CORPORATE NEWS

MASSIVEBIO

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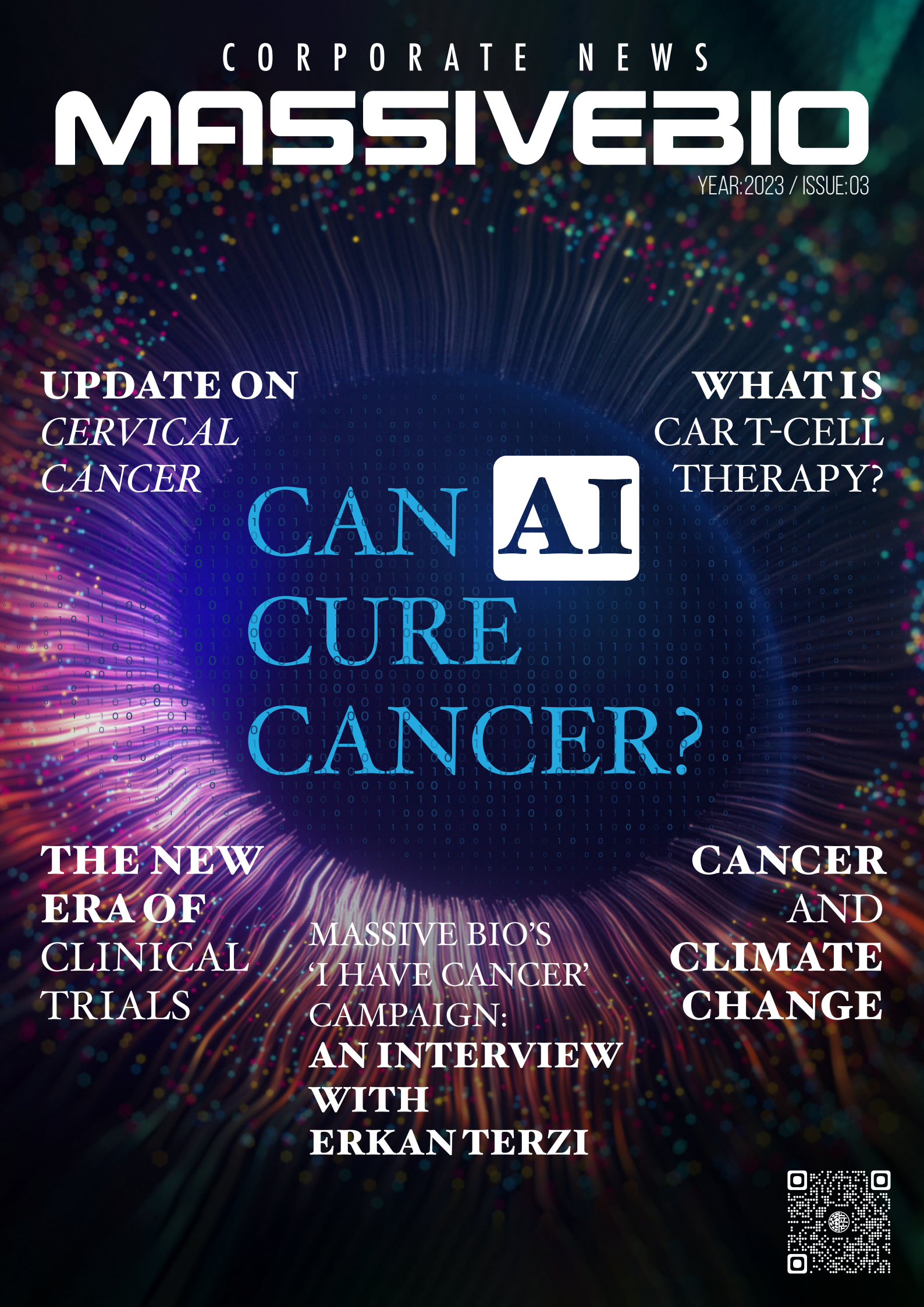

UPDATE ON *CERVICAL CANCER*

WHAT IS CAR T-CELL THERAPY?

CAN AI CURE CANCER?

THE NEW ERA OF CLINICAL TRIALS

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CANCER AND CLIMATE CHANGE

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MASSIVEBIO

A MESSAGE FROM SELIN

Welcome to the third issue of *Massive Bio* magazine, which arrives at the start of a new year that we believe will exceed the excitement and accomplishment of 2022. To be sure, the past 12 months were a remarkable time of growth for Massive Bio. Notably, the company achieved an important milestone last year when we onboarded the 100,000th cancer patient to our platform—nine months ahead of schedule. Massive Bio also developed new partnerships with many patient advocacy groups, as well as several other companies in this space, all with the goal of helping more cancer patients find their clinical trial. In late 2022, we launched "I Have Cancer" (#Ihavecancer), a social media campaign aimed at increasing awareness about cancer and giving voice to patients coping with this disease. (You can learn more about "I Have Cancer" in an interview with Erkan Terzi, Massive Bio's chief marketing officer, on page 18)

Looking ahead, we plan to continue growing, with the goals of adding new team members and expanding our global footprint, supporting 100 clinical trials by the end of 2023, and onboarding 250,000 cancer patients by the middle of 2024. In the months to come, we will also develop more partnerships, as well as launch a new platform that takes our company in a new direction outside of the world of clinical trials—think of it as Massive Bio 2.0.

Of course, none of this would be possible without the many patients who turn to us for guidance and support, and the tremendous faith and belief of our customers. On behalf of everyone at Massive Bio, I'd like to wish you all a happy and prosperous 2023.

Selin Kurnaz
PhD, Co-founder and CEO

Massive Bio News Briefs

Massive Bio CEO Selin Kurnaz is Featured in the *Wall Street Journal*

Massive Bio CEO and Co-Founder Selin Kurnaz, PhD, was featured in an article about current venture funding challenges facing the biotech industry that appeared in the *Wall Street Journal* in December. The article, by *Journal* reporter Brian Gormley, noted that by mid-December of last year, U.S. biotech companies had received $29.7 billion in funding, down from the record high of $38.7 billion in 2021. Yet even as funding became more difficult for companies to secure, Massive Bio has obtained $23.3 million in venture capital, Kurnaz told the *Journal*. She added that the company is now seeking $50 million in new funding to finance new programs, including one that matches patients to drugs. Kurnaz said she was optimistic, overall, because venture firms have money to invest and that, as a revenue-generating company, Massive Bio has market traction. Yet she also expressed concern that venture firms will try to take advantage of their current position. "We are a real company, not a story company on a PowerPoint," Kurnaz told the *Journal*. "Are you going to be able to evaluate me fairly? If the answer is yes, I will work with you."

Massive Bio Launches 'I Have Cancer' Campaign

In keeping with its mission to improve the lives of cancer patients, Massive Bio aims to raise mass awareness about cancer, cancer treatments, and clinical research with "I Have Cancer," the company's new social media campaign. "I Have Cancer" will focus on the problems experienced by cancer patients and their loved ones while bringing attention to the importance of cancer prevention. Learn more about the "I Have Cancer" campaign in an interview with Massive Bio Chief Marketing Officer Erkan Terzi on page 18.

THE WALL STREET JOURNAL
WSJ

KP MORGAN

SELIN KURNAZ, PHD WAS A KEYNOTE SPEAKER

at the 8th Annual CMPRR Summit, *in a session titled*

"Disrupting Oncology Clinical Trial Enrollment With AI and Services."

Nov 22nd-23rd Barcelona, Spain

Selin Kurnaz Delivered a Keynote Speech at the 8th Annual CMPRR Summit

Massive Bio CEO and Co-Founder Selin Kurnaz, PhD, delivered a keynote speech at the 8th Annual Clinical Monitoring and Patient Recruitment Retention (CMPRR) Summit, which was held in Barcelona, Spain, on November 22-23, 2022. CMPRR brings together clinical and medical professionals seeking new ideas and tools for clinical monitoring and patient recruitment and retention. Sessions presented during the two-day event examined the role of technologies such as the Internet of Things and artificial intelligence (AI), quality standards, compliance oversight, risk-based and centralized monitoring, clinical monitoring, and new approaches to patient engagement, among other critical topics.

In her address, titled "Disrupting Oncology Clinical Trial Enrollment with AI and Services," Kurnaz shared her vision for what the future could hold for the enterprise of evaluating the safety and effectiveness of novel cancer therapies. "I imagine a world where, when a patient has been diagnosed with cancer, at that moment in time there is an intervention and a cancer patient has been prescreened for a clinical trial," said Kurnaz. Attaining the goals of increasing access to and enrollment in oncology clinical trials will require overcoming significant barriers, however, such as lack of access to trial sites, underrepresentation of demographic minorities in trials, and underuse of next-generation sequencing to identify candidates for new targeted oncology therapies.

Massive Bio's AI-based platform and concierge-level services are helping to minimize and eliminate those barriers, explained Kurnaz. Moreover, she added, "it's very important to be able to monitor and collect outcomes from these patients." Not only does monitoring and data collection provide essential data about the patient's response to an investigational therapy, but analytics can provide insights that can help improve the patient experience in clinical trials and aid in design of future trials. "Massive Bio has the motivation and aspiration to bring the knowledge that we accumulate from the data, the technology, and the monitoring of those patients over time to further enhance and enrich further the drug development process in oncology clinical trial enrollment," said Kurnaz.

Massive Bio Supports Cancer Associations

Massive Bio has launched "Donation for Life," a new awareness campaign that will support cancer associations and foundations in the United States and Europe. During the campaign, Massive Bio will select different organizations that support cancer patients to be recipients of donations. The campaign will continue for a year, with updates announced on Massive Bio's website and social media platforms. Massive Bio officials aim to provide thousands of donations by the end of 2023 and hope that "Donation for Life" will inspire other companies to support cancer associations and foundations.

"We believe cancer associations and foundations are vital in educating patients about cancer and specific aspects of the disease, such as participation in clinical trials. That's why we are partnering with these groups to provide them the financial and operational

Arturo Loaiza-Bonilla, MD, MSEd
CO-FOUNDER AND CHIEF MEDICAL OFFICER, MASSIVE BIO

New Podcast

Massive Bio's Efforts to Make Clinical Trials More Accessible for Cancer Patients

support to further accelerate and expand their efforts," said Selin Kurnaz, chief executive officer and co-founder of Massive Bio. "The burden of cancer is so large that it can't be resolved by one organization, and our role is to be the glue to bring multiple stakeholders together to fight this very unfortunate disease together, one patient at a time."

One of the biggest problems that cancer patients face is difficulty making their voices heard, added Erkan Terzi, Massive Bio's chief marketing officer. "Foundations and associations are the most effective organizations working to protect patients' rights, make their voices heard all over the world, and support the struggle of patients to make treatments accessible," said Terzi. "Moreover, these organizations rely heavily on volunteers and often have modest budgets. At Massive Bio, we continue to work to erase cancer from the map. In this way, it will always be our priority to support and collaborate with organizations working toward the same goal."

Massive Bio Co-Founder Appears on 'The Scope of Things' Podcast

Massive Bio Co-Founder and Chief Medical Officer Arturo Loaiza-Bonilla, M.D., joined *Clinical Research News* senior writer Deborah Borfitz on her podcast, "The Scope of Things." Describing Massive Bio's efforts to make clinical trials more accessible to cancer patients, Loaiza-Bonilla said that 85% of patients were unaware that clinical trials were an option at the time of diagnosis, 80% of trials did not meet enrollment timelines, and two-thirds of oncology trials had low enrollment. "As nearly 2 million people are diagnosed annually, the underutilization of cancer research as a viable treatment option has quickly become a worrying problem," said Loaiza-Bonilla. "One of the first hurdles we face in cancer is that many patients do not have a detailed conversation with their medical oncologist."

Many cancer patients are reluctant to enroll in clinical trials because they believe that participating in one will prevent them from receiving the traditional standard of care, which is a misconception. "You're never put in a position where you don't get the right treatment," Loaiza-Bonilla reassured listeners, emphasizing the importance of educating patients about clinical trials and helping those who want to participate in one to find and enroll in the right study. "If the patient is familiar with potential clinical trials—before their first appointment—then it will encourage trial adoption and the patient's enrollment to participate in the trial. You can increase it by 50%." Loaiza-Bonilla explained how Massive Bio's artificial intelligence-powered platform matches cancer patients to oncology clinical trials, regardless of where they live.

