



# Product Reach



With passionate dedication to emotional awareness and intellectual execution, people at Promega connect with each other and with scientists around the world to *co-create solutions* to the most relevant problems in life science.

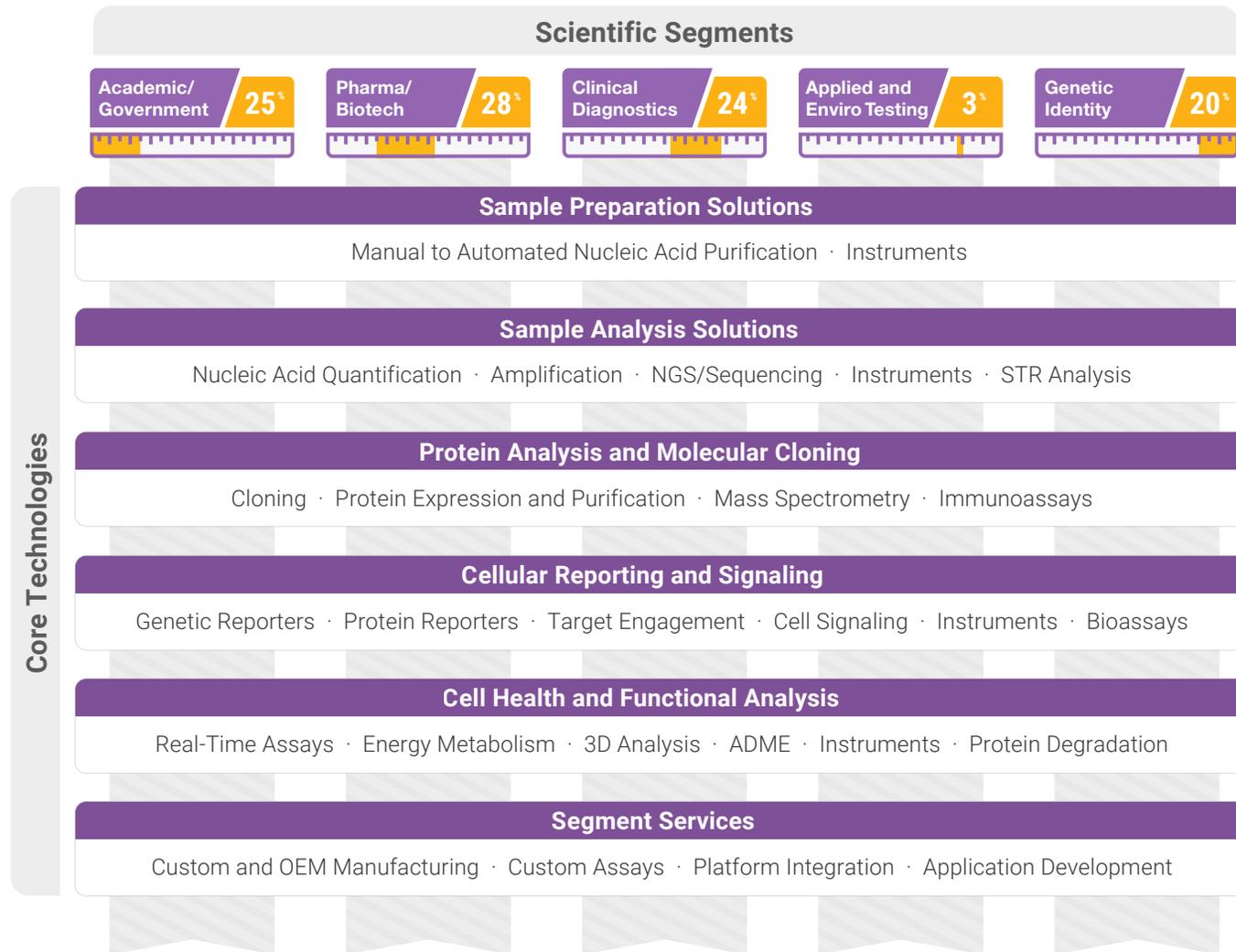
PONCHO MEISENHEIMER  
Senior Director, Research and Development

### Product Reach

Developing innovative solutions to meet the complex and ever-changing needs of our customers begins with listening. We build solid relationships with our customers by investing time to truly understand their work and anticipate their needs so we can problem solve together. Our alliance with them, coupled with determined scientific exploration and flexible manufacturing capabilities, enable us to support our customers in their work to improve the world in profound ways using science.

