare genes, down to a single transcript—from a biological sample. This Molecular Cartography approach is based on single-molecule fluorescent *in situ* hybridization (smFISH), in which

iterative rounds of direct imaging are performed as transcript-specific probes are added to the sample and light up when detected. Each color-coded dot in the resulting image shows exactly where all targeted

A new generation of technologies has finally made it possible to detect large numbers of genes and proteins in a sample and map them to their precise location in a biological microenvironment.

transcripts are present in the sample, down to subcellular resolution.

In general, spatial biology tools based on smFISH offer superior resolution and accuracy compared to

technologies based on sequencing data or other methods where location is inferred from a barcode rather than observed with direct imaging.

Resolve Biosciences is headquartered in Germany with a rapidly growing North American office and laboratory facility located in San Jose, California. Its team works closely with scientists in California and throughout the U.S. to enable new insights into cancer based on spatial biology, answering important questions that were not possible to address with previous technologies

and approaches. Already, Molecular Cartography has allowed researchers to make new discoveries about the tumor microenvironment in prostate cancer, melanoma, liver cancer, and more.

Here to make progress.

Cedars-Sinai Cancer Pioneers "Molecular Twin" Initiative to Advance Research and Care

At Cedars-Sinai Cancer, we deliver exceptional care to the most diverse population in the country. That means we make groundbreaking strides for communities often left behind in research.

One of those strides is our "Molecular Twin" initiative, a new multi-omic profiling of the patient and their cancer that uses the power of big data and artificial intelligence to accelerate cancer research and advance care. This technology creates virtual replicas of a patient and their tumor so that we can identify the best intervention for every individual, including taking their ethnic and racial profiles into account.

Paired with our evidence-based community outreach, we're helping today's patients with tomorrow's treatments to end cancer as we know it.

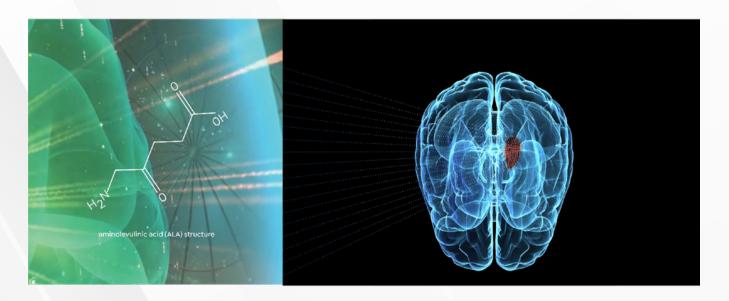
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SonALAsense is Advancing a Novel Technology for Treatment of the Most Challenging Cancers

Sonodynamic therapy shows great promise to treat intractable brain tumors.

Submitted by SonALAsense



 Medical science has made tremendous headway against cancer, but there is still a long way to go. Chemotherapy and radiation have helped many patients, but their side effects can be debilitating, and their impact often wanes over time. Immunotherapies can also be quite effective, but they only help a relatively small number of patients. Targeted therapies inhibit cancerdriving genetic variations, but like chemotherapy and radiation, tumors often become resistant.

SonALAsense is working to overcome these challenges with a novel, noninvasive technology platform called sonodynamic therapy (SDT). It could provide a new option for patients with glioblastoma, diffuse intrinsic pontine glioma (DIPG), pancreatic, ovarian and many other cancers.

What is Sonodynamic Therapy (SDT)?

The Cancer Moonshot supports novel ways to fight cancer and SDT is indeed innovative. SDT utilizes SONALA-001 (a drug called 5-aminolevulinic acid or ALA), which is required for heme synthesis but when delivered to tumors in excess, disrupts their heme metabolism. All our cells need heme to survive, but while normal cells self-regulate their ALA intake, fastgrowing tumors rarely say no when provided with extra amounts of ALA. Such tumor cells have a hard time fully metabolizing ALA, and accumulate high concentrations of protoporphyrin, a highly reactive heme precursor. In SDT, noninvasive focused ultrasound energy targets the tumor and is absorbed by protoporphyrin, which then transfers the energy to molecular oxygen in the cell, producing reactive oxygen species that selectively destroys the cancer cells.

SDT is a promising anti-cancer therapy for several reasons. Although SonALAsense's initial clinical indications are deadly brain cancers, the same quirk in heme metabolism is seen in cancers arising from the lining of tissues (carcinomas). Because of this, SonALAsense will next target pancreatic and ovarian carcinomas with SDT. Since these cancers also require ALA for their own heme metabolism, they are unlikely to develop resistance to SDT over time.

In September 2021, SonALAsense and the Ivy Brain Tumor Center in Phoenix, Arizona, announced positive results for a phase 0/1 clinical trial for recurrent high-grade gliomas (rHGG).

and induced cell death in rHGG and was well-tolerated in patients. SonALAsense will begin recruitment in a phase 2 study of SDT in recurrent glioblastoma in the coming months.

> In addition, SonALAsense was awarded a \$2 million National Cancer Institute (NCI) grant to support its Phase 1/2 SDT trial for DIPG led by Roger Packer, M.D., at Children's National Hospital. The trial will assess safety and tumor size reductions.

> This public/private partnership between NCI and SonALAsense created a path forward for a novel therapy against a rare pediatric disease that has virtually no treatments.

The Cancer Moonshot

The Deadliest Cancers

SonALAsense is deploying SDT against two incredibly deadly brain cancers: glioblastoma multiforme and DIPG. Glioblastoma is the most common brain tumor, but treatments have hardly improved over the past 50 years. The five-year survival rate is under 7%.