Massive Bio Reaffirms Global Growth Strategy with Key C-Suite Hires and Executive Director Appointments

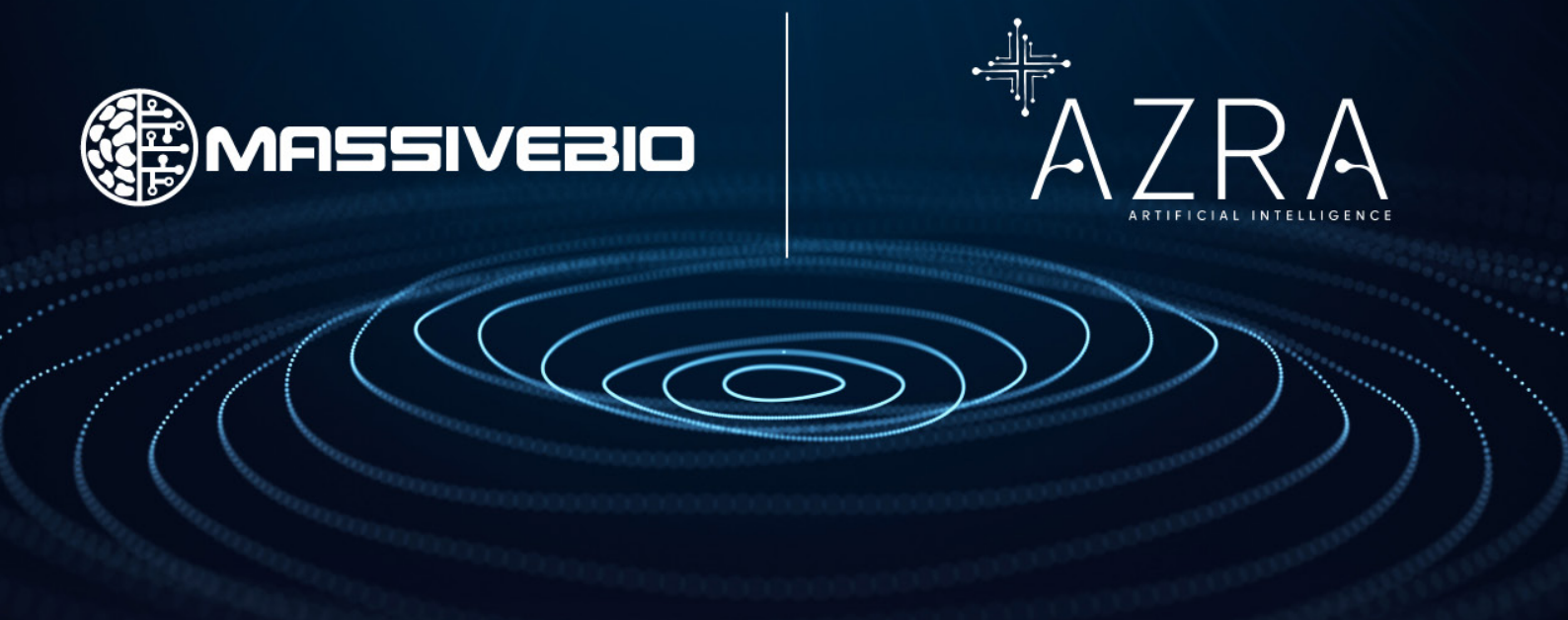
In December, Massive Bio announced the addition of two executives to its C-suite. Verily veteran Özgür "Oz" Huner joins as Massive Bio's first Chief Product Officer, and Erkan Terzi has been promoted to Chief Marketing Officer. Both executives will report to CEO and co-founder Selin Kurnaz and work alongside co-founders Chief Medical Officer Arturo Loaiza-Bonilla and Chief Technology Officer and Chief Operating Officer Cagatay Culcuoglu in leading and driving Massive Bio's product and growth strategy.

Huner and Terzi bring robust leadership experience and strong legacies of success to the company. Oz brings more than 20 years of experience leading development of clinical and genomics products for cancer research and treatment. His prior roles include Molecular Products Lead at Verily Life Sciences, Alphabet Inc.'s research organization devoted to the study of life sciences, and extensive prior leadership experiences in oncology and genomics solutions at Sema4, QIAGEN, Genomic Health, Lifelabs, NexJ and Deloitte. Oz will lead the development of scalable product management processes to support Massive Bio's accelerated growth and catalyze development of novel software and data products to enable new opportunities in the clinical trials value chain.

Terzi oversees creative and brand marketing, advertising, public relations, product management, digital marketing, and business intelligence. Erkan has extensive experience in developing and managing innovative marketing programs for many leading brands, including Allianz, Comcast Spotlight, LG Electronics, and Aselsan, and has led Massive Bio through a successful growth period. Terzi has also authored several marketing books.

"Our mission is to create hope and empower cancer patients by helping them find the best treatment options, which often requires urgent access to trials," said Selin Kurnaz, co-founder and CEO of Massive Bio. "This is a monumental point in time where advanced technology is intersecting with medical science to meaningfully change lives. The addition of these highly seasoned experts will be instrumental in pushing the envelope in our mission as we move into 2023 and continue to execute on our strategic priorities."

The new hires are an outcome of Massive Bio's latest $16.5 million funding round, which brought the company's total raise to $23.3 million from its inception. The latest round of investors were Revo Capital, Kenan Turnacio-



glu, IFC (World Bank), DEG-Deutsche Investitions-und Entwicklungsgesellschaft mbH, TFS Services, ImpactAssets, and SiteGround Capital. The global nature of their investors helps Massive Bio to capture the global oncology clinical trial enrollment market and further accelerates its multi-country expansion plans.

In addition to the C-suite additions, Massive Bio hired Gretchen O'Neill as Executive Director of Clinical Operations, overseeing program management, client relations, and strategic partnerships. A PPD veteran, O'Neill has extensive experience in patient recruitment and retention, supporting top pharmaceutical and biotech companies, leading a best-in-class project management organization, governance-level client management, and oversight of study service delivery.

"Massive Bio's strategy and commitment to individuals diagnosed with cancer sets us apart," O'Neill said. "The care factor for the people we help is unrivaled and it comes from the top down."

The company also announced the addition of David Henka as Director of Global Strategic Partnerships. Henka will be tasked with expanding Massive Bio's relationships with payors, self-insured employers, health systems, research networks and other collaborators to provide access to cancer clinical trials from anywhere in the world. Henka served as the Senior Director of Partnerships and Business Development at Memorial Sloan Kettering Cancer Center, leading cancer screening, awareness, prevention, and High-Risk Surveillance Management (HRSM) for employers and plan sponsors. Henka brings decades of experience consulting with employers and health plan sponsors on a wide range of employee benefit issues, including plan design, benefit strategies, funding, and plan management.

"Oz, Erkan, Gretchen, and David bring proven track records of expertise in building strong product, growth, business and technology teams for market-leading companies in the oncology and clinical research industry, and will enable Massive Bio to continue its hypergrowth towards becoming the leading global AI-powered company in cancer clinical trials," said Arturo Loaiza-Bonilla, MD, Massive Bio's chief medical officer.

Massive Bio and Azra AI Partner to Expand AI's Potentially Lifesaving Impact on Cancer Patients

Last November, Massive Bio announced a strategic partnership with Azra AI, a healthcare technology company that uses proprietary AI software to identify cancer diagnoses in real time and accelerate the patient care process. Combined with Massive Bio's ability to surface personalized clinical trial options for patients, the two companies working together provide early identification and precise treatment options, further improving cancer clinical care.

Today, clinical care teams have limited bandwidth to review important diagnostics like patient pathology reports. Each report takes a clinician one to two minutes to read, delaying trial opportunities for patients with an urgent life-changing health situation. Azra AI's technology, used in over 200 hospitals including HCA Healthcare, reads pathology reports in a fraction of a second, enabling clinicians to focus on the approximately 10 percent of positive pathology reports immediately to treat patients sooner and give them the best chances for survival.

"Our mission is to create hope and empower cancer patients by helping them find their best treatment options, which often requires urgent access to trials," said Selin Kurnaz, co-founder and CEO of Massive Bio. "We are excited to collaborate with Azra AI and expand our growing ecosystem of like-minded leaders who are as committed to transforming cancer clinical trials as we are. This is a monumental point in time where advanced technology is intersecting with medical science to meaningfully change lives."

Where Azra AI focuses on identification of cancer, Massive Bio's platform provides cancer patients with relevant clinical trials using AI, empowering patients to find treatment options faster and enabling life sciences companies to conduct broader, more-inclusive, population-based recruitment rather than traditional site-specific recruitment. The companies' collaboration has the potential to make an immediate impact on thousands of cancer patients – Azra AI's technology touches nearly one in 10 cancer patients in the U.S. while Massive Bio recently announced onboarding more than 100,000 patients onto its trial matching platform.

By utilizing AI technology in cancer identification and trial matching, clinical care teams can improve healthcare access and equity by eliminating unconscious bias or human errors that can prevent successful patient enrollment. Further, healthcare teams can automatically operationalize the volumes of data collected to enhance the patient experience in ways they could not do before.

"We are eager to partner with Massive Bio to connect these two parts of the cancer journey," said founder and CEO of Azra AI, Chris Cashwell. "We can revolutionize the clinical trial process by automating the identification of potential patients early on using artificial intelligence. We are combing through millions of pathology reports and identifying cancer types more quickly. The data sent to Massive Bio's platform closes the loop on serving that patient the best treatment options for their cancer. This enables our clinical teams to focus on cancer care and use the AI to offer the best patient experience."

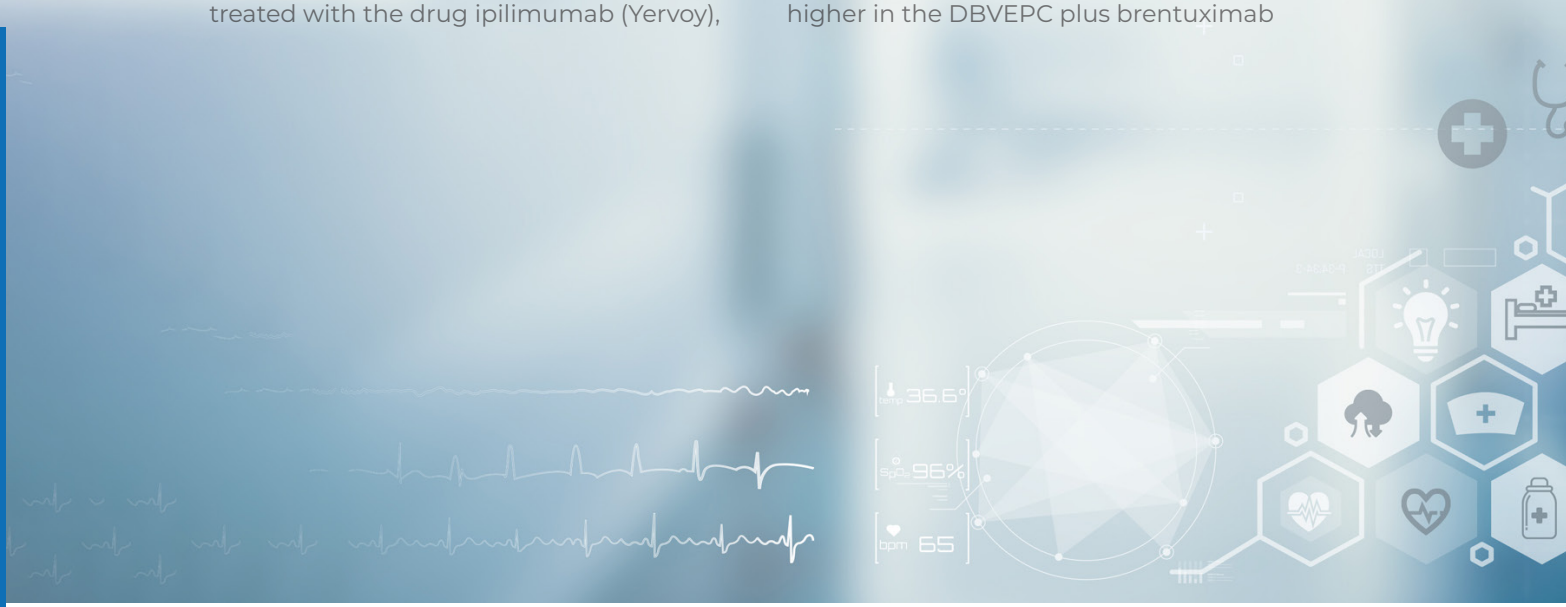
Clinical News

First Phase III Trial of T-cell Therapy in Solid Tumors Shows Promise

T-cell therapy can be highly effective in the treatment of certain blood cancers, but it has been a greater challenge to show benefit for patients with solid tumors. However, in December a team of doctors in the Netherlands reported the first successful use of T-cell therapy in a phase III randomized clinical trial involving patients with advanced melanoma in the *New England Journal of Medicine*. The form of T-cell treatment they used is called tumor-infiltrating lymphocyte (TIL) therapy. In TIL therapy, a doctor removes a sample of tissue from a tumor and sends it to a lab. Protective cells called T lymphocytes that have managed to infiltrate the tumor, or TILs, are removed from the malignant tissue and grown to increase their numbers to billions. The patient undergoes chemotherapy, then TILs are infused back into his or her bloodstream with the goal of waging a massive onslaught against the tumor. In the Dutch study, 49 percent of patients with metastatic melanoma who were treated with TILs had their metastases shrink; in one in five patients, the metastases disappeared altogether. Compared to other patients in the trial treated with the drug ipilimumab (Yervoy), those given TIL therapy were 50 percent less likely to die or have their disease worsen. The company that makes this form of TIL therapy is working with the FDA toward the goal of getting it approved for the treatment of advanced melanoma.