Every day, research scientists, technicians, and analysts in laboratories and industrial facilities around the world rely on our products and technical expertise to succeed in the work they undertake. With high-quality, reliable products at their disposal, researchers, applied scientists, clinical practitioners, forensic analysts, quality assurance personnel and others have more freedom to focus on specific questions at the forefront of scientific discovery. This results in the acceleration of research discovery, better health care, and more consistent justice.

# Breadth of Capabilities



## CUSTOMER FOCUS

### Forensics and Paternity Laboratories

Forensics and paternity testing laboratories deal with unrelenting caseloads and tight turnaround times. Dependable results, fast throughput and reliable product supply are critical in this setting. Forensic labs use limited, often challenging samples to develop investigative leads from crime scenes. Sexual assault kits and property crime evidence are some of the more challenging samples for labs to process. Forensic labs process large numbers of reference samples to populate reference databases that help law enforcement connect arrestees to other crimes, with the goal of identifying possible repeat offenders. Ongoing testing of the rape kit backlog has identified over 1,000 suspected serial rapists in the United States alone.

In addition to analyzing evidence collected at crime scenes, forensics labs help bring closure to families whose loved ones are missing or lost in mass disasters, and even help exonerate those who have been wrongly convicted of a crime. These researchers and analysts require optimal and reliable results from valuable and often irreplaceable evidence samples.

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**We have worked with forensic and paternity laboratories for more than 30 years and support their challenging workflow procedures by providing advanced technologies for efficient DNA extraction through discriminating STR analysis.**

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With the emergence of new tools and technologies on the horizon, labs will be able to gain more information from challenging sample types, save time with increased sample processing capacity, triage samples for more efficient workflows, solve more cold cases with investigative genealogy and database searches, and even bring the entire workflow to the scene of the crime or event.

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### Government and Academic Research Laboratories

In the face of increasing pressure and demands, today's academic and government researchers work on the front line of discovery. They require the newest available tools with enhanced sensitivity and specificity to address more complex biological questions compared to methods used just a few years ago. Promega continues to develop and improve technologies from next-generation nucleic acid isolation and PCR to advanced assays for cellular biology, metabolism, 3D cellular structures and organoids, protein manipulation and CRISPR knock-ins for tagging cell lines. To help modern researchers successfully publish their results, fulfill their research programs and nurture carefully planned careers, Promega is committed to developing the most advanced bioassays, target engagement and protein degradation tools.



Rhinoceros in South Africa.

Forensic analyst swabbing the head and ears of a rhino during a dehorning procedure in Port Elizabeth.

### Forensics

#### CSI SAVANNA: OVERCOMING THE CHALLENGES OF ISOLATING HUMAN TOUCH DNA FROM POACHED RHINOCEROS

Rhinoceros numbers are on a steep decline, from 500,000 in the 20th century to an estimated 30,000 alive today. Poaching is the main driver for this decline, which comes from consumer demand for rhino horn. Although the trade of rhino horn is banned, the demand remains high. With prices averaging \$60,000 per kg, the sale of rhino horn on the black market is a lucrative venture. To preserve rhinoceros species, poaching must be stopped.

Poaching cases can be extremely difficult to investigate and prosecute due to the nature of the evidence available at the scene. Current practices use rhino DNA profiling to match horns with carcasses, but due to low genetic diversity among some rhino species there is decreased confidence in matching a horn to a specific animal. Human DNA profiling using touch DNA from poachers could be a better approach.