DIPG is a rare pediatric cancer that diffuses through the pons. The only current standard of care treatment is radiation, which slows the disease but cannot stop it. Only 10% of children with DIPG survive two years.

In September 2021, SonALAsense and the Ivy Brain Tumor Center in Phoenix, Arizona, announced positive results for a phase 0/1 clinical trial for recurrent highgrade gliomas (rHGG). SDT generated oxidative stress SonALAsense and the Cancer Moonshot both embrace America's innovative drive to find new pathways against cancer. Joining this network would help SonALAsense pursue other indications, in the same way the NCI grant supported an SDT trial for DIPG. By providing the necessary resources to pursue difficult work, the Cancer Moonshot both boosts cancer research and expands its horizons.

At present there are four anti-cancer modalities: surgery, chemotherapy, radiation and targeted therapies. If the potential of SDT is borne out, it could become a fifth modality, providing a radical new approach to address many of the most intractable cancers.



Through Advocacy and Cell Therapy, Gilead Aims to Reduce Disparities and Revolutionize Cancer Care

Submitted by Michael Boyd, SVP of government affairs and policy, Gilead Sciences



The effects from cancer on our families and communities is devasting. Although we've made great strides in reducing rates of mortality and improving the quality of life for cancer patients and their caregivers, there's more work to be done. That's why we were excited to see the Cancer Moonshot Initiative reignited and support its goals to cut the death rate from cancer by at least 50 percent over 25 years and improve the experience of people and their families living with and surviving cancer.

At Gilead and Kite, we're committed to improving the lives of those impacted by cancer and pursuing systemic change that improves care for everyone. We have proven success in bringing curative treatments to patients in virology and strengthening health systems to improve equitable access to care, and we're driven to create similar success in oncology.

Reducing disparities in triple-negative breast cancer (TNBC)

Disparities in TNBC are pervasive. TNBC is an aggressive form of breast cancer that <u>disproportionally impacts</u> <u>Black, Hispanic, and younger women</u>. TNBC is <u>aggressive, often diagnosed at later stages, and</u> <u>presents a higher chance of becoming metastatic than</u> other types of breast cancers. Black women have <u>three</u> <u>times</u> higher odds of being diagnosed with TNBC, are at an <u>increased risk</u> of being diagnosed at later stages, and have the <u>lowest survival rate</u> at each stage of diagnosis compared to white women.

It's crucial to address barriers to care and treatment faced by women with TNBC. In response, Gilead has

supported a policy white paper series authored by leading breast cancer organizations to examine the state of health disparities and inequities in TNBC, amplify the voices of patients, and identify areas for policy change to improve early detection and survival.

The Cancer Moonshot Initiative serves as a vehicle to drive change, presenting an opportunity to seek policy reform to improve patient access to transformative medicines. Gilead has a deep commitment to advancing solutions that improve outcomes of

people faced with life-threatening illnesses, and we are excited to build on this experience to further support the goals of Cancer Moonshot.

The policy white paper series on TNBC inequities can be accessed here:

- Screening and Diagnosis by Tigerlily Foundation
- Care and Treatment by Susan G. Komen
- Patient Support, Wellbeing, and Treatment by Cancer Support Community

Revolutionizing cancer care with CAR T-cell therapies

Kite, a Gilead Company, is driven every day by its singular focus of cell therapy to treat and potentially cure cancer. Kite is deeply committed to developing the next generation of cell therapies and grounded in the shared goals of the Cancer Moonshot Initiative. CAR T-cell therapy is literally a "living treatment" in that it is individually created for each patient using their own cells. Harnessing the power of a person's own immune system to target and attack their cancer, CAR

Kite's innovation can

only have impact if

it reaches patients

at scale, and our top

priority is bringing CAR

T-cell therapy to every

eligible patient as early

as possible in their

treatment journey.

T-cell therapy is a truly transformative one-time treatment that has seen momentous advancement in the last five years alone. From the early days of treating a few hundred patients and dismissed as science fiction, today CAR T-cell therapy is a proven FDA approved treatment for thousands of patients with many different kinds of blood cancers. While more trials are completed with long-term follow-up and real-life success stories build, Kite is already changing the way cancer is treated.

Earlier this year, Kite received approval of the first CAR T-cell therapy for second-line large B-cell lymphoma, upending high-dose chemotherapy and stem cell transplant as a decades-long standard of care for some patients and fundamentally changing the way people think about cancer treatment for advanced blood cancers. We are hopeful that as the data matures, CAR T cell therapy will be used not as an attempt to delay progression, but as a potential cure.

Kite's innovation can only have impact if it reaches patients at scale, and our top priority is bringing CAR T-cell therapy to every eligible patient as early as possible in their treatment journey. We are committed to developing innovation that reflects the aims of the Cancer Moonshot by ensuring the right treatments are given to the right patients and speeding progress against some of the deadliest and hard to treat cancers.

Multi-Cancer Early Detection Tests Will Be Key to Achieving the Cancer Moonshot

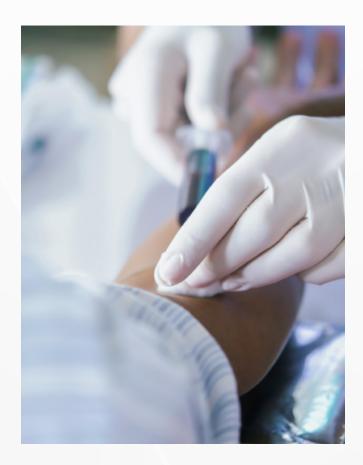
Submitted by Megan Hall, vice president of medical affairs, GRAIL

When President Biden reignited his Cancer Moonshot agenda earlier this year, he highlighted the critical role of early detection in achieving the ambitious-but-attainable goal of reducing the cancer death rate by at least 50 percent in the next 25 years. Importantly, the President's plan recognizes that the rigorous study of multi-cancer early detection blood tests (MCED), to date, has brought us to a crucial inflection point, where detecting many cancers at once is now an essential pillar of any effort to end cancer as we know it.