Targeted Therapy Offers Hope in Pediatric High-Risk Hodgkin Lymphoma

In what many doctors are calling a "paradigm shift" in practice, adding the targeted therapy brentuximab vedotin (Adcetris) to standard chemotherapy improved survival and reduced the risk of relapse, death, or second cancer in pediatric patients with Hodgkin's lymphoma. This important finding, reported in the *New England Journal of Medicine*, comes from a study of 587 patients aged 2 to 21 with untreated advanced Hodgkin's lymphoma who were randomly chosen to receive one of two regimens: the standard pediatric regimen of doxorubicin, bleomycin, vincristine, etoposide, prednisone, and cyclophosphamide (DBVEPC) or DBVEPC plus brentuximab vedotin. At an average follow-up of 42.1 months, event-free survival (time during which cancer didn't return or get worse) was nearly 10 percentage points higher in the DBVEPC plus brentuximab



vedotin group. There was also a 59 percent reduction in the risk of relapse, death, or second cancer in this arm of the study. Side effects were similar in both groups. The U.S. Food and Drug Administration approved brentuximab vedotin for children 2 and older in this patient population last November, the first time the drug was approved for pediatric patients.

Think Twice About CBD Oil for Cancer Symptoms

If you have been considering CBD for managing side effects of cancer treatment, a recent study may dampen your enthusiasm. CBD, or cannabidiol, is a substance in marijuana that is now available in many retail outlets and online in various forms, such as oils, capsules, and even gummies. CBD does not produce a feeling of euphoria, or a "high," but it is widely used to treat nausea, vomiting, pain, insomnia, and other symptoms common in people undergoing cancer treatment. However, evidence that CBD has medicinal benefits is uneven. In a recent study published in the *Journal of Clinical Oncology*, researchers at the Mater Research Institute in Queensland, Australia, recruited 144 patients with advanced cancer to participate in a clinical trial: half took 400 milligrams of CBD oil daily, while the others got empty placebos. After a month, there was no difference in the two groups, suggesting that CBD had no effect on quality of life or symptoms such as fatigue and nausea. However, many of the participants in both groups said they felt better or much better during the trial, which suggests that people who insist CBD eases their symptoms may be experiencing a placebo effect.

'Basket' Trial Yields Exciting Results for Biomarker-Based Therapy

A growing number of oncology clinical trials are taking a novel approach: Instead of including patients who have the same cancer, researchers are recruiting patients with diverse cancers that are linked to a common gene mutation. Known as "basket" trials, these studies evaluate the benefits of treatments that target specific gene mutations. At a conference in Barcelona, Spain, last October, a team reported the results of a basket trial evaluating a drug called ipatasertib, which blocks a protein called ATK. Normally, ATK promotes healthy cell growth, but a mutated version known as AKT1 E17K is linked to a small number of breast and endometrial cancers, as well as some other solid tumors. The trial included 32 patients with various cancers that had failed to respond to multiple therapies. After taking ipatasertib (in pill form) for a month, over half of the patients (56 percent) had stable tumors (meaning they had not worsened) and 22 percent of the patients' tumors shrunk. A larger study is necessary before ipatasertib can be approved and recommended for treating cancer patients with this mutation, but this study helps to validate the concept of targeting biomarkers in cancer treatment.

CAN AI CURE CANCER?

Artificial intelligence is reshaping our lives. While it's helping researchers in the quest for a cure for cancer, it's already having an impact on oncology in many ways, such as driving Massive Bio's clinical trial matching platform.

Artificial intelligence is rapidly becoming ubiquitous in daily life as the force that operates everything from the digital assistant that you ask to check the weather to self-driving cars that increasingly fill the highways. To be sure, sometimes there seems to be no limit to the promise of what "AI" can do. But is this technology powerful enough to achieve a goal that has eluded humankind for centuries—find a cure for cancer?

That's a tall order, of course, and it's probably best to think of AI as an invaluable tool that scientists can use in conducting cancer research to process huge amounts of information rapidly and find patterns in data that may not be apparent to the human eye. If and when researchers find a cure for cancer, AI will undoubtedly play a vital role.

Yet AI is already transforming the treatment of cancer, and no less an authority than the U.S. National Cancer Institute (NCI) is bullish on its promise. "Integration of AI technology in cancer care could improve the accuracy and speed of diagnosis, aid clinical decision-making, and lead to better health outcomes," states the NCI on its website. Here's a look at what lies ahead for AI in cancer care—and how it's already being used today, including by Massive Bio to help patients gain access to innovative new oncology treatments.

What is AI?

AI is technology that gives machines the ability to process information in a manner that closely resembles human thought. AI-based software uses algorithms—which are sets of rules used for problem solving—to interpret data, predict outcomes, and make decisions. There are different subtypes of AI, which include machine learning (ML). This form of AI allows computers to recognize and adapt to patterns in the data it processes, teaching

itself to become even "smarter," without any input from humans. When you ask Siri or Alexa to recommend some new music and the digital assistant picks out a song you love, that's ML at work. However, as you will see, oncology researchers have higher aspirations for the potential of ML and other forms of AI.

Imaging and Lab Studies

The U.S. Food and Drug Administration has approved a number of AI-powered medical devices, which includes imaging tools that are already changing how malignant tumors are detected and evaluated in some hospitals and clinics. AI technology is also in development that could enhance the ability of pathologists to analyze tissue samples to detect cancer. While AI is unlikely to eliminate the need for radiologists, pathologists, and other healthcare professionals who interpret the results of imaging and lab tests, recent studies suggest that AI-based tools can be integrated into practice to help reduce human error and lighten the burden of overworked doctors.

For example, researchers at Tulane University in New Orleans, Louisiana, used more than 13,000 slide images of colorectal cancer from 8,803 patients to "train" an ML program to recognize a malignancy. When put to the test, the program identified colorectal cancer with 98 percent accuracy, which was slightly better than human pathologists scored, according to a 2021 study published in *Nature Communications*.

In another study, researchers at the University of Massachusetts Medical School trained an AI program to read mammograms, then fed it 131 mammograms of women with breast cancer and 154 mammograms of women who were cancer free. The AI tool identified cancer more accurately than each of five human breast imaging specialists; on average, the AI tool was 14 percent more accurate at correctly spotting a breast tumor. Another study demonstrated that radiologists who worked with an AI program improved their ability to identify breast cancer from benign masses on ultrasound images by 37 percent. An earlier study found that an AI tool was more accurate than pathologists at identifying cervical cancer.

Decision Making

Doctors have been interested in using computer technology to aid in decision making about patient care since as far back as the 1970s, but the idea has only begun to flourish recently with growing interest in AI technology. Importantly, adding AI to the equation when diagnosing and treating cancer can help doctors personalize therapy to the patient, based on his or her unique profile.

For example, recent studies suggest that AI can help doctors select the optimal therapies for cancer patients. Because of the unique ways that our bodies metabolize drugs, no two cancer patients have the same response to an oncology therapy. That's why a treatment that shrinks one patient's tumor may have no benefit for a patient with the same cancer. Fortunately, AI-based tools are in development that will help doctors predict patients' response to therapy. Researchers at the Georgia Institute of Technology and Ovarian Cancer Institute used gene-expression data from 499 cell lines to develop an ML tool that accurately predicted the response to seven chemotherapy drugs in 23 ovarian cancer patients with 91 percent accuracy. The researchers hope to replicate these

findings in a larger pool of patients.

Recent studies have also shown that that ML can accurately predict whether a person with cancer will have severe side effects from radiation therapy and chemotherapy. That critical data could help oncologists tailor treatment recommendations to patients by recommending a lower dose of radiation or choosing an alternative form of chemo.

In other studies, researchers have demonstrated that AI-based programs can estimate survival in patients with breast, prostate, and lung cancers with greater accuracy than conventional predictive tools. Having a more accurate prognosis can help a doctors personalize treatment plans by taking a more-aggressive approach with high-risk patients, and possibly choosing not to administer therapies with high potential for severe side effect in those who are at low risk and are therefore less likely to benefit from the treatment.

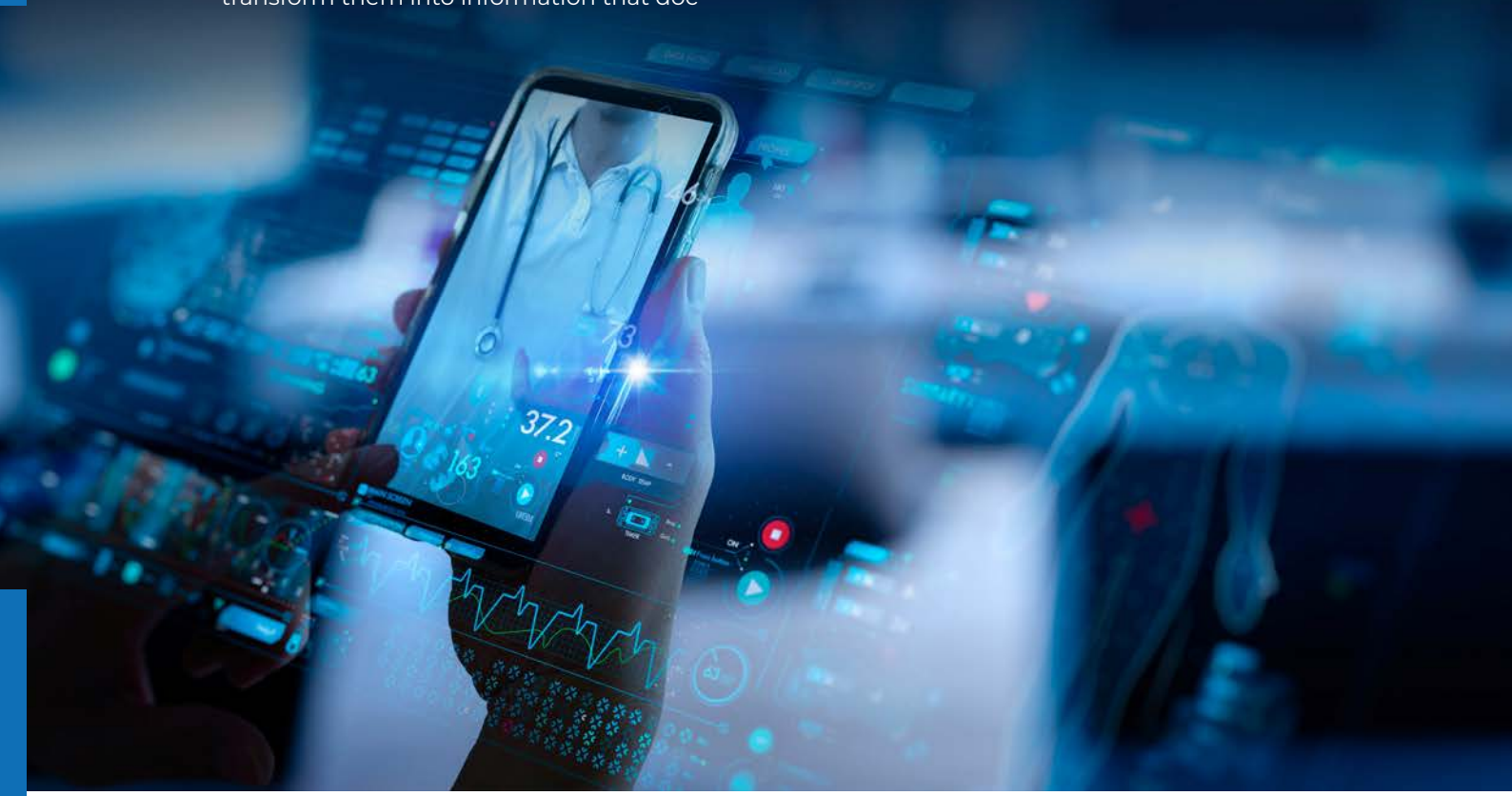
Another form of AI, called natural language processing (NLP), can interpret and understand spoken and written human language. An example of NLP you may have encountered is a chatbot, which is software that simulates human speech; some businesses and other organizations use chatbots on their websites to answer basic questions from human users.