Humans have very unique DNA profiles, increasing chances of linking a poacher to the scene. However, sample collection challenges exist with this approach that need to be overcome. Human touch DNA samples have

low abundance of DNA, and the dry, rough, dirty surface of rhino skin compounds the recovery issue. Optimal sampling techniques combined with sensitive extraction and DNA amplification technologies will therefore be needed to establish human DNA profiles.

Researchers from the University of the Free State in South Africa are investigating various methods of touch DNA recovery from rhino back, rump, ears, legs, head and horns. Several Promega technologies designed for low-level DNA samples have been instrumental in their work.

The Promega Casework Direct Kit, designed for extraction from low-abundance DNA samples, is being used to prepare lysates for downstream PCR amplification. The sensitive PowerPlex® ESI 16 System and Direct Amplification from swabs method is being used to generate the DNA profiles from these low-abundance touch samples. Preliminary results have uncovered mixed and partial profiles, generating hope that human touch DNA could one day be an essential tool in linking or excluding suspects involved in these crimes against wildlife.



Dr. Soly Ismail, Postdoctoral Fellow, Francis Crick Institute

## Research Laboratories

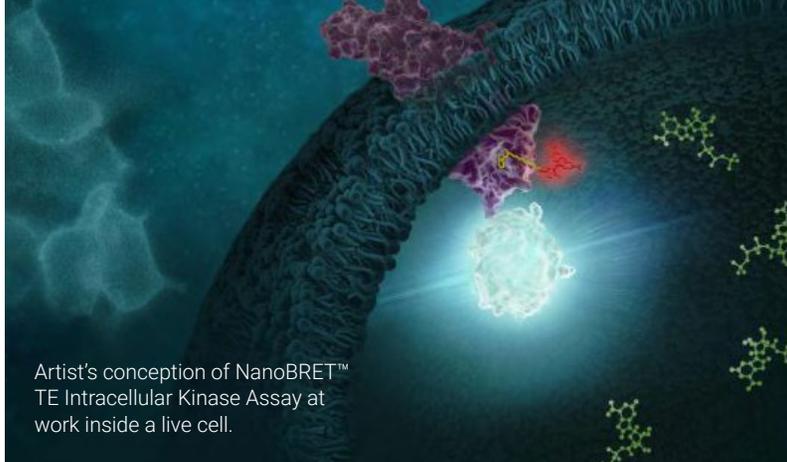
### MEETING THE SCREENING CHALLENGE ON PROTEIN:PROTEIN TARGETS TO UNDERSTAND MALFUNCTION OF HEALTHY CELLS

Billions of new cells are made in the body every day, replacing worn-out, dead or damaged cells and keeping us healthy. Cells multiply by dividing—an existing cell splits in half to create two new ones. This process is very tightly organized so that new cells are made only when and where they are needed. Faults in key genes controlling cell division (known as oncogenes) make cells multiply out of control, leading to cancer. The Oncogene Biology Laboratory headed by Julian Downward at the Francis Crick Institute in the UK investigates how the molecular signals received by cells make them grow and multiply, and how faulty signals lead to cancer. They focus on oncogene function in healthy cells and find out what happens when they go wrong. Some types of cancer can even become ‘addicted’ to certain oncogenes, relying on just one faulty gene to drive their unchecked growth.

Dr Soly (Mohammed) Ismail, a post doctorate researcher within the Oncogene Biology Laboratory, is particularly interested in a target known as Ras. This oncogenic protein is found to be faulty in almost 30% of human cancers, including bowel, pancreas and

lung tumors, and so it is a very important target to understand. Much work has been done on inhibitors of Ras, specifically those that inhibit the Ras-Raf and Ras-P13K protein:protein interactions. In the past 10 years, the Oncogene Biology Laboratory has shown that inhibition of the Ras-P13K interaction has a significant effect on tumor initiation, development and maintenance so finding out how to switch off Ras signaling could be a powerful way to treat cancer. Soly’s aim is to discover and characterize specific inhibitors that could block RAS/P-13K and RAS/RAF for future targeted therapies.