Let's take a step back and explore what multi-cancer early detection is, and why it is featured so prominently in both the cancer expert and bipartisan policy maker vision for the future of cancer care.

About 40 percent of Americans receive a cancer diagnosis in their lifetimes, amounting to more than 600,000 American deaths in an average year. Cancer represents a "chronic pandemic," in which we need new tools to improve quality of life, reduce persistent disparities, and bend the cancer mortality curve.

But early cancer detection is suffering from a common ailment in medicine and public health: the streetlight effect. We are looking for five cancers "over here," under the streetlight where we have five individual screening tests, but 70 percent of cancer deaths are occurring "over there," in the dark where we aren't even looking



for cancer. We simply are not detecting enough cancer in the population through existing screening tools, meaning most cancers are still detected only when symptoms present, which means the cancer is usually late stage and has often already spread, and when outcomes are generally poor.

New technology can extend the benefits of cancer screening and early detection to more cancers. Multicancer early detection tests simultaneously screen for more cancers, and can detect them at earlier stages, before symptoms have appeared and when there is a better chance for successful treatment. These blood tests, including GRAIL's Galleri® test, are fundamentally different from existing single-cancer screening approaches in that they leverage next-generation sequencing and machine learning technologies to look for a shared cancer signal in the blood, allowing for simultaneous screening for and—in the case of Galleri localization of multiple cancer types.

GRAIL has initiated what we believe is the largest clinical program in genomic medicine to-date. Our clinical development program consists of studies that collectively include more than 325,000 participants—likely the largest linked datasets of genomic and clinical data in the cancer field. We are partnering with hundreds of highly respected institutions for evidence generation, from Sutter Health in California all the way to the United Kingdom's National Health Service. Validated by a portion of these studies

that includes more than 21,000 participants, Galleri® is now being adopted by forward-leaning health systems, employers, and physician practices.

One of the most exciting examples in our clinical development program is a public-private collaboration with the U.S. Department of Veterans Affairs (VA) Veterans Health Administration, America's largest integrated health care system, and the Veterans Health Foundation, to provide GRAIL's groundbreaking MCED blood test to 10,000 veterans over the next three years through our real-world evidence program. As the largest national integrated health system in the U.S., the VA delivers unparalleled care to our veterans, many of whom are at elevated risk of developing cancer.

Our clinical development program consists of studies that collectively include more than 325,000 participants—likely the largest linked datasets of genomic and clinical data in the cancer field.

An estimated 1.2 million veterans who have used VA health care since the beginning of fiscal year 2021 have received a cancer diagnosis, with too many caught in late stages. This exciting public-private partnership,

> among others, is expected to make a real impact on veterans' lives through earlier diagnosis of cancer.

Multi-cancer early detection tests will enable us to dramatically increase cancer detection through population screening, and this greatly improve public health. We feel a tremendous responsibility and urgency to make this groundbreaking technology available to patients and providers to help meet the ambitious Moonshot goals, and we stand with policymakers who are dedicated to meaningfully addressing

the burden of cancer on patients, loved ones, and communities through early detection.

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Prostate Cancer Lab Convenes a Crowd to Help Advanced Cancer Patients with Complex Testing and Treatment Decisions

Submitted by Brad Power, Founder, CancerHacker Lab



Brian McCloskey has advanced prostate cancer. He's been through the standard of care: a prostatectomy, radiation, and androgen deprivation therapy—multiple lines of treatment over seven years. He responded to the treatments, but his PSA is rising again, indicating that his cancer is resisting the latest treatment. With biomarkers identified from DNA and RNA sequencing, and help from Cancer Commons, CureMatch, and Massive Bio, he has identified 21 viable treatment options. But the question remains—which one should he take, and should he combine them in some way?

Problem: many cancer patients face complex decisions

Some cancer patients (like me) are lucky. They get a diagnosis (lymphoma) and there's a standard treatment (a chemotherapy cocktail) that leads to a durable response. Other patients, like Brian, get the standard of care, and it fails to hold the cancer back. Once they are beyond the standard of care, or if there is no standard of

care that has good outcomes, physicians and patients face complex decisions.

Solution: bring a crowd to help make complex decisions

At CancerHacker Lab, we bring together a diverse crowd of patients, diagnosticians, molecular biologists, bioinformaticians, researchers, and physicians across institutions in a hackathon and health learning system to help advanced prostate cancers patients make complex testing and treatment decisions.

Our community provides several services for patients, like answers about their testing and treatment strategy and best next options, a consumer's guide to testing, and a learning system for future advanced cancer patients on what works. CancerHacker Lab also collaborates

across the existing cancer review boards at various hospitals and academic research centers to share experience, insights, and outcomes.

This unique process gives patients hope. When they're told there's nothing more that can be done for them, Prostate Cancer Lab offers other possible treatment options. While tests and treatments may not succeed,

Our community provides several services for patients, like answers about their testing and treatment strategy and best next options, a consumer's guide to testing, and a learning system for future advanced cancer patients on what works.

this process helps patients and their medical teams feel confident knowing what they learn will provide the best shot at a durable response. This process also encourages education. Everyone in the Prostate Cancer

> Lab community is constantly learning about the best tests, treatments, and experts in the field.

