WE ARE WHERE...

SCIENCE PROTECTS LIVES

Our solutions supported the healthcare sector amid the COVID-19 pandemic as specialists pushed ahead with research, clinical development and then the production of vaccines in record time. We consistently helped smooth the design and development process for medical and surgical solutions tailored to individual patient needs.

2020 and the COVID-19 crisis proved the wisdom of Dassault Systèmes' acquisition of Medidata, which was completed in late 2019. This acquisition – the largest in Dassault Systèmes' history – fits perfectly with our long-term strategy, at a time when life sciences are undergoing major transformation. The combination of virtual technologies, analytics and artificial intelligence is a powerful tool when seeking to visualize the molecular structure of a virtual or to achieve innovation in clinical trials. The patient-centric healthcare model requires a better understanding of the human body's complexity, from DNA to cells, tissue, organs and the organism as a whole. In addition, surgery is entering the era of digital simulation. The virtual twin of humans is becoming a reality to help prepare for procedures and design the medical devices that a patient needs – make in order to prevent illness, provide care, target treatments and repair damage where necessary.

The virtual twin of healthcare to help people live healthier lives

Throughout 2020 and all around the world, we saw healthcare systems come under enormous pressure. The COVID-19 crisis also showed us how much virtual twins have revolutionized the whole sector, from carrying out research to caring for patients. The life sciences industry's response was unprecedented. It worked in a collaborative and rapidly adaptable way, which is why it was possible to produce vaccines in only nine months, whereas it usually takes 15 years. 2020 was also the year in which Bernard Charlès revealed our ambition of moving "from things to life". What difference is there between a manufactured object and life? Life is not made up of spare parts, it cannot be standardized, it's personalized by its very nature.

In healthcare, it's crucial to have a relevant model, calibrated by real-world data. Because to understand the human body, whether it's in good or poor health, we need to bring together a set of very different scientific and medical disciplines, taking a holistic approach to individuals, their experience and their context. Our aim is to get all of these disciplines working together, so that we can visualize, understand, test, and predict what cannot be seen – from the way drugs affect a disease to surgical outcomes – before a patient is treated. We want to improve the patient's overall experience, and this is made possible by the Dassault Systèmes and Medidata innovation platform, the only business and science-based platform to power the innovation cycle end-to-end.

With the **3D**EXPERIENCE platform, our aim is to serve the whole healthcare ecosystem. Together, we are bringing together knowledge and know-how, we are disseminating medical best practice, we are visualizing and predicting responses to particular treatments and interventions. Naturally, patients are central to this vision and so we must address matters of trust, ethics and personal data protection. With the combined power of brands such as MEDIDATA (which is involved in 60% of the world's COVID-19-related clinical trials), BIOVIA, SIMULIA, CATIA, SOLIDWORKS, DELMIA and NETVIBES, we are powering access to vaccines and therapies all around the world, for everyone.

To deal with future crises, however, the industry needs to become more agile. We have a wonderful opportunity to transform it: in the world of precision medicine,

the patient is at the center and every aspect – from how a therapy is designed to how it's administered – must be reconsidered. Current systems are not set up to deal with the complexity of the production process, or the need to make adjustments very rapidly.