Targeting the interaction of proteins represents a particular challenge for drug screening largely due to the strength by which they bind or their solubility. Promega NanoLuc® Binary Technology (NanoBiT®) was originally developed to detect protein:protein interactions in live mammalian cells. Instead Soly successfully adapted this NanoBiT cellular assay into a biochemical, cell-free format using mammalian cell lysates. The NanoBiT Biochemical Assay now offers an attractive tool for drug screening against challenging protein:protein interaction targets, including the interaction of RAS with PI3K.



Artist's conception of NanoBRET™ TE Intracellular Kinase Assay at work inside a live cell.

## Pharmaceutical and Biotechnology Industries

Scientists within the pharmaceutical industry are continuously developing new small-molecule drugs that can enter cells easily and affect specific target proteins. Targeted cancer therapies that block the growth and spread of cancer by interfering specifically with the diseased cells, but not normal healthy cells, are one example where small-molecule drugs are used therapeutically. At early phases of drug development, researchers may screen more than 100,000 compounds at once to identify leads that can be further optimized and turned into new drugs. The availability of high-throughput-compatible, reliable and predictable assays serves a crucial step toward discovering new safe and effective drugs.

Promega has developed a broad portfolio of assay reagents that meet the needs of these pharmaceutical researchers and have been used widely during various phases of drug discovery and development. For example, our NanoBRET™ Target Engagement Assays allow researchers to quantitatively measure the interaction between a molecule and a protein in live cells reliably in a high-throughput manner. This is a significant advancement as these cellular assays can better predict compound performance. In addition to common drug targets like kinases, this NanoBRET™ Target Engagement technology has also been applied to CRISPR-Cas9 gene edited cells to help identify drugs that can lead to oncoprotein degradation.

## Pharmaceutical

### AIDING IN DRUG DEVELOPMENT AND DISCOVERY

The cell is the basic structural and biological unit of all organisms. How our cells function, including if they divide or die, is tightly controlled by a large collection of proteins called kinases. When these proteins mutate and their signaling capabilities become faulty, cell growth and division can be negatively impacted and diseases such as cancer can occur.

Live-cell model systems are an important tool for laboratory researchers in their quest to develop and evaluate cancer drugs against target kinases. The most helpful live-cell models represent the endogenous biology, or true-to-life conditions, observed within the human body. Studying potential drug compounds in a live cell is a relatively new practice. Scientists typically use biochemical methods with enzymes purified from ruptured cells, but this testing approach isn't always relevant to how drugs behave in the body. Live cells, with the enzymes inside, would provide researchers a more predictive model of drug behavior. Obtaining this more predictive data in the early stages of drug exploration will allow researchers to move through R&D faster and continue to advance human health.

Promega scientists developed a unique way to study kinases using an energy transfer technique and specially designed cell-permeable detection probes that enable testing in a live-cell environment. The NanoBRET™ TE Intracellular Kinase Assays use Bioluminescence Resonance Energy Transfer, or BRET, to measure the binding of the drug to the kinase. This new technique helps researchers determine if the drug gets into the cell, if it interacts with the intended target, and how long it stays bound despite other things in the cell trying to bump it off. With this new live-cell approach, pharmaceutical researchers can arm themselves with the comprehensive data they need for a more complete picture of kinase target effects as they move to the next phases of development.



Over 20 million olive trees in Italy and other parts of Europe are infected with *Xylella*.