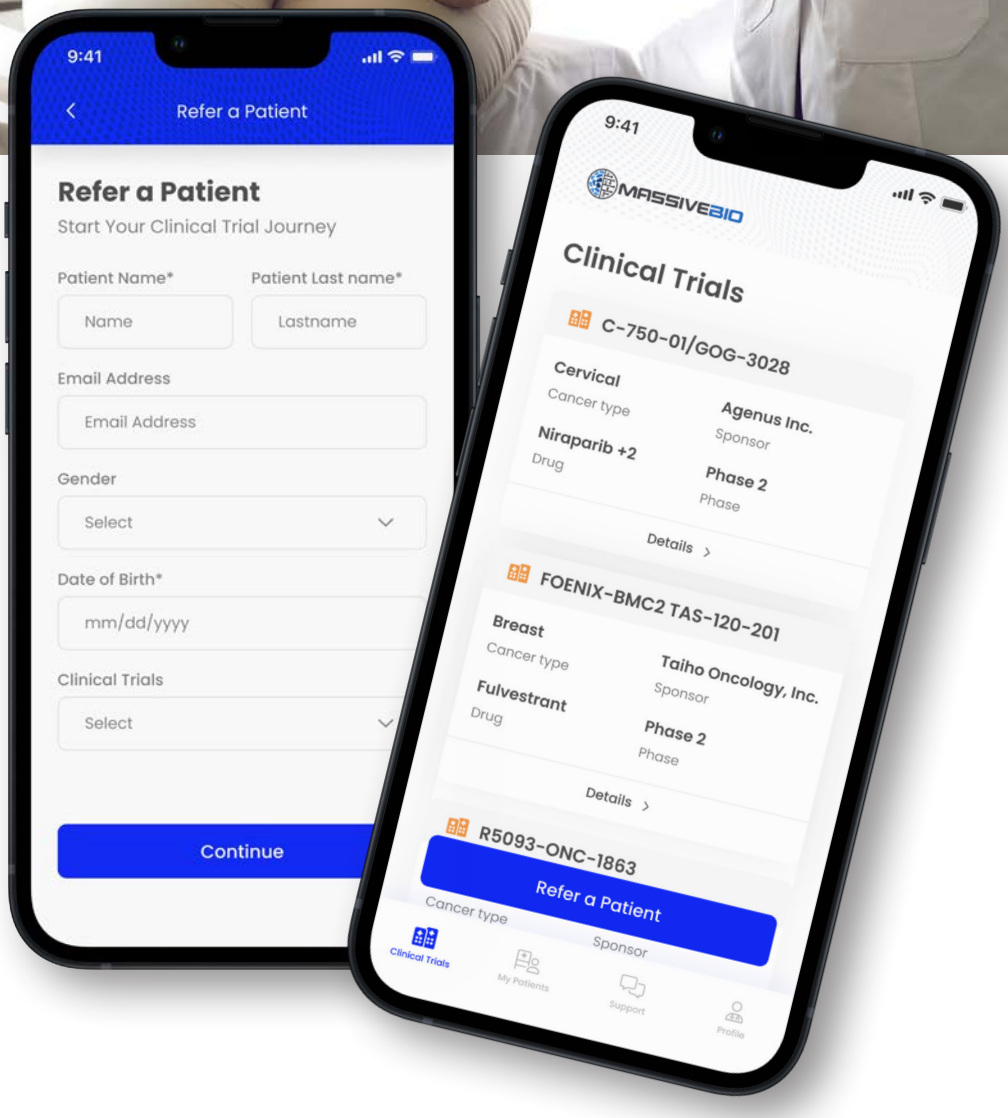
In medicine, NLP can process large amounts of disparate data, such as electronic health records, clinical notes, and lab reports, and transform them into information that doctors can use to make decisions about patient care. Studies indicate that using NLP-based software tools can help oncologists choose the best cancer treatments with the lowest risk of side effects.

Massive Bio Uses AI To Help Cancer Patients

Massive Bio's artificial intelligence-powered platform, SYNERGY-AI, uses NLP, ML, and other forms of AI to match cancer patients to clinical trials of promising new therapies—exponentially faster and with greater precision than would be possible by a patient's healthcare team. After a patient signs a consent form granting us access to his or her medical records, we upload that data to SYNERGY-AI, which uses over 170 algorithms to craft personalized recommendations based on a patient's gender and age, where the patient lives, his or her type and stage of cancer, what medications he or she has received, the results of blood tests, and a long list of other variables. Once SYNERGY-AI has created a precise profile, it rapidly searches a database of more than 14,000 clinical trials to identify only those that are evaluating the best treatment options for the patient and his or her diagnosis.

The result: Massive Bio matches patients to clinical trials in 67 seconds, on average, and we can have you enrolled in one within a few days, compared to the weeks or even months it can take a doctor or nurse. And when you participate in a clinical trial recommended by Massive Bio, we pair the power of AI with the human touch, as our team stays at your side through every step of the journey.





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I HAVE
CANCER
#ihavecancer #cancerawareness #massivebio

Massive Bio's 'I Have Cancer' Campaign

An Interview with Erkan Terzi

Erkan Terzi is Massive Bio's chief marketing officer and creator of the company's new "I Have Cancer" campaign. In this interview, Terzi describes the origins of "I Have Cancer" and the impact he believes this initiative will have.

Q: What was the inspiration for the I Have Cancer campaign?
A: Three years ago, COVID-19 emerged and millions of people around the world died in a short period. We were all in shock and quickly changed our behaviors by wearing masks in public and practicing social distancing, for example. Yet, every year millions of people die of cancer, but we have not adopted that same level of consciousness about its impact and the threat it poses to us. That led me to believe that we need to do more to understand the experiences of cancer patients and increase awareness about how we can all protect ourselves and our loved ones.

Q: Has cancer touched your life? Has a family member or friend had cancer? How did that influence your inspiration for this campaign?
A: About 15 years ago, I lost my cousin to cancer. She was 25 years old and it was not an easy time for my family and me. Cancer is one of the greatest threats to humanity, yet there is too little consciousness about how to lower your risk for being diagnosed. Changing the status quo could save lives.

Q: What audience are you trying to reach with the I Have Cancer campaign?
A: We are targeting everyone in society with this campaign. Cancer is one of the most serious global problems and we don't even know what causes many forms of the disease. Cancer can strike any of us, regardless of age, race, or gender. With the I Have Cancer campaign, we want to remind all segments of society about these realities.

Q: Do you think most people understand what it's like to live with cancer? Why is it important to bring awareness to the experiences of people who have cancer?
A: We are all familiar with cancer in some

way, but we do not understand exactly what the disease means until it happens to us or someone close to us. The fact is, most of us think it will never happen to us. However, the chances of being diagnosed with some types of cancer are growing, due to climate change and other factors. I believe we need to create greater awareness of cancer not only so that we can offer aid and comfort to those struggling with it, but in order to protect ourselves, too.

Q: Why do you think the voices of cancer patients are largely "unheard"?
A: There may be many reasons for this. As I mentioned, coping with cancer is a very difficult and long-term challenge for both patients and their loved ones. Living with cancer is both psychologically and physically exhausting, due the disease itself and the side effects of treatments patients must endure. Some patients respond to this by closing themselves off from the world. That's not healthy and we hope that the I Have Cancer campaign will encourage patients to speak up and be heard about what they're experiencing.

Q: In many cultures, cancer remains a taboo subject and people don't like to talk about it. What effect does silence have? How will the I Have Cancer campaign address that problem?
A: Whether it's due to fear, stigma, or whatever the reason, many people find it difficult to talk about cancer. That includes patients, but also the people they may encounter in their daily lives, too. But silence is never an acceptable solution. On the contrary, letting people with cancer talk about what they're going through can help improve their morale and motivation to keep fighting. It also helps patients feel less lonely. In fact, no patient is alone—there are millions of people, from

young to old, struggling with this disease all over the world. We believe that I Have Cancer can help connect them.

Q: What is the key message you want to deliver with this campaign?
A: We would like to remind everyone that cancer patients are not alone and that anyone could someday face this disease.

Q: Describe how you will get this message across.
A: The main target audience of the campaign is the United States. Outside of the USA, the campaign will also target Italy, Spain, Poland, Israel, and Turkey. We are using all of Massive Bio's social media platforms to get the message out, including Facebook, Instagram, TikTok, Twitter, LinkedIn, and YouTube.

Q: What can people do to take part in the I Have Cancer campaign?
A: Anyone can support the campaign by sharing their stories on social media with the hashtags #ihavecancer, #cancerawareness, and #massivebio.

Q: What impact do you hope this campaign will have?
A: When we produce any campaign at Massive Bio, we don't think about how many people we can reach, the way most companies do. With any outreach effort we create, we believe that if we save one patient's life or increase awareness for even a single healthy person, we have succeeded. As a company, Massive Bio has a strong commitment to social responsibility. Our goal is to save lives and improve the quality of people's lives, both patients and their loved ones. In the first week of the I Have Cancer campaign, we reached over one million people in the United States alone. In the months to come, I hope we save many lives with this campaign.

It's a long road, but not a lonely one.

We have found a clinical trial for your breast cancer near you.

Find a Clinical Trial Near You

PATIENT STORIES

Taking a Chance

A twist of fate helped Jen Heatherly confront her fears and adopt a new approach to fighting breast cancer.

One day in 2017, Jen Heatherly was shopping with one of her daughters when she stumbled and fell off a curb. “My femur snapped in two,” says Jen, 50, of Vista, California, who soon found herself being whisked to a hospital. Lying in the back of an ambulance, she recalls, “was one of those moments when you know that your life is changing.”

To be sure, breaking her leg would ultimately start Jen on a new path in the treatment of her breast cancer, which had been diagnosed three years earlier. Today, Jen is participating in a clinical trial of a novel cancer drug—something she never dreamed of doing just a few years ago.

Jen was diagnosed with breast cancer in 2014. But when an oncologist recommended chemotherapy, Jen—who favored Eastern medicine over conventional Western therapies—wouldn’t hear of it. “I mean, I never even took Tylenol or Advil, and you’re going to put chemo in my body? I don’t think so,” she recalls telling herself at the time.