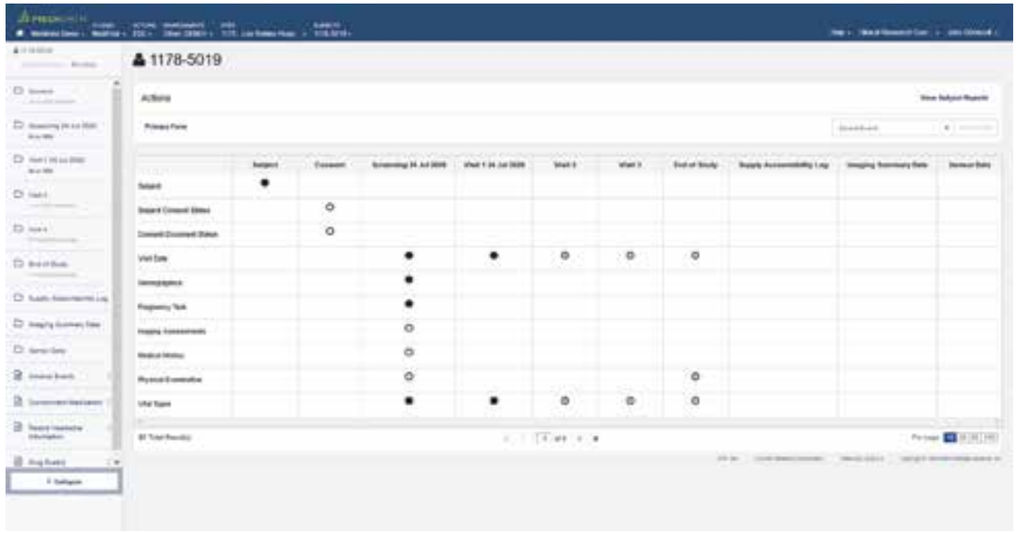
Dassault Systèmes' 4,000 life sciences and healthcare professionals are united in pursuit of that objective, and have the unique advantage of being able to combine the power of virtual worlds – using modeling and simulation technologies – with advanced analytics and data (clinical & real-world). Just as there was a time before and a time after the Boeing 777, there will be a time before and a time after the virtual twin of the human body.

Tarek SHERIF
Co-founder and co-CEO, Medidata
Chairman of the Life Sciences & Healthcare Board

> "The way we provide knowledge to practitioners will be influenced by the quality of the data, greater engagement and artificial intelligence."

PATIENTS PLAY AN ACTIVE ROLE IN CLINICAL TRIALS **WITH MYMEDIDATA**

myMedidata is a new platform that can acquire data from various sources, from treatments as well as from direct interactions with practitioners, and so can play a major role in patient-centric research. myMedidata comprises all Patient Cloud tools and the Rave platform, both of which comply with current regulations. myMedidata also includes eConsent, an electronic system for obtaining patients' consent to take part in clinical trials; eCOA (electronic Clinical Outcome Assessments), a tool for assessing the results of clinical trials; ePRO, which is used to integrate results obtained electronically from patients; wearable sensors, which collate data collected by biosensors and wearable tech and virtual trials.



More than
23,000
clinical trials have already been carried out using MEDIDATA solutions

More than
40%
of clinical trials around the world rely on MEDIDATA solutions

A new dawn and mobilization around healthcare

Although MEDIDATA initially focused on processing data produced by clinical trials, we also use data from other sources. In 2020, hundreds of millions of patients and thousands of researchers had active, simultaneous access to more than 30 terabytes of raw data, generated from sources that are updated daily, within the MEDIDATA environment. The system uses billions of documents, and we are proud to be part of this new era for the whole of society and the mobilization around healthcare in general.

New methods and tools will emerge in all therapeutic areas. Before COVID-19, everything worked on the assumption that the caregiver and patient would be present in the same room. That's what happens when a patient volunteers to take part in an on-site clinical trial or, even more frequently, when a patient consults his or her doctor. But this was not the right assumption. We are now seeing a wave of innovation around virtual trials and new ways of thinking about research.

Precision medicine originated in the field of oncology, based on analyzing the molecular and genetic characteristics of tumors. Research has shown how genetic damage occurs within normal cells, triggering the processes that lead to cancer, which vary from patient to patient. Progress with genome sequencing has allowed us to develop molecular tests and therapies that target these cancer-causing phenomena. These are examples of a convergence of biological and digital domains.

> "The transition to genuine precision medicine will transform the way we carry out research and the way we think about data."