## Environmental Testing

### XYLELLA FASTIDIOSA: SEEKING EARLY DETECTION OF A MICROSCOPIC THREAT TO AGRICULTURE ECONOMIES

Agriculture is the lifeblood of human existence. We rely on the cultivation of plants as a source of nourishment for our bodies and the generation of plant-derived products to support our economies. Agriculture offers a connection to the land and a way of life for generational growers. Destruction of our agricultural ecosystems can have devastating impacts on our livelihoods. Sadly, a global agricultural threat is growing at an alarming rate, and the causative agent is a microscopic one. *Xylella fastidiosa* is a bacterium that infects and reproduces in xylem, a tissue found within vascular plants that transports water and nutrients from roots to stems and leaves. The bacterium is mainly spread by insects feeding on plants. Infection with this bacterium deprives plants of the nutrients they need, resulting in starvation and death. Most plants die within 1–2 years of infection and there is currently no cure.

Globally, infection with *Xylella* has affected over 20 million olive trees in Italy and other parts of Europe, bringing the olive oil industry to its knees. In Brazil, the majority of orange trees have been killed in efforts to control

the disease. In the US, Spain and Middle East, almond trees are infected. With such immense socio-economic impacts at stake, quick detection of this bacterium can go a long way to manage the spread of the disease. Labs are exploring new ways of detection, and DNA purification from plants is becoming one of the key aspects of analysis.

Promega is positioned to help in the quest for early detection and continuous monitoring of *X. fastidiosa* infection. We provide tools for DNA extraction and automated processing that can meet the needs of plant pathogen testing labs as the number of samples continues to grow. Together with the laboratory community, we have developed plant and insect DNA extraction methods that are robust and reliable for use with a variety of materials. The Maxwell® line of instruments provides a walk-away, automated approach to extracting plant DNA from up to 48 samples simultaneously. When used together, this system provides purified DNA to plant pathogen testing labs in under one hour for subsequent immediate use in qPCR and other molecular detection methods.



Our Environmentally Preferable Products require less packaging, include fewer hazardous components and generate less waste to support sustainability efforts of customers. To learn more, visit: [Promega.com/EnvironmentallyPreferred](https://www.promega.com/EnvironmentallyPreferred)

## Environmental and Food Testing Laboratories

Demand for food and water testing is increasing as laboratories seek rapid, reliable solutions to ensure products are safe and food ingredient claims are authentic. Biotechnology offers tools for testing labs to detect bacteria or other contaminants in food, water or plants. From GMO testing and pathogen detection in food to water quality and contamination analysis, assays need to satisfy the requirements of food and water testing laboratories, including sensitive detection of unwanted microbes and undeclared ingredients.

To screen plants for GMOs, analyze food for pathogen contamination or authenticate ingredients, DNA must be extracted from the samples. The resulting DNA needs to be pure enough to work in PCR-based analysis, the method most food testing labs use for detection. In Europe, Promega DNA purification reagents have become a reference standard in authenticity determination of meat products, and European Union Reference Laboratory for Animal Proteins in feeding stuffs (EURL) has developed a Standard Operating Procedure for DNA extraction based on our purification chemistry. In addition, our Maxwell® RSC PureFood GMO and Authentication Kit was recently selected by the European Reference Laboratory on GMO Food and Feed Testing for developing new Standard Operating Procedures for food DNA extraction, influencing food companies to use Promega products as part of their routine quality control testing.

Water treatment facilities and desalination plants test water quality and biofilm formation to reduce energy consumption and improve plant operational efficiency. By partnering with these facilities, we have been able to improve our luminescent bacterial detection assay for specific use with water sampling to help with industrial processes like biocide dosage and timing for water cooling systems. Promega Water-Glo™ microbial analysis uses bioluminescence to measure the amount of adenosine triphosphate (ATP) in drinking water, desalinated water and other samples to monitor water quality.

## Clinical and Molecular Diagnostics Laboratories

In 2020, Promega's impact on the clinical diagnostic world was demonstrated through our rapid and robust response to COVID-19 testing. Promega solutions supported COVID-19 diagnosis in over 25 million samples around the globe in the first quarter alone. GoTaq® Probe 1-Step RT qPCR System was added to the CDC's 2019-Novel Coronavirus Real-Time RT-PCR Diagnostic Panel Emergency Use Authorization on March 31, 2020, further expanding testing options and capacity for labs in the United States. Promega Viral RNA sample extraction solutions, ranging from manual to high throughput, provided options for clinical labs processing samples in a time of unprecedented demand on public health labs. Promega custom manufacturing supplies critical reagents that are part of 15 COVID-19 diagnostic tests marketed by other diagnostic manufacturers.