Complication: accessing and adopting new tests

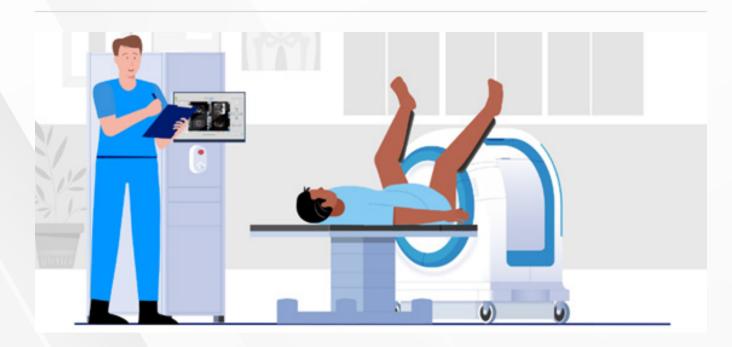
There is great promise for personalizing cancer treatment decisions by using new tests (beyond DNA sequencing), such as RNA sequencing, proteomics, liquid biopsies, and functional drug testing, but most patients don't know about them, and most clinicians either don't know about them, how to use them, or have the time to pursue them.

Breaking down barriers: increasing awareness

The Cancer Moonshot could increase awareness and rally support for a truly patient-centered approach that's focused on the complex navigation that advanced cancer patients face, not a slight improvement to a process which benefits industry incumbents like pharma, payers, and providers.

Supporting the Fight Against Prostate Cancer with Promaxo's New, Portable MRI-Guided Technology

Submitted by Promaxo



Since the first prostate cancer case was diagnosed back in 1853, the incidence rate has increased exponentially to become the second leading cause of death among men. The <u>American Cancer Society</u> projects new prostate cancer cases will surpass 268,000 by the end of 2022, with almost 35,000 deaths. President Biden's <u>Cancer Moonshot</u> 2.0 has been reinvigorated to address all types of cancer, and Promaxo is working hard to support this worthy initiative in the prostate cancer arena.

Promaxo's MRI and MRI-guided ecosystem, consisting of imaging, robotics¹, and artificial intelligence (AI), are all being designed to optimize healthcare system performance and quickly achieve the goals of the Cancer Moonshot program. The Team aims to improve patient experience, enhance clinical experience, and enable better outcomes in a more cost-effective manner.

Advancements in screening and diagnosis

Current prostate cancer screening methods like digital rectal exams (DREs) and prostate-specific antigen (PSA) tests have significant drawbacks. These methods routinely produce false positives, leading to avoidable procedures that are costly and may include unwanted side effects. To address this, Promaxo is taking a complete solution approach to manage the entire prostate cancer care continuum by uniquely combining MR-imaging, robotics¹, and AI in a compact machine to aid in the diagnosis through biopsies, treatment, and eventual screening¹ of prostate cancers.

The device improves patient experience by making use of the world's first truly open, low-field MRI to eliminate claustrophobia and guide targeted prostate interventions in the physician's office or outpatient facility while maintaining the same quality of care as a high-field MRI in a hospital or imaging center.

This ability to perform MR-guided procedures at the point of care allows healthcare providers (HCPs) to use data to diagnose aggressive prostate cancers more accurately. Subsequently, physicians using this

approach can make informed decisions on which cancers to treat and which ones to monitor.

Developing personalized medicine options

Once diagnosed, Promaxo's technology enables physicians to develop personalized prostate cancer care plans using its open MRI architecture by selecting the most suitable course of treatment. A few options include whole gland ablation, radiation, focal treatment, or robotic interventions to remove the prostate completely.

Promaxo's in-office MRI-guided biopsy offers clinically superior diagnostic yield compared to the current standard of care TRUS approach: 71% cancer detection rate and identifies 23% more clinically significant cancers () Gleason 3+3)². Not only that, the technology breaks down the barrier of high capital and operational expenses (vs traditional MRIs) by enabling direct access to MRI for Urologists in their office.

Overcoming obstacles and challenges

Making progress in any field comes with challenges. Finding and treating cancer is no exception. Promaxo is breaking new ground every step of the way, facing both technical and non-technical challenges in the path to commercialization. Nevertheless, their leadership has hand-picked a world-class team of experts who

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of treatment.

remain laser-focused and dedicated to bringing this new MRI-guided technology to market.

The availability of comprehensive prostate cancer data along with device insights is currently lacking, and when made available, empowers HCPs to accurately identify prostate cancer at an earlier stage when it is still treatable. Using this data, providers will treat only those patients who truly need it most, while enrolling others into an <u>active surveillance</u> program. This will help offer peace of mind and

maintain the quality of life for patients and their families.

Leveraging partnerships and agreements

Promaxo has formed both industry and clinical partnerships which aim to build out the company's commercial pipeline. To support this goal, the organization is leveraging significant expertise in A.I. and individual health data analytics to advance its screening, diagnostic, and treatment capabilities on the technical side. Multiple clinical partnerships have been formed that enable Promaxo to collect anonymized data to help train the next generation of computer-aided diagnostic and tissue characterization tools.

Driving meaningful participation

At Promaxo, the opportunity to participate in the Cancer Moonshot effort fulfills our employees' long-standing passion for helping others. Each team member brings their personal experiences with cancer to the table, driving meaningful participation in this remarkable initiative. The team is all working to achieve change for the better and is proud to be a part of making that change happen.

^{1.} Not yet cleared by the FDA.

^{2.} Promaxo data on file.