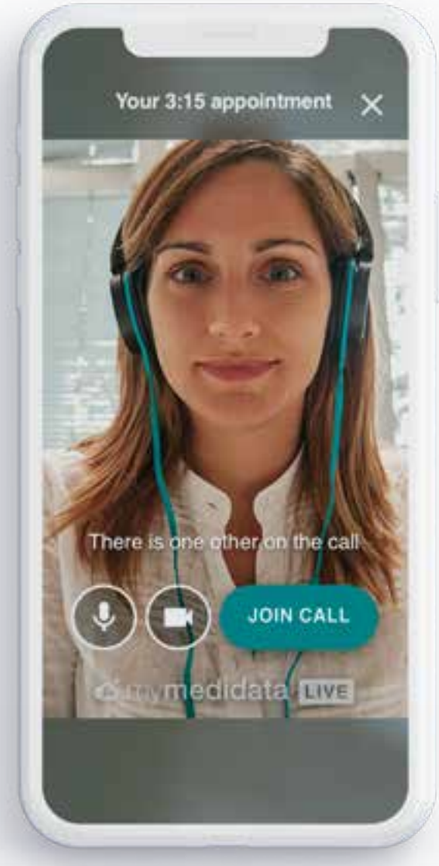
However, precision medicine creates a paradox. Precision medicine means, almost by its very nature, that there will be a decreasing number of patients benefiting from the therapies it produces. The more precision we achieve, the more closely we define the patient population, the more data we need to collect, and the harder it is to collect them and generate the evidence required. The transition from therapies based on large cohorts to genuine precision medicine will transform the way we carry out research and the way we think about data. And when I talk about convergence, I'm also thinking about how we can represent the various therapies on a Venn diagram, with one set corresponding to molecules, another to medical devices and another to digital therapies. Convergence means that the intersections between these various sets will increase. Finally, we must ask questions about access to care: How do we offer therapies to patients in a fair way, regardless of their socioeconomic circumstances and geographical situation?

Glen DE VRIES
Co-founder and co-CEO,
Medidata

When data save lives
Using data that come from various and sometimes heterogeneous origins, sources (and formats, and which are generally not in a coherent, combined form) represents a very promising area of medical research. When these data are restructured and cross-referenced, mutual enrichment takes place and they become a real asset when seeking to make therapeutic progress. When studying COVID-19, for example, researchers used databases consisting of reimbursement requests made to insurance companies and demographic and lifestyle-related data produced by credit institutions and governments. These data, alongside those produced by laboratories, have been and are still being used to support studies of how COVID-19 affects specific groups of people and to predict hospitalization rates.

However, when we talk about the widespread use of cross-referenced, restructured and aggregated data, we immediately run into the question of confidentiality. Data do not consist of abstract figures but are intimately linked to the experiences of patients and citizens. The use of personal data must be clearly circumscribed; but if the rules are too strict, this will prevent effective use of the data; for exemple, if rules prevent singularization, correlation and inference. Singularization means the ability to identify, within a group, the person to which the data refer. Correlation means the ability to connect data from various sources to a single person. And inference means the ability to deduce something about a person simply because he or she is part of a group. Even if the person in question cannot be named, the data set cannot be regarded as anonymous if any of these three elements is possible.

Maintaining medical secrecy and confidentiality
In addition, pharmaceutical and IT companies are working on solutions that allow people to take part in studies remotely or from home. As a result, new issues are raised around obtaining patient identification and consent, as well as maintaining medical secrecy and confidentiality. Remote services must take place with the same level of confidentiality as if they were happening face-to-face behind closed doors in the doctor's office or clinic. Complete segregation of the data, involving both physical and logical separation, is probably part of the solution. When carrying out clinical trials, major pharmaceutical companies send personal data around the world, for exemple, in order to submit data to regulators and to comply with legislation. After marketing authorization has been obtained, data from several countries must be assessed for pharmacovigilance purposes. As a result, legal ways of transferring data, for example from the European Union to the United States, are needed.