OncoMate™ MSI CE IVD became available to the European market in March of 2020. This new molecular diagnostic tool enables labs to determine microsatellite instability status in tumor tissue, an important step in diagnosing and treating cancer patients. Until 2015, MSI testing was part of a workflow to determine if a patient tumor was hereditary, enabling relatives to have preventive testing. More recently, in addition to hereditary tumor testing, MSI Dx Analysis System status is recognized as a key factor

## Clinical Diagnostics

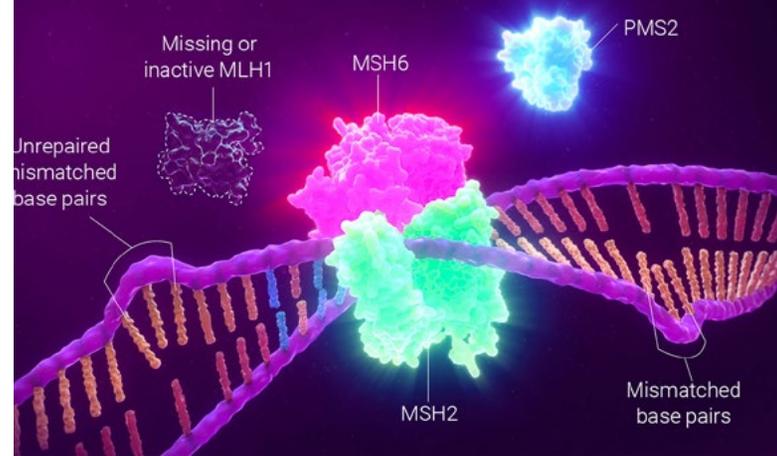
### SUPPORTING TAILORED TREATMENT WITH TUMOR CELL TESTING

Promega first developed the Microsatellite Instability Analysis (MSI) system over fifteen years ago, but the advent of immune checkpoint inhibitor therapy has revealed new applications for the technology. Tumors with defects in the expression of functional mismatch repair (MMR) proteins often have somatic mutations that produce “foreign” proteins that can be detected by the immune system. As a result, these tumors are effective at priming an immune response and subsequently susceptible to immunotherapies. MSI analysis can identify the presence of mismatch repair (MMR) deficiency, and thus predict a positive response to immunotherapies such as immune checkpoint inhibitors.

In late 2019, Promega announced a global collaboration with Merck to develop the Promega MSI technology as an on-label, solid tumor companion diagnostic (CDx) for use with Merck’s immune checkpoint anti-PD-1 therapy, KEYTRUDA® (pembrolizumab). KEYTRUDA®, like other immune checkpoint inhibitors, works by activating the body’s own immune system to identify and attack tumor cells. The Promega MSI technology was used in clinical trials to identify tumors that were likely to respond to this type of treatment. The global collaboration will initially seek regulatory approval for the Promega OncoMate™ MSI Dx Analysis System in the United States and China. Plans to seek approvals in additional territories may follow.

In March 2020, the OncoMate™ MSI Dx Analysis System (OncoMate™ MSI) also received CE marking as a new in vitro diagnostic (IVD) medical device in Europe.

Promega’s research-use-only MSI technology has been validated in labs around the world to characterize solid tumor MSI status. As scientists understand more about the biology of MSI-high tumor cells, even more tailored and effective therapies can be developed against tumors expressing the MSI biomarker.



in determining if patients are eligible for a new and effective class of oncology drugs, PD-1 inhibitors, that are having dramatic results in extending the lives of late-stage cancer patients. In November of 2019, Promega signed a global companion diagnostic development agreement with Merck to further develop the OncoMate MSI assay as a companion diagnostic for Keytruda, a PD-1 inhibitor. Clinical trials are underway in China for this indication.