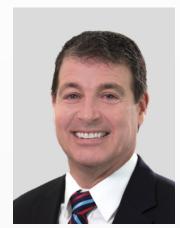
The Power of Data Visualizations with Aggregated Data

Submitted by Veranex

Data visualizations can be a powerful tool to investigate, understand and present insights into cancer studies. Clinical data visualization helps to tell stories by curating data, making it easier to understand and highlight trends. In a non-small cell lung cancer usability study, the use of visualization tools was found to increase understanding of study results using 28% less time than if a standard presentation was used.¹ When taken with the availability of large amounts of data, the opportunity to improve analytics for clinical trials from patient recruitment needs to genetic biomarker-cancer interactions can be enhanced. But this shift to using 'big data' contains challenges. What are these challenges and what are the benefits of visualizations through the use of aggregated data, especially for oncology trials?

Benefits and challenges of data visualizations

Data visualization is the graphical representation of information and data. Effective data visualization is a delicate balancing act between form and function. The plainest graph could be too boring to catch any notice, or it may reveal a powerful point; the most



Richard Murg, Senior Vice President of Business Development, Veranex Solutions

stunning visualization could utterly fail at conveying the right message or it could speak volumes. The data and the visuals need to work together, and there's an art to combining great analysis with great storytelling.

Benefits and challenges of aggregate data

In clinical research, data can be collected in the cloud in a centralized repository designed to aggregate, process, and secure clinical data across compounds, indications, and programs, using structured and unstructured data. Data from wearables and other data sources and systems (EDC, IRT, ePRO, labs, excel files) can be incorporated. Aggregating clinical data affords clinicians the ability to study data from different domains and sources, current and historical.

However, there may be a temptation to bring in all available data, which can yield a 'data swamp,' with data that has quality issues or is of a size resulting in poor performance optimization. Additionally, lack of data governance can expose users to data that they should not see whether it is blinded data or from an era for which the viewer does not have responsibility or relevant knowledge.

Data visualizations, aggregated data, and use in clinical trials

Using visual elements like charts, graphs, and maps, data visualization tools provide an accessible way to see and understand trends, outliers, and patterns in data. For oncology studies, relating RECIST scores to dosing, AEs to age, or biomarkers to diagnosis across all or a subset of studies can be accomplished prior to a more structured statistical analysis. Visualization software such as Power BI, Spotfire and Tableau have a user-friendly interface and capabilities that can empower users to make data-driven decisions, while maintaining study blind and user permissions. Data from SDTM data sets of closed studies can serve as historical data. This data is maintained by the sponsor as it is submitted to the regulatory authorities. Ongoing study data can be incorporated to form real time data upon which to generate visualizations. There are different mechanisms to bring this into the data, but it is normally accomplished by periodic FTP transfers or real time API integrations.

In summary, the ability to generate effective visualizations on aggregate data can be a powerful tool for clinical trial research.

Veranex is an experienced partner in generating visualizations from aggregate data for our sponsors. We are here to help.

 Tong,M; Hsu,W; Taira, R, 2017, Evaluating a Novel Summary Visualization for Clinical Trial Reports: A Usability Study, AMIA Annu Symp Proc, 03-Aug-2022, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5333215/



How One Nonprofit is Developing a Test to Determine If Immunotherapy Will Work Before Treatment Begins

Submitted by The Jackson Laboratory



Immunotherapy can be a crucial tool for patients undergoing cancer treatment, vastly improving outcomes for many.

Yet everyone's immune system is unique, and responses to the same therapy—including success rate and detrimental side effects—may vary greatly from patient to patient based on each individual's immune system differences. How can immunotherapy be most effective when every person has a different reaction?

James Keck, Ph.D., the scientist leading product development at The Jackson Laboratory's JAX® Mice, Clinical & Research Services (JMCRS), is working to answer that question. At JAX's Sacramento-based campus, Keck is creating mouse-based experimental platforms that enable pharmaceutical researchers to simultaneously evaluate both the safety and efficacy of a given treatment. Keck is working to develop tests for these drug treatments using a specific patient's immune cells and the genetic profile of their tumor. To do this, he works with immune-deficient mice developed at JAX, which may be supplemented with human stem cells or immune cells for the purpose of replicating the human immune system in a mouse for studies of cancer, as well as immunology and infectious diseases such as HIV-AIDS or COVID-19.

"Our ultimate goal is to know, before treatment even begins, which drugs are going to be efficacious, and which are going to have a toxic side effect," Keck said. In new research conducted with a pharmaceutical partner, published in abstract form in *The Journal* of *Clinical Oncology*, Keck tested two similar

immunotherapy drugs to evaluate clinical success in relation to liver toxicity, a serious, potentially fatal side effect. The study yielded important findings related to dosage and an overall conclusion that preclinical safety assessment using humanized mouse models as used for these studies could be an important step in the course of the development of novel immunotherapy for the safety of patients, as well as mitigating drug

"Our ultimate goal is to know, before treatment even begins, which drugs are going to be efficacious, and which are going to have a toxic side effect," Keck said.

development cost. The research builds on Keck's earlier work testing immune therapies like pembrolizumab, the cancer immunotherapy known by the trade name Keytruda for efficacy targeting different tumor types.

Recognizing his tremendous contributions to accelerating drug development, Keck was recognized in 2021 as JAX's first-ever President's Innovation Fellow. The award highlights scientific impact and economic value created through research and product development at the global biomedical

research institution.

Research like Keck's, which builds on JAX's world-renowned mouse models and bridging partnerships with the pharmaceutical world, has the potential to lead to pivotal drug discoveries and spark new startup companies dedicated to improving human health.

Keck has devoted his career to leading drug discovery efforts that may

improve people's disease prognoses and may help countless patients lead healthier lives.