Jen not only refused chemotherapy, but said no to radiation therapy, too. Instead, she turned to a naturopathic doctor for treatment. The practice of naturopathy uses natural remedies such as herbal medicine, acupuncture, and other non-Western treatments to promote healing. Jen had sought

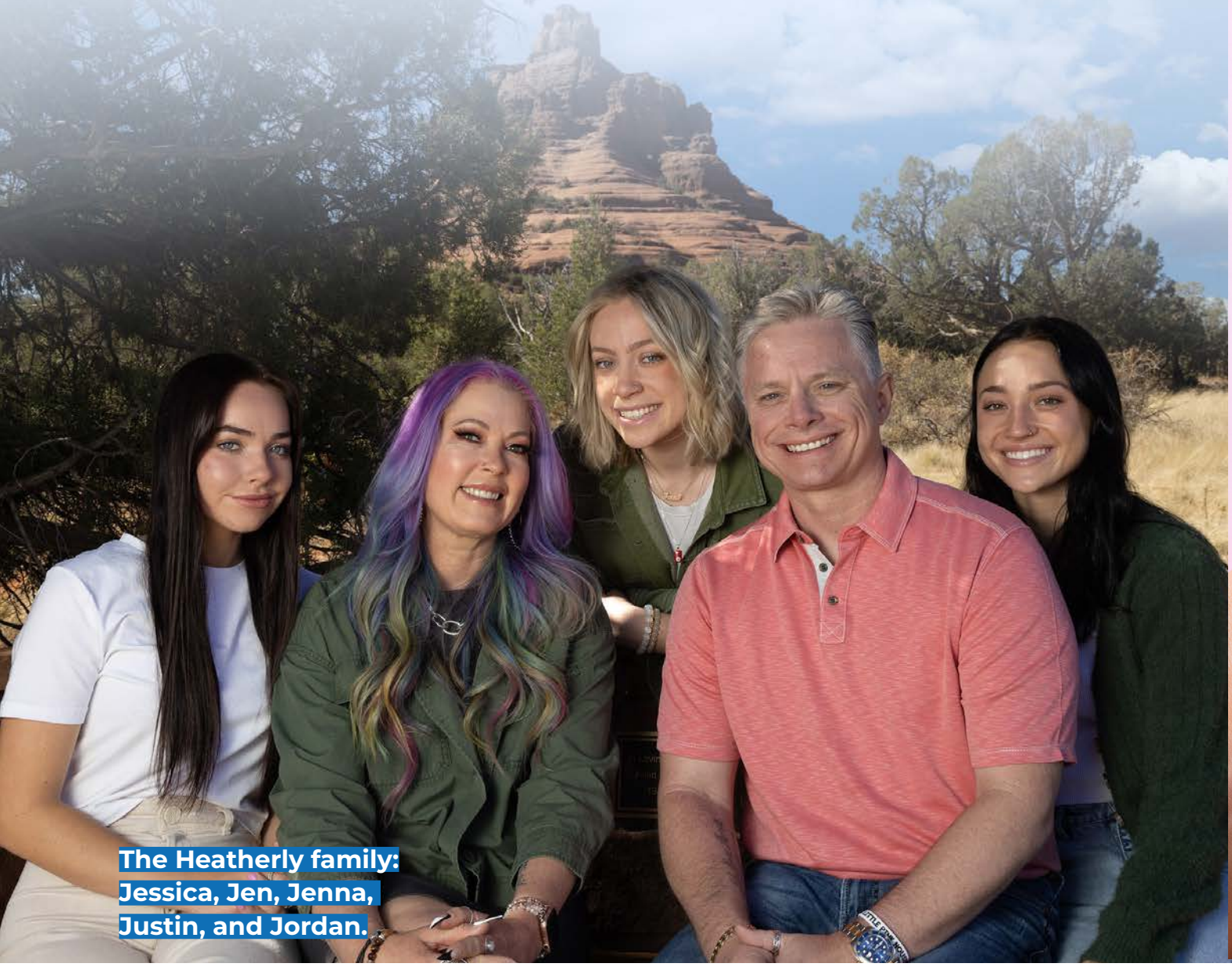
treatment from the naturopath previously, so it only seemed logical to return to her.

The naturopath's recommendations for Jen included a process known as detoxification, which involved steps such as eating primarily organic foods (which she mostly did anyway), switching to organic makeup and skin care products, and only using non-toxic household cleaners. She even cut off relationships she considered toxic, while learning to slow down her life and feel more gratitude. Jen also took dietary supplements and used several devices recommended by the naturopath to promote healing at the cellular level.

"Things were going great," says Jen, that is, until 2017, when she developed severe pain in her left leg. X-rays revealed a spot on her femur, but several doctors dismissed it as most likely just evidence of an old injury, which made sense to Jen. "I was a total tomboy, as a kid," she recalls. "I used to jump ditches on dirt bikes and play tackle football in the street with my brothers." It wouldn't be surprising, Jen thought, if she had banged up her leg at some point, but forgotten about it.

However, when Jen fell and broke her leg, tests showed that the femur had been weakened by spreading cancer; often, a fracture in a long bone such as the femur is the earliest sign that cancer has migrated from its original site, or metastasized. At the hospital where she had her broken leg repaired, Jen learned that the malignancy had spread to eight other bones, in addition to her femur, and that she had stage 4 metastatic breast cancer.

When Jen was initially diagnosed with breast cancer, she made a deal with her husband, Justin: If Eastern medicine couldn't control the disease, she would accept the treatments that conventional Western medicine had to offer. Not that it was an easy transition. While she was still in the hospital, doctors started her on the drug Tamoxifen, which treats



The Heatherly family: Jessica, Jen, Jenna, Justin, and Jordan.

metastatic breast cancer. “It literally took me 30 minutes of bawling my eyes out with that pill in my hand before I could actually take it,” says Jen. “That’s how petrified I was of cancer medication.”

But she took the medicine, which began a new phase in Jen’s breast cancer story.

Since then, she has had the gamut of cancer treatments. She had her ovaries removed and a bilateral mastectomy (surgical removal of both breasts). She has been on several different targeted therapies, which deactivate certain proteins involved in cancer, as well as drugs that block hormones that promote the growth of the type of breast cancer Jen has. She had a total of 66 rounds of radiation and took oral chemotherapy, too. All treatments were effective for a time, but her cancer kept coming back. With malignancies in Jen’s bones, lungs, and liver, intravenous chemotherapy was her next option, but her doctor knew Jen was reluctant to accept that approach. So she gave her an alternative: How about participating in a clinical trial of a new oral drug?

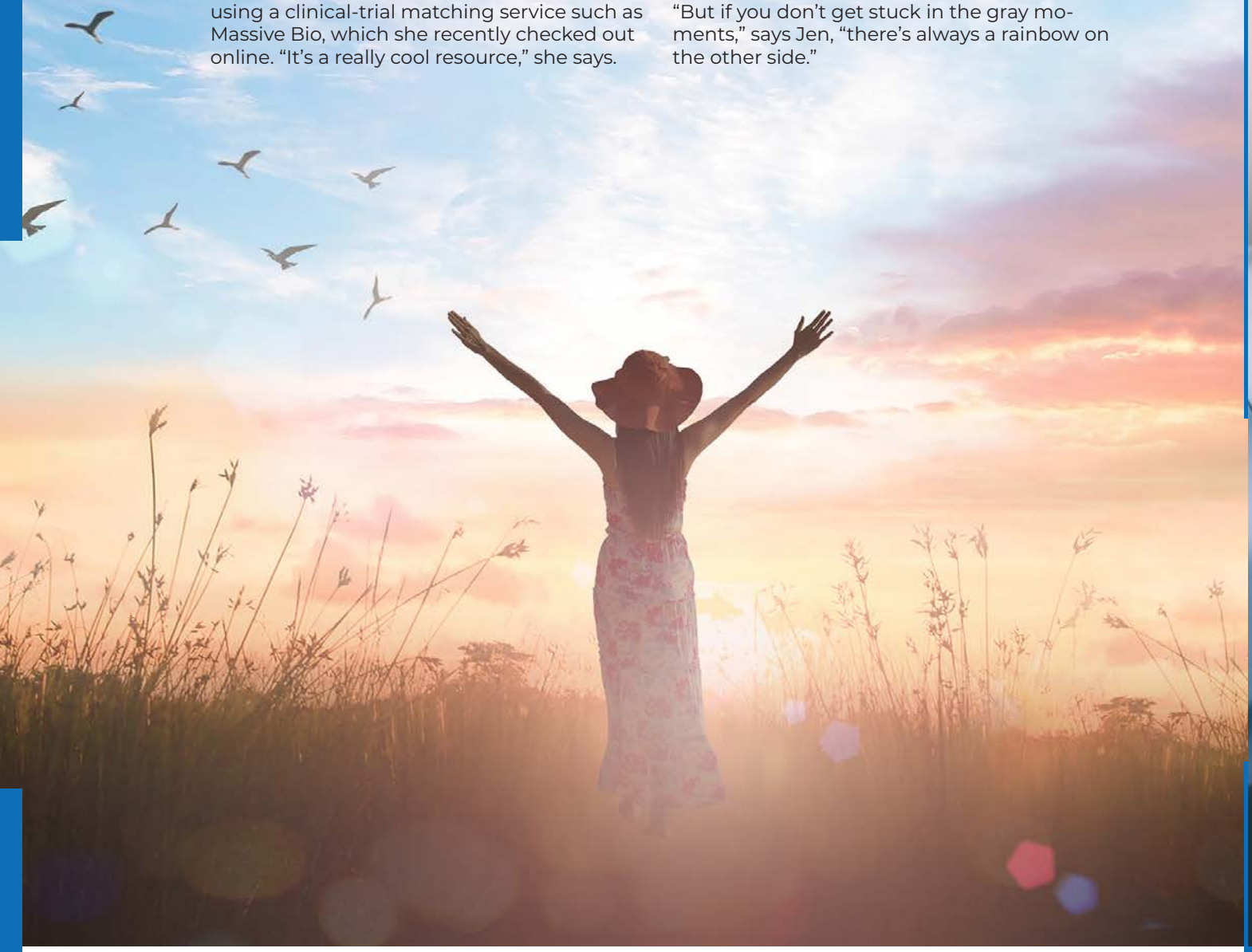
After much consideration, Jen enrolled in the clinical trial in June, 2021. Every morning after breakfast she takes two tablets of a drug that is still only known by a code name, ARV-471, which degrades estrogen receptors on tumors, preventing hormones from attaching to them and causing cancer to grow. “I was really nervous about making that decision,” says Jen, but she is satisfied with her choice: Blood tests and bone scans show no signs of cancer. Taking pills at home also means she doesn’t have to report to a clinic every few weeks for an infusion of chemotherapy. “That would really limit my ability to just pick up and go at the drop of a hat,” says Jen who loves to travel and has a spontaneous streak. A week before she spoke with us, a friend had offered her an extra ticket for an Elton John concert in Phoenix, Arizona that Friday. “I said ‘Heck, yes’, but if I had IV chemo the following Monday morning, there’s no way I could have gone.”

ARV-471 has only caused Jen to have one significant side effect, an increase in hot flashes. Before starting the treatment, Jen had begun experiencing hot flashes occasionally at night, “but now they’re happening in the daytime, nighttime, it doesn’t matter—they’re non-discriminatory.” She says applying peppermint oil to the back of her neck, and turning on a fan or two, helps.

To participate in the trial, Jen must drive from her home in the San Diego area to Los Angeles County, where she receives treatment and monitoring at several UCLA Health sites. On a good day, the trip takes less than two hours, but if there’s an accident on the 405 or somewhere else on the route, it can take three times as long. But after needing to make frequent trips early on in her involvement, today she only has to be on site once a month, with an extra visit every third month for a computed tomography (CT) scan. Overall, says Jen, her experience in the clinical trial “has been pretty great,” adding that should be open to enrolling in another trial in the future if the need arises. And she would consider using a clinical-trial matching service such as Massive Bio, which she recently checked out online. “It’s a really cool resource,” she says.

Jen is involved in the breast cancer community and has taken trips to the Florida Keys and Nashville with other “metastatic ladies,” as she calls her fellow survivors. Recently, a friend suggested that she make a “Living Legacy” video with Sharsheret, a nonprofit organization with the mission of supporting Jewish women diagnosed with breast cancer and ovarian cancer, though the group’s programs are available to all. Interviews with some women who participated in the program are featured on Sharsheret’s website (sharsheret.org), though the Living Legacy videos are intended solely for their families and friends, and Jen welcomed the idea of creating one for her three daughters. “I liked the fact that Sharsheret is open to help anybody, not only if you are of Jewish heritage,” says Jen, who is a Christian. “They’re a resource for all women with ovarian and breast cancer.”

Jen says her faith helps her get through every day. “And I try to make each day a good day,” she says. Sometimes life gets in the way and that doesn’t always happen, she concedes. “But if you don’t get stuck in the gray moments,” says Jen, “there’s always a rainbow on the other side.”



The New Era of Clinical Trials

Take part in a clinical trial—in your living room? What's an umbrella trial? Clinical trials are getting a makeover, which is making them more accessible and inclusive.