### Medical Affairs

Accelerating the impact of research on the practice of improving human health and well-being is the highest priority for the Medical Affairs team. Our dedicated team of scientific experts focuses on providing technical and scientific support to the clinical research and healthcare communities around the world.

Medical Affairs plays a critical role in the interchange of scientific and medical knowledge as it relates to patient care. We engage with key scientific leaders and clinicians to provide perspective and input on the evolving needs for medical information, education and support of new product development efforts.

From infectious disease to oncology, impactful science and emerging resilience tie Medical Affairs to our global community.

## INVESTMENT IN INNOVATION

To sustain our contributions to scientific exploration and application, Promega invests in the development and discovery of new technologies. In 2019, over 11% of total revenue was allocated to research and development. Research is not solely focused on the development of new products; our Advanced Technology Group and a group funded by the Federal Government perform basic research.

Our growing investment in innovative research resulted in 79 new patent filings in 2019, bringing our intellectual property library to over 434 granted patents and 206 pending patents. Promega research scientists had 21 scientific papers published in the last year. We also work with academic institutions and other entities to license and develop promising technologies.

## Patents

### Issued and Pending Applications



## QUALITY PROCESS AND PRODUCT

Promega Corporation has a long history of supporting our customers with high-quality products, services and information. Promega Madison, WI, USA, was first certified to International Organization for Standardization (ISO) for quality management systems in 1998, and our commitment continues with our current ISO 13485 and ISO 9001 certifications. The ISO series of quality management system standards are developed and maintained by the International Organization for Standardization. An organization achieving ISO certification has demonstrated to a third party that the organization meets all requirements of the standard and has implemented a quality system capable of developing, manufacturing, testing and delivering high-quality products around the world. ISO certification assures our global customers that Promega is committed to quality and has established reliable and effective processes. ISO certification exemplifies commitments to our customers, to our business, and to all those who rely on and benefit from the use of our products. Currently, 16 Promega locations around the world are certified to meet the requirements of ISO 9001, ISO 13485 or both.

In February 2016, ISO 18385:2016 was published as the first international standard specific to the forensic manufacturing community. In 2017, Promega became the first major forensic manufacturer to achieve third-party certification of the published ISO 18385 standard to minimize the risk of human DNA contamination in products used to collect, store and analyze biological material for forensic purposes. Promega products manufactured in alignment with the ISO 18385 standard include a “Forensic Grade” certification logo.

## GOING ABOVE AND BEYOND FOR OUR CUSTOMERS

I am so thankful and proud to work for Promega and with such amazing co-workers! We received a call from a clinical lab late yesterday afternoon, after our corporate office had closed. The lab was in a pinch with clinical samples to run on their Maxwell® AS3000 Instrument. Their external computer had crashed, and they could not get the replacement computer to connect to the instrument. They had pending patient reports that they needed to release to clinicians and needed to run additional samples today, on Christmas Eve. Team members from multiple departments globally connected late into the evening to begin the troubleshooting and devised a plan to help this lab before Promega closed for the holidays. I visited the lab the next day to trouble-shoot on-site with the remote support of several Promega team members. We were all taking time away from family Christmas eve celebrations. After trying multiple different things over several hours, we were able to access the patient sample run data files and print them to pdf per their SOP. One of the runs was a viral screen of a child pending results. The lab was able to move forward per their SOP and release the results to the doctors. The level of support this lab felt from Promega was astounding. We were literally jumping for joy when we were successful. They are back in business and will be running samples through the holiday. The gratitude and joy the customers and I felt were awesome. Promega co-workers truly are a family and a support network that can always be relied on! This would not have worked without everyone's input and tenacity.

— Amy Parman, Sr. Regional Manager  
with gratitude to Rebecca Roberts, Brian Leininger,  
Jessica Rossol-Allison, Promega Korea, Promega Australia