MYMEDIDATA ECOA

- Online eCOA
- Patients connect to myMedidata to fill in all necessary patient data forms
- Patients can access their personal assessments

MYMEDIDATA ECONSENT

- Online consent allowing patients to sign up virtually for a new trial
- Video guide and appropriate consent documents provided before virtual signature

RAVE ECOA

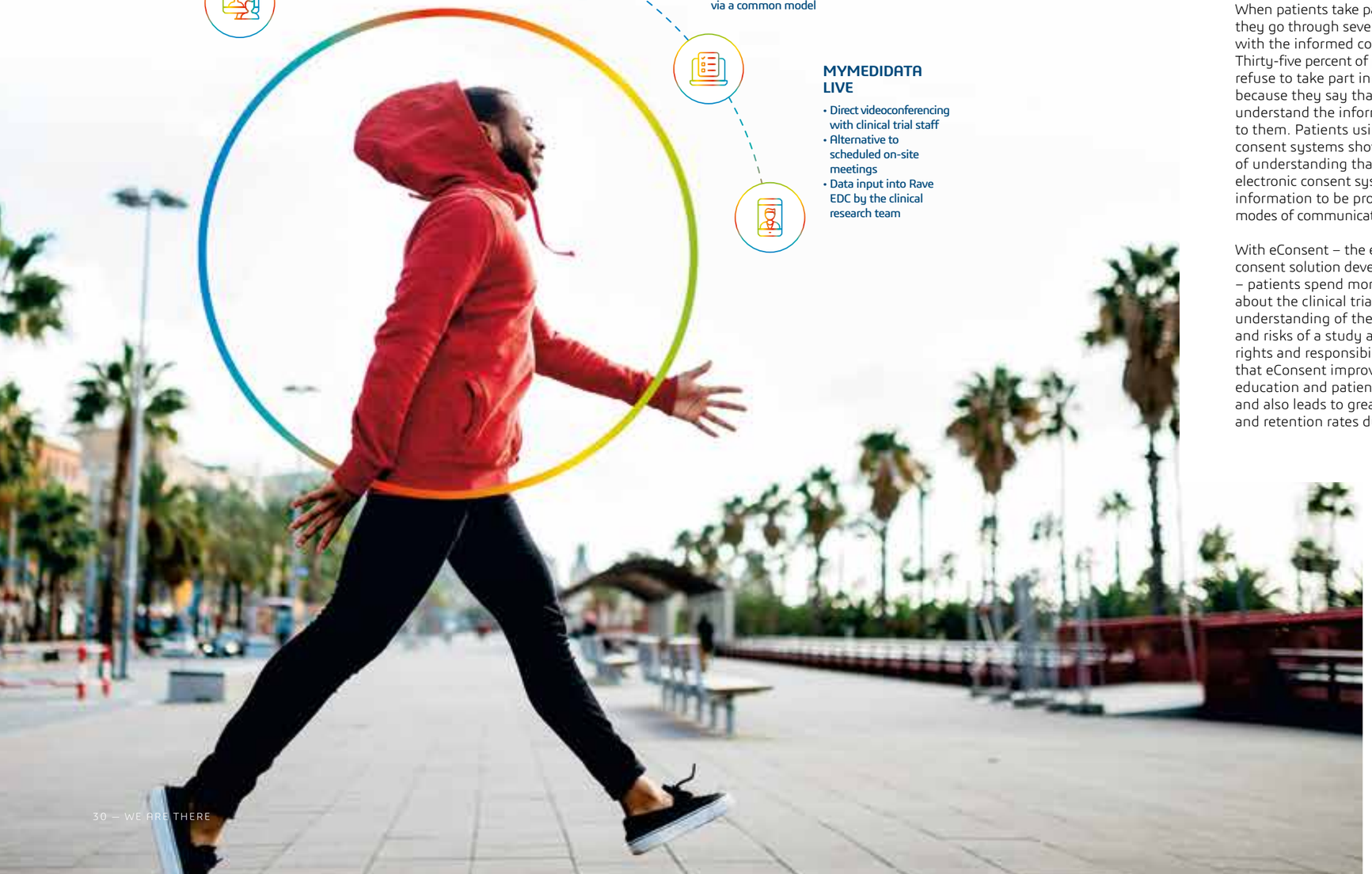
- Account access during the clinical trial
- Electronic assessment of clinical results (Clinical Outcome Assessment)
- Patients fill in forms online