Before a cancer drug or any other medicine can be offered to a patient, it's subjected to a rigorous test of effectiveness and safety called a clinical trial. In fact, most medications must pass through three phases of clinical trials before they can be considered for approval by the U.S. Food and Drug Administration (FDA). To be sure, the clinical trial—in which volunteer patients receive an experimental therapy and are compared to similar patients not given the treatment—is the gold standard for determining whether a new medication relieves symptoms, improves survival, or has any other medical benefit.

But that doesn't mean there isn't room for improvement. Several developments in medicine in recent years have led some scientists to toss out old rules for conducting clinical trials and try fresh approaches. These new-style trials are eliminating barriers to participating in clinical research and giving patients access to a wider variety of treatment options.

COVID-19 and the Rise of Decentralized Clinical Trials

One of the greatest challenges facing developers of new medicines is recruiting an adequate number of patients to participate in a clinical trial. The reasons that eligible patients choose not to enroll in clinical trials are

complex, but one significant barrier is geography: A patient may simply live too far from the hospital or clinic where a novel treatment is being studied, making frequent visits to participate inconvenient, if not impossible. One solution to this problem is inspired, in part, by an unlikely source: the COVID-19 pandemic, which disrupted many clinical trials, yet has also led some researchers to adopt new approaches to running trials that make them more accessible.

Clinical trials have traditionally been conducted at one or more research hubs, or clinical sites, where volunteer patients go to enroll, receive experimental treatments, and have their responses to these novel therapies monitored. However, the COVID-19 pandemic resulted in the failure of some trials, as many patients dropped out or refused to enroll in the first place, fearing that visits to a hospital or clinic would expose them to the coronavirus.

At the same time, though, "virtual" office visits became the norm across healthcare, as doctors and other clinicians used telemedicine—primarily in the form of video conferencing—to treat patients without meeting in person and risking transmission of the virus. This trend helped give momentum to an idea that was already taking shape: Using telemedicine and other tools to conduct "virtual" clinical trials, which are now widely known as decentralized trials.

There are different forms of decentralized trials, but all are designed to reduce the need for participating patients to receive treatment and monitoring at a clinical site. In some decentralized trials, patients may be able to receive all or most of their treatment in the home, whether by self-administering a therapy or receiving a visit from a healthcare worker. Wearable medical devices can monitor many vital signs, which can be wirelessly transmitted to clinical investigators. However, more common is a "hybrid" version of the decentralized trial, which allows some participation to occur offsite, but still requires patients to visit a research hub on occasion for more complex treatments (such as infusions) and assessments (such as X-rays or other medical imaging).

Decentralized trials have the potential to increase diversity and inclusiveness in research by allowing patients to participate who wouldn't be able to otherwise due to travel costs, the inability to take time off from work,

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Cancer treatment finder

or mobility problems. By minimizing geography as a barrier to participation, developers of new drugs and other medical products have access to a larger pool of patients. That makes development more efficient and lowers the risk that a trial could fail simply because too few patients volunteered to enroll.

Scientists who design decentralized trials need to overcome certain obstacles, such as ensuring that investigational medicines administered at home are stored properly, as well as guaranteeing the accuracy and privacy of patient data collected by biometric wearable devices. However, solving these logistical concerns could have significant long-term advantages for patients. “A wider embrace of decentralized clinical trials will help accelerate the development of new therapies in oncology and other areas of medicine,” says Selin Kurnaz, PhD, co-founder and chief executive officer of Massive Bio. “Breaking down barriers to participation in clinical trials makes them more democratic and helps bring new treatments to market faster. Both are good for patients.”

Basket Trials? Umbrella Trials?

Another significant development in oncology that’s having a profound impact on how some clinical trials are designed is the rise of genomic medicine. The mapping of the human genome has allowed researchers to identify hundreds of gene mutations—that is, genes with DNA that’s altered—that cause cancer to grow and spread. Advances in genomic medicine have led to the development of oncology drugs that target these gene mutations and the proteins they produce, which can slow the growth and spread of cancer.

The emergence of genomic medicine in oncology is contributing to changes in some clinical trials. In a traditional clinical trial, scientists recruit patients who have the same

type of cancer to participate—all enrollees have breast cancer, for example, or all enrollees have melanoma. However, genomic researchers have made two key discoveries: a single gene mutation may promote or worsen several different forms of cancer; and many forms of cancer are linked to multiple gene mutations.

These discoveries have inspired scientists to design several new types of clinical trial:

Basket trials
Instead of recruiting patients who all have the same type of cancer, a basket trial involves patients with different types of malignancies that are linked to a common gene mutation, or biomarker, which is targeted by the treatment being studied. There are currently about 30 investigational treatments under study in basket trials, while a number have already been reported. (Basket trials are also known as bucket trials.)

Umbrella trials
These trials include patients with one cancer type, but whose tumors are linked to different gene mutations. Each tumor's unique genetic alteration is treated with a specific targeted therapy.

Platform trials
A platform trial is a hybrid of a basket trial and umbrella trial. What sets apart a platform trial is that it is conducted in an ongoing or perpetual manner, in which multiple drugs and/or multiple disease populations can be added to the trial as it proceeds.

While the design of clinical trials is evolving, their goal remains the same: To help ensure that only safe, effective therapies find their way to the clinic and your medicine chest. If you're considering a clinical trial as part of your care, finding the best treatment option for you is essential. Massive Bio can help you make the right choice.

There is always hope!

Explore all treatment options available to treat your advanced multiple myeloma

Find a Clinical Trial Near You

What is CAR T-Cell Therapy?

This innovative treatment trains immune cells to hunt down and kill cancer cells.

What if your own cells could be trained to seek out and destroy cancer cells? Thanks to advances in medical science and technology, that's now possible for some forms of cancer, with a treatment called CAR T-cell therapy.

CAR T-cell therapy is a form of immunotherapy. As the name suggests, immunotherapy is a treatment that works on the immune system, which is your body's natural defense network. The immune system is like a team of security guards in an office building: It's constantly on the lookout for intruders that don't belong in the body, such as germs and other foreign cells.

Immune cells perform this task by scanning every cell they encounter for a protein called an antigen. An antigen is like an ID card that an employee uses to enter an office building. Normally, the immune system recognizes the antigens on healthy cells, so it leaves them alone and lets them pass by. But when an immune cell encounters a foreign cell that doesn't belong in the body, such as a virus or bacteria, it doesn't recognize its antigen. When that happens, immune cells called T cells attach themselves to the foreign cell and signal other immune cells to surround and attack it.

Cancer cells certainly don't belong in a healthy body. Unfortunately, the immune system doesn't always attack them. That's because cancer cells are made by our own bodies, so the immune system may not realize they're dangerous and need to be destroyed. And even if the immune system detects a tumor, some cancer cells can modify themselves in a way that lets them evade detection. For example, some cancer cells have a protein that acts like a fake ID, which fools immune cells into leaving them alone. That allows a tumor to grow, spread, and possibly turn deadly.

The goal of immunotherapy is to make the immune system smarter and stronger, which improves its ability to find and kill cancer cells. There are several types of immunotherapy. Some forms take away a

cancer cell's fake ID, making it easier for the immune system to detect. Others boost the ability of immune cells to destroy cancer cells.

CAR T-cell therapy is one of the newest forms of immunotherapy for treating cancer. CAR stands for "chimeric antigen receptor." The word "chimeric" comes from chimera, which is a mythical fire-breathing creature with the head of a lion, body of a goat, and a serpent for a tail. In science, a chimera is an organism that has cells from different species. In CAR T-cell therapy, a patient's T cells are fused with proteins called receptors. These new receptors essentially give T cells sharper vision, which makes them better able to identify a specific type of cancer, explains Arturo Loaiza-Bonilla, MD, chief medical officer of Massive Bio.

"We harvest T cells from the patient and train them to identify cancer by changing their 'eyesight' so they can locate what they're looking for," says Dr. Loaiza-Bonilla. "We are not only harnessing the immune system to attack cancer, but we're telling it 'only attack these specific markers in cancer cells'." As a result, CAR T-cell therapy causes less harm to healthy cells, which limits side effects.

Scientists have been interested in using T cells to fight cancer since the 1960s. However, a turning point occurred in the early 1990s, when a physician-scientist

named Michel Sadelain at the Massachusetts Institute of Technology first used genetic engineering techniques to modify T cells with the goal of targeting and killing cancer cells.

In 2003, Dr. Sadelain showed that it was possible to use his techniques to train T cells to detect and kill leukemia cells in mice. In 2013, he and several colleagues published the results of the first clinical trial of CAR T-cell therapy in humans. The new form of immunotherapy eradicated tumors in five out of five patients with a blood cancer called acute lymphoblastic leukemia, who all went into remission. In 2017, the U.S. Food and Drug Administration approved the first form of CAR T-cell therapy. The treatment, called tisagenlecleucel (Kymriah), is approved for treating one form of leukemia and two types of lymphoma that have relapsed or not responded to other therapies. Today, there are a half dozen forms of CAR T-cell therapy used to treat various forms of blood cancer.

CAR T-cell therapy works like this: First, the patient goes to a hospital or clinic, where a sample of his or her blood is drawn. T cells are removed from the blood and sent to a lab, where they are modified to become CAR T cells. These powerful new cells are grown to increase their numbers, then infused back into the patient's bloodstream. As Dr. Loaiza-Bonilla explains, CAR T cells act like a SWAT team that has been given a photo of a criminal and the address where he's hiding out, as they hunt for the antigen on cancer cells they have been trained to detect and help mount an attack on the tumor.

CAR T-cell therapy has been remarkably successful for many cancer patients. In fact, the first pediatric cancer patient to receive the therapy, Emily Whitehead, recently celebrated 10 years of remission; she was treated for acute lymphoblastic leukemia at age 6, and now Emily is a senior in high school. However, some patients don't respond to this novel treatment, and CAR T-cell therapy is still only available for treating a small number of blood cancers. However, there are options for patients who can't benefit from CAR T-cell therapy. Enrolling in a clinical trial can give you access to new treatments months, and even years, before they're available to other patients. These advanced therapies can be life changing and some may even offer a cure. Whatever form of cancer you're confronting, give yourself the gift of hope by learning about all of your treatment options.

Update on **Cervical Cancer**

Better screening and the HPV vaccine have reduced cervical cancer rates, but vigilance is essential and there's more work to be done.

January is Cervical Cancer Awareness Month, an occasion that calls to mind the remarkable success medicine has had in reining in the threat this malignancy once posed in much of the world—and the work that remains to be done.

Until the mid-20th century, cervical cancer was one of the deadliest forms of cancer among women in the United States and many other countries. However, that all changed with the introduction of the Pap test (named for its creator, George Papanicolaou, MD), which can detect precancerous changes in cervical cells, as well as early-stage cervical cancer, which is highly treatable. Routine screening with the Pap test caused rates of cervical cancer and deaths from the malignancy to plummet. This year, a little over 14,000 women in the United States will be diagnosed with cervical cancer and roughly 4,300 will die of the disease. By comparison, 287,850 new cases of invasive breast cancer will be diagnosed in women and 43,250 will die.

Over the last generation, women have also had the option of being screened for the human papilloma virus (HPV), which causes almost all cases of cervical cancer. Both the Pap and HPV tests are effective at preventing cervical cancer, and can be performed at the same time in the form of a "co-test."

What's more, in 2006, the first HPV vaccine was introduced, which has been shown in multiple studies to prevent infection with the virus that can trigger cervical cancer. However, even more compelling support for this shot in the arm came in 2020, when a huge

Swedish study involving 1.7 million women found that those who received the HPV vaccine prior to age 17 reduced their risk for cervical cancer by nearly 90 percent.

Yet, while screening tests and the HPV vaccine have made cervical cancer one of the most preventable forms of malignancy, the numbers show that this protection is nonetheless failing to reach many women.