"The role of the immune system is wide across many therapeutic areas," he said. "And we're just scratching the surface in understanding on how these cells can be targeted to improve human health."



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Ending Cancer Starts with a Culture of Sustainable Innovation

Submitted by Protagonist Therapeutics



There are at least 137 different blood cancers, and no one strategy to address them all. Some studies have suggested blood cancer survival rate has reached 70% over the last five years. That adds up to hundreds of thousands of hours of life for patients—a huge victory that speaks to the extraordinary value that can be delivered by innovation. But more than a third of blood cancer patients still do not survive five years after their diagnosis, and advanced blood cancers remain some of the most difficult to treat. Solving for this next level challenge will require not just a culture of disruptive innovation, but one of tenacity and unwavering long-term commitment from multiple disciplines, individuals, and companies.

Protagonist Therapeutics, a drug innovation company in the midst of a decade long journey to fulfill unmet needs of patients with cancer and other disease, is tackling polycythemia vera (PV). Affecting about 100,000 patients in the US, PV causes excessive production of red blood cells. It can lead to fatal thrombotic events if left untreated.

Protagonist's journey started with the discovery of Rusfertide, a novel mimetic of the natural hormone hepcidin, which regulates iron absorption, storage, and distribution in the body. Today, Protagonist is conducting a 250-patient phase 3 registrational study for PV.

"As they say, it takes a village, and that has certainly been true for Protagonist in the context of Rusfertide," Protagonist CEO Dinesh Patel, PhD, said. "Our team has collective expertise in the discovery, development and commercialization of more than a dozen innovative drugs, and all of that has been put to great use to arrive at multiple drugs including Rusfertide. Over nearly four

decades in the life sciences, our team has learned what it takes to build an innovation ecosystem that can be sustained over the many years it takes to generate a new and sometimes unconventional idea and bring it to commercial reality."

Here is some of what Patel shared:

1. Begin with bold science that has the potential to deliver exponential value to patients. Protagonist

was founded on the idea that mother nature is the best teacher and innovator of new medicine. Protagonist focused on naturally occurring peptides—a natural bio-defensive mechanism in a wide variety of living organisms, plants, and animals—as a starting point for drug discovery. Using computational tools, its scientists created and screened large virtual libraries of conformationally constrained peptidic scaffolds and integrated them with other tools such as molecular biology and medicinal chemistry. That's what led to the discovery of Rusfertide.

"But for us, it was never about a single program," Patel said. "The company's leadership team has maintained unwavering belief and committed investment to our platform to deliver a continuum of product innovation."

Protagonist has applied it to develop agonists and antagonists of a diverse array of difficult targets—cytokines, cytokine receptors, integrins, transmembrane solute transporters, GPCRs, and ion channels. In addition to Rusfertide for potential treatment of PV, the company also has two other novel drug candidates in clinical development, one of which is partnered with Janssen Pharmaceuticals of Johnson & Johnson.

 Prioritize diversity of talent. Getting to best outcomes when working in unique and challenging disease indications requires going beyond classical approaches. It means bringing together diverse scientific talent with a singular focus on unmet need. Protagonist focused on continuously building competency in computational science,

"The company's leadership team has maintained unwavering belief and committed investment to our platform to deliver a continuum of product innovation."

molecular biology, peptide chemistry and medicinal chemistry. Unlike the popular approach of speeding up drug discovery and development,

> the company's leadership team believes that delivering differentiated innovation *at scale* requires the patience to develop expertise in multiple areas as well as the discipline to work together as a coordinated engine, rather than in silos. And while scientific diversity is at the heart of the company's approach, it's the diversity of talent that Patel said enables success.

"It comes from cultivating an environment where people are valued both for their individual areas of expertise and their ability to work in a coordinated way toward a common purpose," he said.

3. Work with humility and commitment. Solving for cancer and other diseases is one of the world's worthiest pursuits. When aiming for truly audacious goals, high standards and accountability to continual progress are key. But setbacks and wrong turns should also be expected and welcomed along the way. Rusfertide's clinical journey started with a rare disease called beta-thalassemia, but the company pivoted to PV after determining the drug was better suited to its treatment. This has enabled the Protagonist team to stay humble, grounded, and truly focused on the long-term objective of getting new medicine in the hands of people who need it the most.

With its goals of investment in the NIH and NCI, development of the Cancer Cabinet and other initiatives, the Cancer Moonshot represents a comprehensive commitment to build a national culture of *sustainable* innovation to end cancer. Like so many companies in the California life sciences ecosystem, Protagonist is proud to contribute to the aims of the Cancer Moonshot through its work to address PV and other diseases.

A New Approach to Achieving Anti-Tumor Effects While Reducing Toxicity

Submitted by Ascendis Pharma

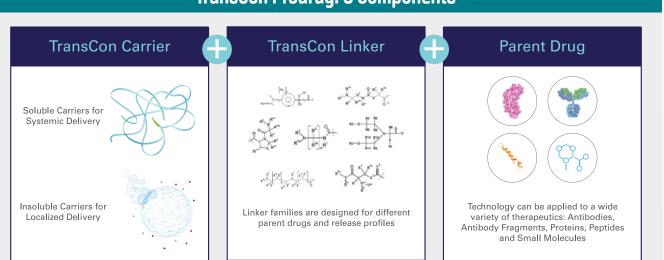
Over the last few decades, groundbreaking oncology research has accelerated our understanding of cancer biology and the mechanisms involved in these devastating diseases, leading to the development of new treatments that have transformed cancer care. Yet many such treatments, including cancer immunotherapies, share a common challenge: dosing at levels that work against the cancer present unique toxicity risks¹ and the potential for later health problems.