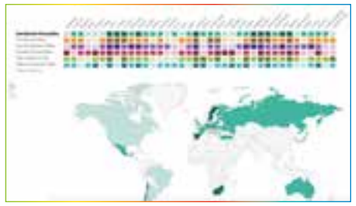
SENSOR CLOUD

- Rapid integration of medical-grade sensors and devices
- Incorporation and analysis of data from any digital health technology
- Standardization of data via a common model

MYMEDIDATA LIVE

- Direct videoconferencing with clinical trial staff
- Alternative to scheduled on-site meetings
- Data input into Rave EDC by the clinical research team





Informed patient consent

When patients take part in a clinical trial, they go through several stages, starting with the informed consent process. Thirty-five percent of potential patients refuse to take part in a clinical trial because they say that they cannot understand the information provided to them. Patients using paper-based consent systems show a lower rate of understanding than those using electronic consent systems, which allow information to be provided via various modes of communication.

With eConsent – the electronic, remote consent solution developed by MEDIDATA – patients spend more time finding out about the clinical trial and gain a better understanding of the aims, advantages and risks of a study and of their own rights and responsibilities. This means that eConsent improves both patient education and patient commitment, and also leads to greater compliance and retention rates during the study.

Processing and using data

MEDIDATA subsidiary Acorn AI uses unparalleled clinical data, advanced analytics and deep human expertise developed over 20 years to propel life sciences companies growth by accelerating insights and speed to market. In particular, the Intelligent Trial solution provides cross-industry, real time operational clinical trial data, enabling customers to gain a competitive edge as they execute clinical trials with increased agility. Synthetic Control Arm®, MEDIDATA's external control arm solution, uses historical, cross-industry patient-level clinical trial data to replace or supplement control arms, especially in diseases lacking clinical equipoise. Thus, Synthetic Control Arm can speed clinical development in situations in which traditional randomized controlled trials are not feasible, or impose undue patient burden.

After acquisition and processing, the use of synthetic control arm also requires special expertise in the data. MEDIDATA Detect is a centralized statistical analysis tool whose algorithms help researchers assess clinical data by focusing on their quality and patient safety. In particular, the solution allows data to be standardized, aggregated and collated from different, complex user experiences and from disparate and heterogeneous sources. MEDIDATA has simplified these advanced analyses by adopting a platform approach, with data being transferred automatically to the cloud, without it being necessary to extract or upload data.

> The European Data Protection Board sets out the legal bases on which we can rely for the data processing.

Translational medicine, targeted therapies and omics sciences

Dr. David Fajgenbaum has changed the way Castleman disease is understood and treated. He had been diagnosed with a form of the orphan disease itself (idiopathic multicentric Castleman disease), and is now in remission because of a precision treatment he identified. He set up and runs a foundation called the Castleman Disease Collaborative Network, which aims to accelerate research and development of treatments for this illness through a collaborative network approach, using both translational medicine and targeted therapies. This has become a model for other rare diseases. The approach integrates patient perspectives to guide high-impact research and identify treatments that can be repurposed for Castleman disease. Omics sciences – such as genomics, proteomics, transcriptomics and metabolomics – have made it possible to develop new technologies, such as biosensors, diagnostic tools and treatments. As Dr Fajgenbaum says, "integrating clinical data using the MEDIDATA Omics platform has genuinely transformed our analysis and interpretation of proteomics data." The approach has saved his life, and the lives of thousands of other patients.