- Cervical cancer remains the fourth most common cause of cancer among women around the globe, with more than 600,000 new cases and about 342,000 deaths reported annually, according to the World Health Organization. Rates are particularly high in lower-income nations that have limited access to screening tests and the HPV vaccine.
- In the United States, cervical cancer remains the second leading cause of cancer death in women aged 20 to 39 years, and half of all deaths from the disease occur in women in their 50s or younger. A recent research letter published in *JAMA* noted that there was a modest uptick in cervical cancer cases among women in the United States aged 30 to 34 between 2012 and 2019, though the authors couldn't say whether that represented a genuine increase in incidence or was due to improvements in early detection.
- Last year, a UCLA study found that the incidence of stage 4 cervical cancer increased 1.3 percent annually, on average, from 2001 to 2018 in the United States. Rates of late-stage cervical cancer were higher among Black women than in white women. However, white women aged 40 to 44 in the southern United States had the highest annual increases in this hard-to-treat form of cervical cancer, with annual increases of 4.5 percent. Authors of the study, published in the *International Journal of Gynecologic Cancer*, speculate that failure to receive routine screenings explained the increased rates.

Massive Bio is working with industry partners who are conducting clinical trials of new treatments for women with advanced cervical cancer, and we're helping to raise awareness about the importance of screening and prevention through our I Have Cancer campaign (see page 18).

What's New in Cervical Cancer Research?

Cervical Cancer Screening Guidelines Are Often Ignored

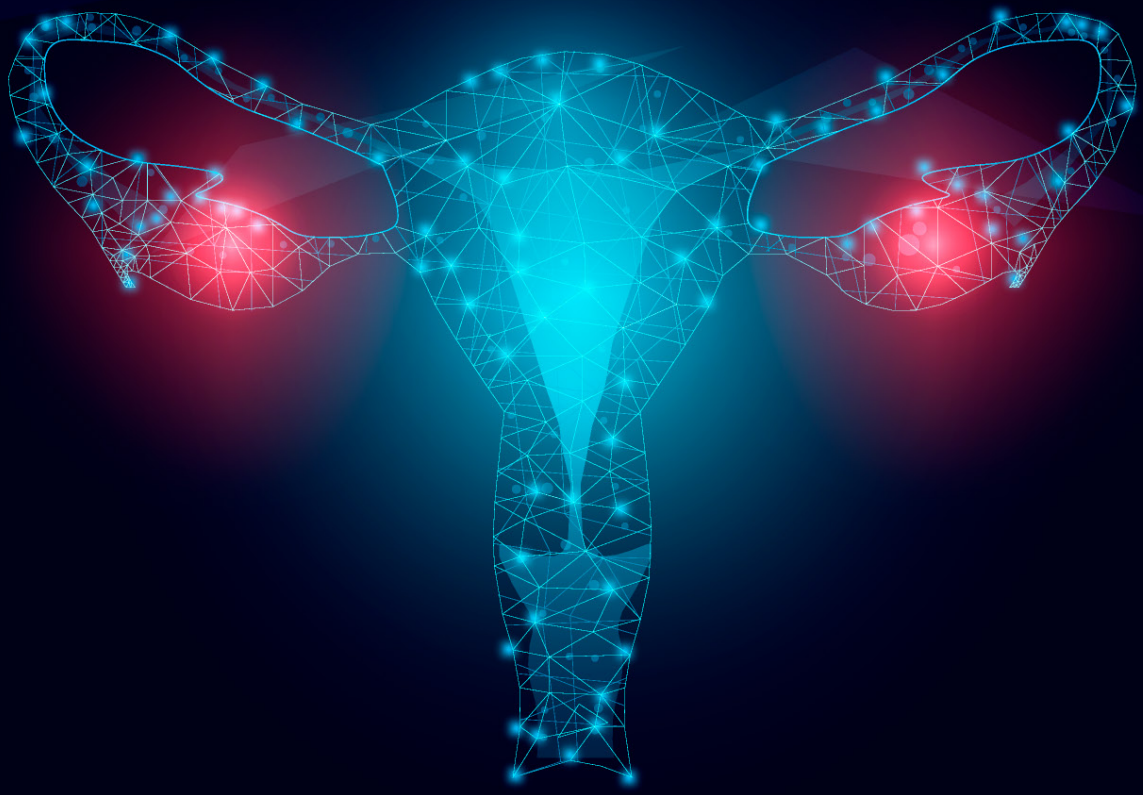
Screening with the Pap test and/or the HPV test can prevent cervical cancer and find small cancers while they are treatable. Yet the benefits of cervical cancer screening diminish over the course of a woman's life. That's why the American Cancer Society and other health authorities say that women can stop getting tested at age 65 if they are of average risk for cervical cancer and have previously been getting screened on a regular basis. Yet, many older women in the United States are getting screened unnecessarily, according to a 2022 study in *JAMA Internal Medicine*. Researchers examined 20 years of Medicare claims and found that, during that period, 1.3 million women over 65 received some form of screening for cervical cancer. If you're a woman over 65 and your doctor recommends cervical cancer screening, ask why.

Single-Dose HPV Vaccine Could Increase Protection in Africa

Standard HPV vaccines are administered in a two- or three-shot regimen, delivered in intervals months apart. Unfortunately, cost and logistics make it difficult to impossible to offer these vaccines to young people in some lower-income countries. Giving a single dose of the vaccine would cut costs and be easier to deliver, so researchers recruited 2,275 young women in Kenya to participate in a study: Some received one dose of the HPV shot, while the others were given a meningococcal vaccination. Just two young women given the HPV injection developed HPV infections, compared to 36 in the group given the meningococcal vaccine. The researchers found that the single dose was 97.5 percent effective in preventing infections by two HPV strains known to cause cervical cancer.

Misinformation About the HPV Vaccine Is Widespread

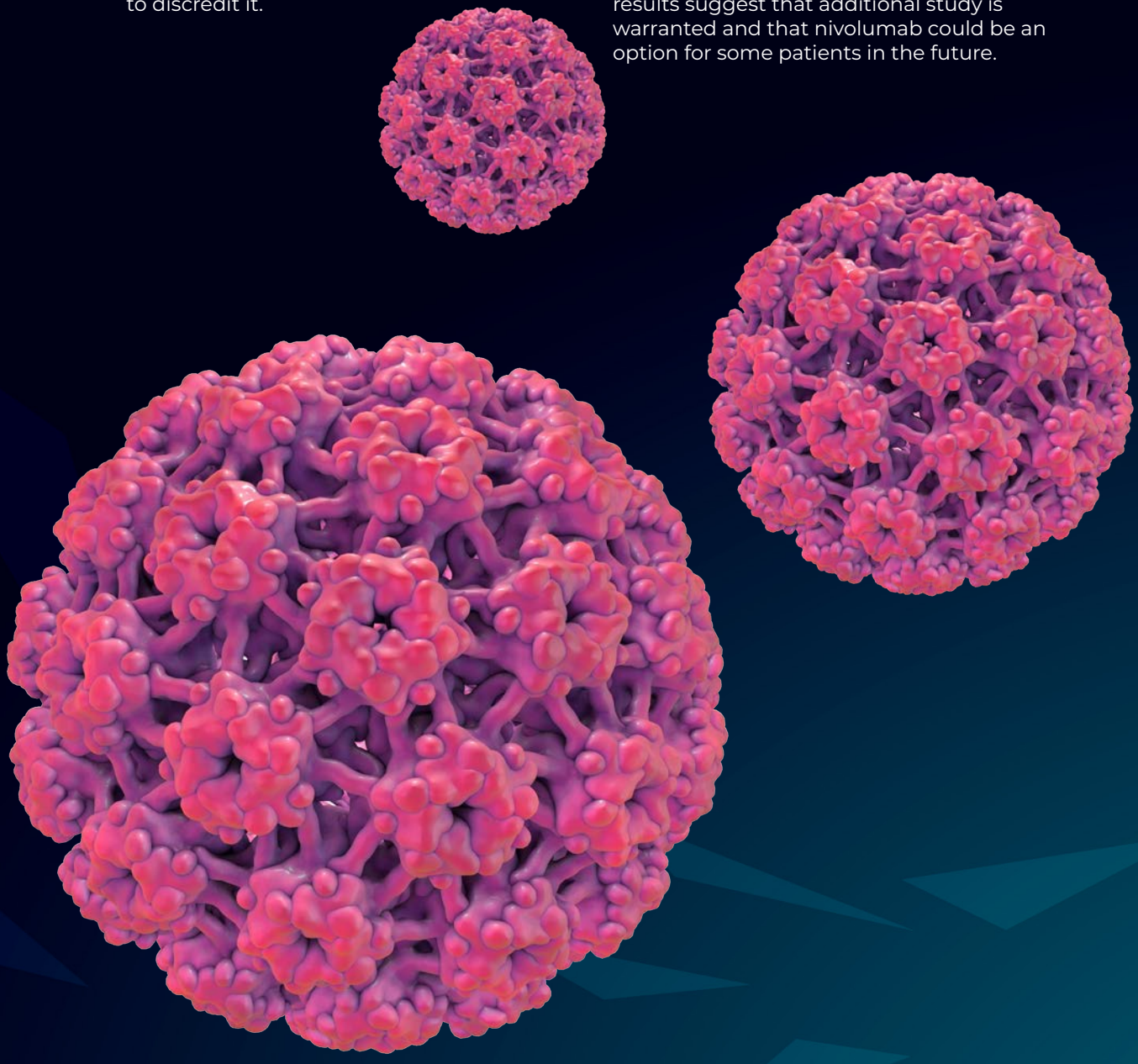
The HPV vaccine is highly effective at preventing infections that increase the risk for cervical cancer, yet acceptance of the immunization has been slow in some countries, including the United States. The Centers for Disease Control and Prevention (CDC) recommends the vaccine for boys and girls at age 11 or 12 (though it can be offered as



early as age 9). Yet in 2019, more than a dozen years after the first HPV vaccine was approved, only about half of teens aged 13 to 17 in the United States were up to date on their shots. A 2022 study published in the *Journal of Behavioral Medicine* suggests that misinformation on social media contributes to this vaccine hesitancy. An analysis of 3876 Twitter posts mentioning the vaccine in 2019 and 2020 found that nearly one in four (24 percent) contained lies and inaccurate information, such as claims that the shot is ineffective or causes harm. Tweets containing misinformation about the HPV vaccine were over five times more likely to be retweeted than accurate posts. The good news is that recent data suggests that acceptance of the HPV vaccine is growing in the United States and other countries, despite nefarious efforts to discredit it.

Nivolumab Shows Promise in Recurrent and Metastatic Cervical Cancer

An early-stage clinical trial suggests that nivolumab (Opdivo) could become a new treatment for patients with recurrent or metastatic cervical cancer. Nivolumab is a type of drug known as a checkpoint inhibitor, which disables the ability of certain cancer cells to "hide" from the immune system. It's approved for treating metastatic melanoma, non-small cell lung cancer, and several other forms cancer. In the CheckMate-358 phase I/II trial, patients received either nivolumab alone or in combination with ipilimumab (Yervoy). After a minimum of two years, 26 percent to 38 percent of patients had a good response to treatment, depending on the regimen they received. Given the challenge of treating advanced cervical cancer, these results suggest that additional study is warranted and that nivolumab could be an option for some patients in the future.



Cancer and Climate Change

Warming of the planet is increasing the risk for some types of cancer. Here's what you need to know.

Cancer is an ancient disease. The oldest evidence of a malignant tumor is from a fossil that's 1.7 million years old. To be sure, most scientists believe that cancer is as old as humanity.

By contrast, climate change is a relatively recent phenomenon that began when humans started burning fossil fuels such as coal, oil, and natural gas to produce energy about 150 years ago. Yet these new and old phenomena appear to be intersecting in some surprising and troubling ways: Changes in our environment brought on by warming of the planet appear to be increasing the risk for some types of cancer.

The Impact Has Already Begun

For example, consider the rising rates of skin cancer around the globe. Burning fossil fuels creates greenhouse gases that trap heat in the atmosphere, causing temperatures to rise. As heatwaves occur more often and last longer, people in many parts of the world are spending more time outdoors, exposing their skin to the harmful effects of the sun's ultraviolet rays.

Unfortunately, depletion of the ozone in the atmosphere by industrial chemicals and human activity is allowing more of those ultraviolet rays to reach the Earth. Together, these phenomena may explain why rates of invasive melanoma—a potentially deadly form of skin cancer—have increased 31 percent over the last decade in the United States. According to a 2020 study in *The Lancet Oncology*, increased exposure to the sun's ultraviolet rays may be responsible for three out of four new cases of melanoma in North America and Europe, as well as in Australia and its neighboring island nations. And the problem will surely become worse over time. For example, scientists predict that the incidence of melanoma in the United Kingdom will rise 7 percent from 2014 and 2035.