An innovative approach

Building on its success with TransCon[™] technologies to develop innovative endocrinology rare disease therapies, Ascendis Pharma is also pursuing its vision to create best-in-class therapies in oncology.

TransCon, or "transient conjugation," is the name for the company's unique ability to temporarily (transiently) link an inert carrier to a parent drug with known biology, for release in the body over time under normal physiologic conditions. Depending on the carrier and choice of parent drug, TransCon prodrugs can be designed to be given systemically (throughout the body) or locally (e.g., inside the tumor) to exert the desired anti-tumor effects.

TransCon molecules have **three components**: an unmodified parent drug with known biology, an inert carrier that protects it, and a linker that temporarily binds the two. When bound, the carrier inactivates and shields the parent drug from clearance. Once injected,



TransCon Prodrug: 3 Components

Ascendis Pharma's TransCon platform for drug development combines known biology with the benefits of prodrug and sustained-release technologies with the goal of optimizing therapeutic effect. Once injected (systemically or locally), physiologic conditions in the body initiate the release of the active, unmodified parent drug in a predictable manner at a predetermined rate.

physiologic conditions in the body initiate the release of the active, unmodified parent drug in a predictable manner at a predetermined rate.

A powerful, flexible technology platform that uses advanced knowledge of chemistry to overcome challenges of developing new therapeutics, TransCon is widely applicable to proteins, peptides or small molecules in multiple therapeutic areas.

Applying TransCon technologies to clinically validated targets offers the potential to increase the likelihood

of success by improving outcomes currently limited by suboptimal efficacy and systemic toxicity, and could also help accelerate timelines to the clinic.

Targeting the cancer immunity cycle

Today, Ascendis Pharma is developing systemic and intratumoral product candidates that target different aspects of the cancer immunity cycle, with the goal of enhancing anti-tumor effects by providing sustained

TransCon molecules have three components: an unmodified parent drug with known biology, an inert carrier that protects it, and a linker that temporarily binds the two.

modulation of tumor microenvironments and activation of cytotoxic immune cells.

By enabling sustained release from one day to months (depending on the product candidate and treatment goal), therapeutic levels can be maintained without the need for frequent administration, avoiding high peaks in circulating drug levels. In this way, TransCon drugs are being designed for prolonged exposure of drugs at efficacious levels, without reaching the high levels of toxicity that often complicate oncology treatment regimens.

Making a meaningful difference for patients

The team at Ascendis Pharma believes that TransCon is well-suited for oncology applications given the large number of validated targets with known limitations and the potential to treat more patients with new combination and multi-agent regimens that otherwise would not be feasible. The result could be solving the limitations of current treatments to ultimately help improve patient outcomes.

1.

In "A review of cancer immunotherapy toxicity" (CA: The Cancer Journal for Clinicians, 16 January 2020) authors Lucy Boyce Kennedy, M.D. and April K. S. Salama, M.D. note that "Cancer immunotherapies.... have transformed treatment algorithms for numerous tumor types [but] lead to unique toxicity profiles distinct from the toxicities of other cancer therapies...."

An Urgent Commitment to Confront the Complexities of Cancer

Submitted by Bristol Myers Squibb



Bristol Myers Squibb (BMS) is united by a single mission: transforming patients' lives through science by discovering, developing and delivering innovative medicines that help them prevail over serious diseases.

As a leader in cancer research with a legacy of developing life-changing medicines, BMS has actively engaged in several collaborations aimed at making significant progress against cancer since President Biden first launched the Cancer Moonshot as Vice President in 2016, including:

A partnership between the National Cancer Institute (NCI) and at least 20 drug and biotechnology companies to expedite researchers' access to investigational and approved medicines.

- The National Institute of Health's Partnership for Accelerating Cancer Therapies, a five-year public-private research collaboration focused on accelerating the development of new cancer immunotherapy strategies for more patients.
- The Strategic Computing Partnership between the Department of Energy and the NCI to Accelerate Precision Oncology, which brings together nearly 100 cancer researchers, care providers, computer scientists and engineers to apply the nation's most advanced supercomputing capabilities to accelerate cancer research.

Today, BMS continues to unravel the complexities of cancer and develop new therapies for patients with significant unmet need. At R&D sites in San Diego and the Bay Area, the company is investigating novel ways to enhance and restore the body's ability to fight cancer.

"A broad array of approaches is necessary to match the many ways cancer co-opts or evades the immune system and develops resistance to current therapies,"



said <u>Neil Bence</u>, vice president, head of Oncology Discovery at the BMS Oncogenesis Thematic Research Center in San Diego. "Collaboration has always been essential to enhancing our understanding of cancer and to our ability to discover innovative and transformative medicines for patients in need."

Leadership from BMS attended the Cancer Moonshot Goals Forum at the White House earlier this year to exchange ideas, expertise and perspective on driving innovation in cancer care. Critical to scientific progress is ensuring fair and equitable access to novel therapies.

When BMS announced a \$150 million, five-year investment to accelerate <u>five inclusion and diversity</u> and health equity commitments in 2020, it included a commitment to increasing clinical trial diversity. Science and research will better reflect the patient populations most impacted by cancer—ultimately helping to improve cancer treatment and patient outcomes for underserved communities.

Approximately 80% of people enrolling in clinical trials conducted in the U.S. today are white. Current clinical trial practices often exclude other groups, such as people with disabilities. In California, BMS conducted activities to support 157 clinical trials at 439 study sites in 2021.

With a strategy centered around the patient experience—from screening and early diagnosis, to access to quality care and innovative medicines, BMS has started by addressing who the investigators are and where the clinical trials are run in its approach to increase clinical trial diversity.