In October 2020, MEDIDATA completed the acquisition of MC10, a company that specializes in developing biomarkers that show a patient's condition or response to a treatment. MC10's solutions are already being used in numerous clinical trials, and add new analysis capabilities to MEDIDATA's Patient Cloud solutions, for example in order to enrich data provided by patients (ePRO) and to assess clinical trial results (eCOA). This will provide the healthcare industry with even more ways of managing clinical trials virtually. When data taken from the real world can then interact with the real world, for example through medical devices, they become much more powerful.

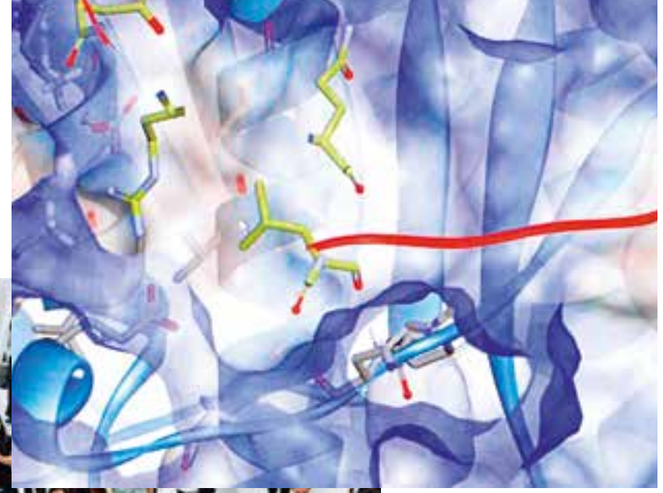
As part of the research on devices, IASO, which takes its name from the Greek goddess of recuperation from illness, is a showcase that illustrates the lifecycle of a biological product combined with an auto-injector platform, intended for the oncology market. It shows the value that the **3D**EXPERIENCE platform can add for those seeking to innovate in the field of medicine or life sciences combined with medical devices.

This model was built with BIOVIA Discovery Studio using PDB structure 6M17 (Human ACE2 receptor in complex with RDB domain from Sars-CoV-2 Spike protein) and 7DK4 (Sars-CoV-2 Spike protein in pre-fusion stabilized conformation with two RBD domain up) and superimposing both structures on the common RDB domain.

Accelerating innovation with *in silico* experimentation

IASO illustrates how 3D design, collaborative engineering and digital simulation advance the development of drug candidates and medical devices. At the manufacturing stage, IASO shows how companies can develop the plant of the future by coming up with new planning and execution solutions. Finally, IASO shows how the **3D**EXPERIENCE platform promotes operational excellence, by optimizing regulatory activities and the quality management system and by providing a holistic and unified view of the patient experience.

Using physical experiments alone is not economically viable, particularly in a rapidly evolving situation like COVID-19. Scientists need a better understanding of how antiviral therapies and vaccines work. To help scientists identify molecules with new properties, BIOVIA has developed BIOVIA Discovery Studio, a modeling and simulation environment that provides a full set of tools, including biological product design and analysis methods, traditional simulations, structure- and fragment-based drug design and virtual screening. The solution also allows users to simulate a drug's pharmacokinetic properties (absorption, distribution, metabolism and excretion or ADME) and predict its toxicity.



Modelisation of a molecular research for the COVID-19 vaccine by the Migal Galilee Research Institute

500,000
people are likely to be enrolled in longitudinal COVID-19 studies in the United States.

30,000
patients have taken part in Phase III trials of Moderna's COVID-19 vaccine.