Worsening Disasters and a Diminished Food Supply

As the planet becomes hotter, wildfires are becoming more destructive: The number of acres burned by wildfires in the United States has doubled since the 1990s, and the problem is likely to get worse. Smoke from wildfires pollutes the air with toxins such as benzene and formaldehyde, which are also found in cigarette smoke and can cause lung cancer. A study published in *The Lancet Planetary Health* last May found that people who lived within 30 miles of areas where wildfires occurred were five percent more likely to develop lung cancer and 10 percent more likely to have brain tumors than people who lived further away. Overall, increasing air pollution from wildfires and burning of fossil fuels will result in an increase in premature death and lung cancer everywhere in the world except Africa, according to the *Lancet Oncology* study mentioned earlier.

Climate change appears to be making some forms of natural disaster more common, which could have long-term effects on our health. In 2017, Hurricane Harvey poured one trillion gallons of water on Houston, Texas, drenching some areas with nearly a year's worth of rain in just a few days. Hurricanes are nothing new, but climate scientists say that the warming of our planet is increasing their likelihood of occurring. In this case, scientists estimated that climate change made Hurricane Harvey 3.5 times more likely to strike. With winds peaking over 130 miles per hour, Hurricane Harvey had a devastating impact, killing 82 people and causing $125 billion in damage. Yet the long-term impact of Hurricane Harvey may not be known for years, since it flooded chemical plants, oil refineries, and Superfund sites. As a result, huge amounts of cancer-causing toxins were released into the local community. Some of these toxins, such as dioxin, can linger in the environment for decades.

Natural disasters can also interfere with cancer treatment by closing roads and shutting down clinics due to loss of power. Missing even a single cancer treatment can worsen a patient's outcome. A 2019 study in *JAMA* found that lung cancer patients who had their radiation treatments delayed due to hurricanes were up to 27% more likely to die than other patients in areas unaffected by these storms.

Extreme weather and environmental alterations caused by climate change may increase the risk for certain cancers in an indirect manner. Parching droughts can destroy fields of nutritious fruits and vegetables. High levels of carbon dioxide in the atmosphere can reduce the nutritional value of essential grain crops. As oceans become warmer and more acidic from climate change, fisheries may diminish, depriving communities that rely on seafood as a dietary staple of healthful omega-3 fatty acids. Reduced access to healthful foods will probably disproportionately affect people in less-wealthy countries and could increase the risk for a variety of medical conditions, including colorectal cancer and other gastrointestinal malignancies.

The rising temperatures of a warming planet will also affect agriculture in other, less-obvious ways. While sun and heat help crops grow, too much can have downsides. For example, hot and humid conditions promote growth of fungi. That includes a form of fungus that produces cancer-causing chemicals, or carcinogens, known as aflatoxins, which can grow on corn, peanuts, and other crops. These toxins increase the risk for liver cancer, and you could be exposed to them by eating contaminated peanuts or consuming meat or dairy products from animals fed tainted corn.

What You Can Do

There are many steps you can take to help slow climate change and make the world a healthier place. Swap incandescent lightbulbs for LED bulbs. Ensure that your home is well insulated and your heating and cooling units function efficiently. Ride a bicycle to work instead of driving. Trade your gasoline-guzzling car for an electric vehicle. These and other changes lower energy use, which will reduce greenhouse gas emissions.

And, of course, take all the necessary steps to keep yourself healthy. Eat a balanced diet and get plenty of exercise. Don't smoke and limit alcohol consumption. See your doctor on a regular basis for checkups and health screenings. And if you're diagnosed with cancer or any other condition, make sure you learn about all of your treatment options.

PATIENT ADVOCACY

SHARSHERET

A resource for Jewish women with breast and ovarian cancers, their caregivers, and anyone seeking support

Rochelle Shoretz was just 28 and had two little boys at home when she was diagnosed with breast cancer. As she tried to learn more about living with the disease, Shoretz found that there was little information available that addressed her unique circumstances as a Jewish woman with breast cancer. Moreover, friends and family tried to connect her with other women with breast cancer for support, but most were much older and couldn't relate to her experience.

Then, a friend introduced Shoretz to Lauryn Weiser, who was 31, Jewish, and had three small children. A bond between the two women quickly formed, as did the idea for Sharsheret, the nonprofit organization they established in 2001 as a resource for Jewish women with breast and ovarian cancers, and anyone seeking support. Sharsheret is Hebrew for "chain," which symbolizes the connections between women, families, and communities facing these diseases. Today, Sharsheret receives 24,000 inquiries a year from patients, their caregivers, and family members who need help coping with can-

cer. Sharsheret has offices in New York, New Jersey, Florida, Illinois, and California.

"There are a lot of unique issues and concerns facing Jewish women regarding breast and ovarian cancers," explains Leora Goor, development associate for Sharsheret. For starters, she notes that women of Ashkenazi Jewish heritage have a one in 40 chance of inheriting a BRCA gene mutation that increases the risk for breast and ovarian cancer, compared to about one in 500 in the general population of women, according to the Centers for Disease Control and Prevention.

What's more, while cancer can be difficult to discuss for some, it can be a particularly sensitive subject in the Jewish community, with its strong emphasis on marrying at a young age and creating families, says Goor. "There's a big stigma around talking about a diagnosis [of cancer], because that might taint your marriage-ability and could affect your ability to have kids and grow your family," she says.

Shoretz and Weiser had a vision for an organization that helped women address these and other concerns with emotional support, education, and counseling. One of the first things they did was create a peer-support network, which continues to thrive and grow. Whether a woman is newly diagnosed or a survivor, Sharsheret can connect her with a peer who has had similar experiences and has volunteered to offer information and support.

"We try to customize the peer connections," says Bonnie Beckoff, MSW, director of support services for Sharsheret. For example, a woman may want to know what to expect from recovery after surgery or what it's like to undergo fertility treatment. "We do our best to connect that woman to someone who has been down that road previously to give her strength and share her experience." In some cases, relationships forged through the peer-support network have become long term, with peers developing close friendships. Women can also seek support and information from the Sharsheret community on the organization's Facebook page. A private Facebook group, Sharsheret Embrace, was created for women with metastatic breast cancer and advanced ovarian cancer.

Another of Sharsheret's missions is to fight stigma and misconceptions about cancer through education and outreach. The organization offers a wealth of information about all aspects of living with breast and ovarian cancers, by phone, online, and in print. Sharsheret holds educational programs in the community on college campuses and in hospitals, for example, and produced about 60 webinars last year, many hosted by doctors and other healthcare professionals offering medical information and updates. "But every now and then we offer a webinar for people who want a break from talking about cancer, such as an art class or instruction on how to do a facial at home," says Goor.

Importantly, Sharsheret has a genetic counselor on staff who is available to offer plain-English

information to anyone interested in learning what it means to be born with a genetic predisposition for breast and ovarian cancer, including patients and their family members. Patients who have undergone genetic testing can provide their lab reports and consult with the counselor for guidance.

Sharsheret also has various programs to help women live better with cancer. Free Survivor Kits include cookbooks, exercise bands, and other tools for healthier living. The group also offers free Best Face Forward kits, which include make-up and other cosmetic products, as well as tips for dealing with hair loss and changes in skin tone. Sharsheret's Best Face Forward 2.0 program provides financial subsidies to eligible women to help them obtain wigs, cold caps (which can preserve hair during cancer treatment), three-dimensional micropigmentation of the nipple and areola, and microblading (tattooing of the eyebrows).

While Sharsheret was created as a resource for women of Jewish heritage with breast cancer and ovarian cancer, the organization welcomes and works with people of any faith or gender who reach out for assistance and support. "We also offer support for caregivers, so any family member or friend of a person with breast or ovarian cancer can call in," says Beckoff.

Rochelle Shoretz passed away due to complications of breast cancer in 2015, but her legacy lives on through these and other services Sharsheret offers. "She believed that we need a community of women to support each other," says Goor. "Wherever you are in the world, Sharsheret can help you."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AWARENESS CALENDAR

January

- Cervical Health Awareness Month

February

- National Cancer Prevention Month
- Gallbladder and Bile Duct Cancer Awareness Month
- World Cancer Day (Feb 4)
- National Donor Day (Feb 14)
- International Childhood Cancer Day (Feb 15)
- Rare Diseases Day (Feb 28)

March

- National Colorectal Cancer Awareness Month
- Multiple Myeloma Awareness Month
- Kidney Cancer Awareness Month
- International HPV Awareness Day (Mar 4)

April

- Esophageal Cancer Awareness Month
- National Cancer Control Month
- National Minority Cancer Awareness Month
- Head and Neck Cancer Awareness Month

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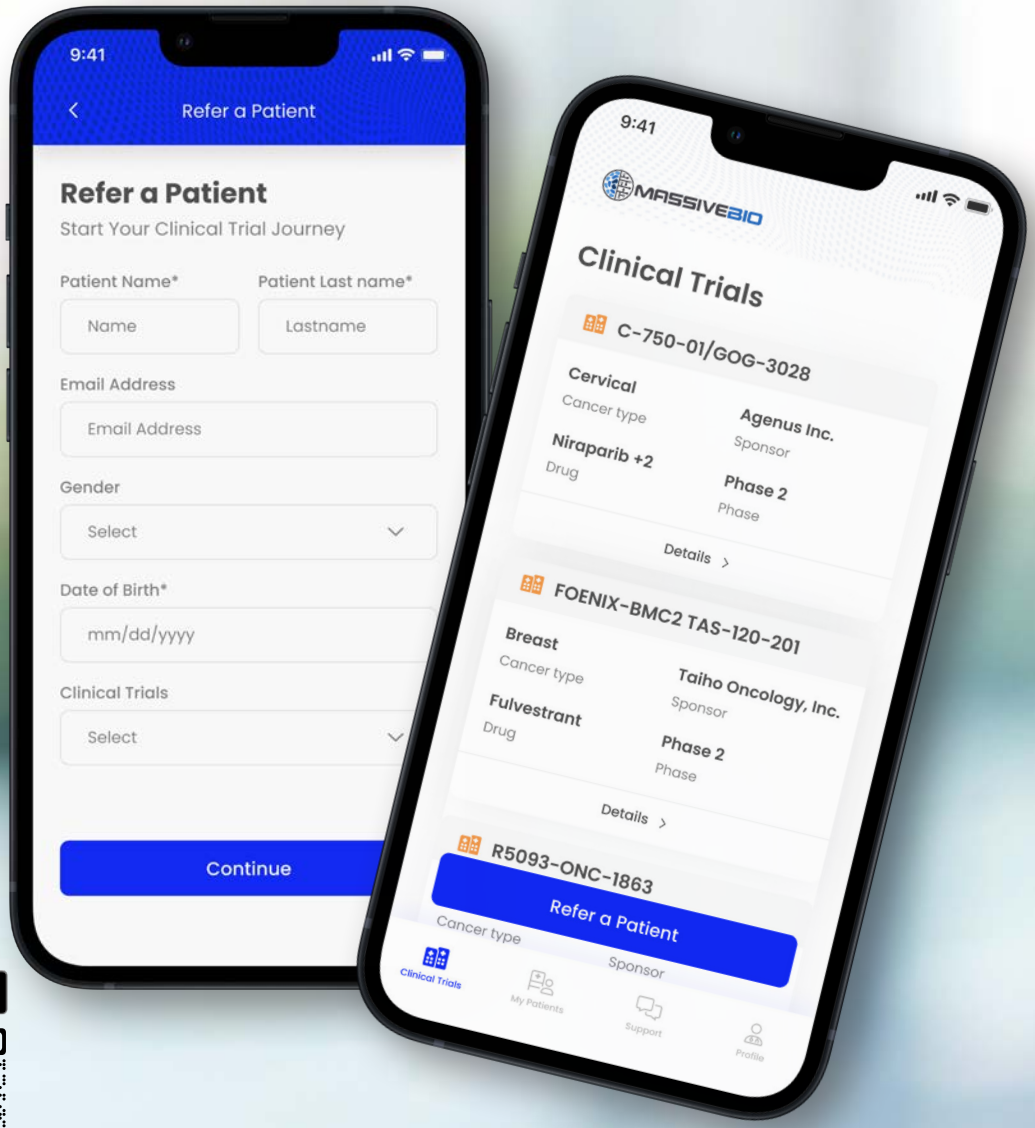

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