By the end of 2022, 25% of BMS clinical trial sites will be located in highly diverse communities. In addition, the Bristol Myers Squibb Foundation has developed the <u>Robert A. Winn Diversity in Clinical Trials Award</u> <u>Program</u> which will train more than 250 diverse clinical investigators. The company also launched the Disability Diversity in Clinical Trials initiative in July 2022 to address the participation of people with disabilities in clinical trials.

BMS is confident that by breaking down the barriers to clinical trial participation with thoughtful and long-term approaches, the company will effect real change and deliver on its R&D mission while supporting the goals of the Cancer Moonshot.



Small Molecules That Modulate Protein Assembly as a Game-Changing Strategy for the Cancer Moonshot

Submitted by Prosetta Biosciences

Cancer comprises the second most frequent cause of death in the United States with 602,350 fatalities in 2020. While lung cancer is the leading cause, responsible for nearly 25% of all cancer mortality, more than 100 different types of cancer have been characterized that contribute to this figure. It has been proposed that ascribing all proliferative disorders to the same blanket term "cancer" overlooks the diversity of possible causes and consequences of disease. Cancer can affect a variety of organs and tissues, from the brain to the blood. It may be attributable to an underlying mutation in the patient's DNA, to a cancer cell's metabolic reprogramming through epigenetic mechanisms, or to a patient's underperforming immune system. Its impact on the patient may be benign or lethal. However, one commonality between all cancers is the crucial role played by protein assembly,-

the largely overlooked dimension of intermolecular interactions falling between gene expression and the formation of functional multiprotein complexes.

At Prosetta Biosciences, we have been working to develop small molecules which modulate protein assembly. The small molecules which have been identified through our screens, including our anticancer compound PAV-951, have shown remarkable properties. The data indicate that assembly modulation is a new mechanism of action with the potential to be advanced into novel, next generation therapeutics— a worthwhile venture for the Cancer Moonshoot to get involved in.

When screened in the Eurofins OncoPanel[™] for anticancer activity, PAV-951 was found to have dose-dependent tumor cytotoxicity in 15 different human cancer cell lines- A172 (male human glioma), BFTC-905 (female human urinary bladder transitional cell carcinoma), COR-L105 (male human lung adenocarcinoma), DB (male human b-cell lymphoma), FaDu (male human pharynx squamous cell carcinoma), H9 (male human t-cell lymphoma), Hs 294T (male human melanoma), MCF7 (female human breast cancer), MDA MB 436 (female human breast cancer), MeWo (male human melanoma), MHH-PREB-1 (male human b-cell lymphoma), SJSA1-OSA (male human osteosarcoma), SU-DHL-10 (male human b-cell lymphoma), SW1353 (female human chondrosarcoma), and U-2 OS (female human osteosarcoma). This data indicates that pan-cancer therapeutics could be developed from our oncology hit compounds.

The anti-cancer activity of PAV-951 has been validated in a xenograft study, where a human A549 non-small cell lung cancer tumor was grafted onto Athymic

Nude mice and treated with either vehicle, PAV-951, Gemcitabine- an FDA approved drug for non-small cell lung cancer. After 14 days, PAV-951 inhibited tumor growth by 72% relative to the vehicle control, performing comparably to Gemcitabine which inhibited growth by 84%. This data indicates that the anti-cancer properties of PAV-951 are not artifacts only attributable to toxicity in cell culture.

We hope to become part of the Cancer Moonshoot effort in order

to advance a chemical series based on PAV-951 into a viable cancer drug. We believe that the demonstrated activity in multiple human cancer lines—derived

The data indicate that assembly modulation is a new mechanism of action with the potential to be advanced into novel, next generation therapeutics a worthwhile venture for the Cancer Moonshoot to get involved in.

from an array of tissues as well as genders, ages, and ethnicity, indicates that the unique mechanism of PAV-951 is broadly applicable to many forms of

> cancer. Since we have already verified that the anti-cancer activity observed in cell culture corresponds to tumor reduction in an animal model, we are optimistic that a chemical series based on PAV-951 could be developed into a pan-cancer therapeutic.

Becoming a part of the Cancer Moonshoot efforts would provide us with support for the costs of synthetic organic chemistry, screening, and other IND-enabling studies on PAV-951 and its chemical

analogs. This would have the potential to substantially decrease the burden of cancer mortality and bring a next-generation therapeutic into fruition.



The next issue of the CLS digital magazine, Life Sciences Insights, will be published in December. For advertising and content submission guidelines, please contact Alex Burch at <u>aburch@califesciences.org</u>

About California Life Sciences (CLS)

California Life Sciences (CLS) is the state's most influential and impactful life sciences membership organization, advocating for the sector and its diverse innovation pipeline. For more than 30 years, CLS has served the community by supporting companies of all sizes, from early-stage innovators and startups to established industry leaders in the fields of biotechnology, pharmaceuticals, and medical technology. As integral components of a healthy and collaborative ecosystem, CLS also works closely with universities, academic and research institutions, the investment community, and other critical partners that promote this vibrant sector. With offices in South San Francisco, San Diego, Sacramento, Los Angeles, and Washington DC, CLS works to shape public policy, improve access to breakthrough technologies, educate lawmakers, and advance equity within our ecosystem by championing innovative solutions for some of the most pressing challenges of our times. In doing so, CLS fulfills its mission to protect and nurture California's life sciences industry, empowering discoveries that lead to healthier lives around the world. Visit CLS at www.califesciences.org, and follow us on Twitter @CALifeSciences, Facebook, LinkedIn and YouTube.



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