Producing usable scientific information
The Migal Galilee Research Institute in Israel has been using BIOVIA solutions for four years as part of multidisciplinary research in projects to develop vaccines against avian coronavirus. When COVID-19 became a pandemic, this university research center – specializing in plant science, precision agriculture, environmental sciences, information technology, nutrition and biotechnology – started using these applications and calculation tools to study mutations in COVID-19. The Institute uses a digital approach to managing experiments. Researchers can quickly analyze data collected over the last four years and model the behavior of viral proteins. Using this method, they can better understand new trial results with reference to previous research, and decide which strategies to use in future. More specifically, the BIOVIA Pipeline Pilot solution with its machine learning capabilities can streamline the research innovation cycle by supporting the rapid deployment of data science workflows, accelerating the production of usable scientific information. At the same time, BIOVIA Discovery Studio offers comprehensive modeling and simulation techniques that allow scientists to explore the nuances of protein chemistry, helping them discover and develop therapies based on large and small molecules.

Data captured by patients
When carrying out trials on its messenger RNA COVID-19 vaccine, Moderna used MEDIDATA's Rave Clinical Cloud platform. Working with the urgency required to address the global pandemic, Moderna's teams used MEDIDATA's cloud platform across the various stages of development. The clinical trial is one of the largest ever to integrate data captured directly by patients, which meant that attendance at medical centers was reduced. In addition, virtualization allowed participants to use their own devices, avoiding the need to carry a device provided by the medical team. Moderna has used several of the Rave platform's technologies, including Rave EDC for electronic data capture, Rave eCOA for the electronic assessment of clinical results, and Rave Detect for centralized statistical analysis.

Using these methods, future clinical trials will maximize patients' chances of quickly obtaining a revolutionary and successful therapeutic solution. Because in the end, all of these advances are pursuing the same objective: improving the patient pathway in terms of medical treatment, whatever it may be, but also surgery and prosthetics.

> We are using BIOVIA Discovery Studio and Pipeline Pilot to extend our research and enrich our IT tools.

Itai BLOCH
Computational chemist,
Migal Galilee Research Institute

A prosthetic leg allowing people to continue doing what they love

The core aim of BioDapt is to develop ever more effective high-performance prostheses for athletes and people practicing outdoor sports, to develop ever more effective and resilient high-performance prostheses. For as long as he can remember, CEO Mike Schultz has loved motorsports, motocross and snowmobile racing. He eventually achieved his childhood dream of becoming a professional snowmobile racer, but in 2008, during an international competition, he suffered a major leg injury. The only way of saving it was to amputate around four inches above the knee.

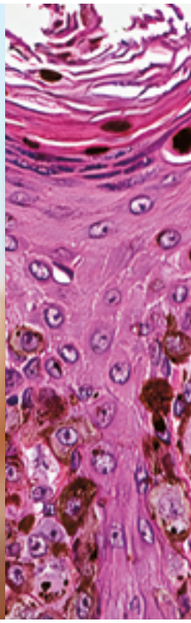
In the spring of 2009, Schultz stood up on his first prosthetic leg. A few months later, he realized that he would need a more elaborate prosthesis if he wanted to resume practicing the sport he loved. And he was confident that he could design it himself. He knew better than anyone how his body needed to perform if he was to become an elite sportsman again. He also knew how the suspension and mechanical components of his vehicles worked. The leg he designed using these twin insights allowed him to win the silver medal in the supercross event in the Summer X Games, seven months after his accident.

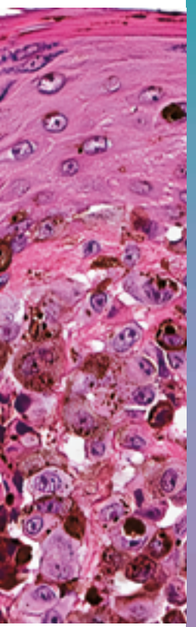
It was then that Schultz understood that his prosthesis could help other amputees. In early 2010, he founded BioDapt, a company aiming to create the most high-performance lower-limb prostheses in the market, intended for use in action sports and motorsports. "SOLIDWORKS makes the process so much easier and quicker and allows us to do so many more things," Schultz enthuses. "We can build the assemblies virtually and then digitally test them with SOLIDWORKS Simulation to see where the weak points are." The solution also allows the BioDapt team to design collaboratively, both in the office and while traveling, which Schultz often is.

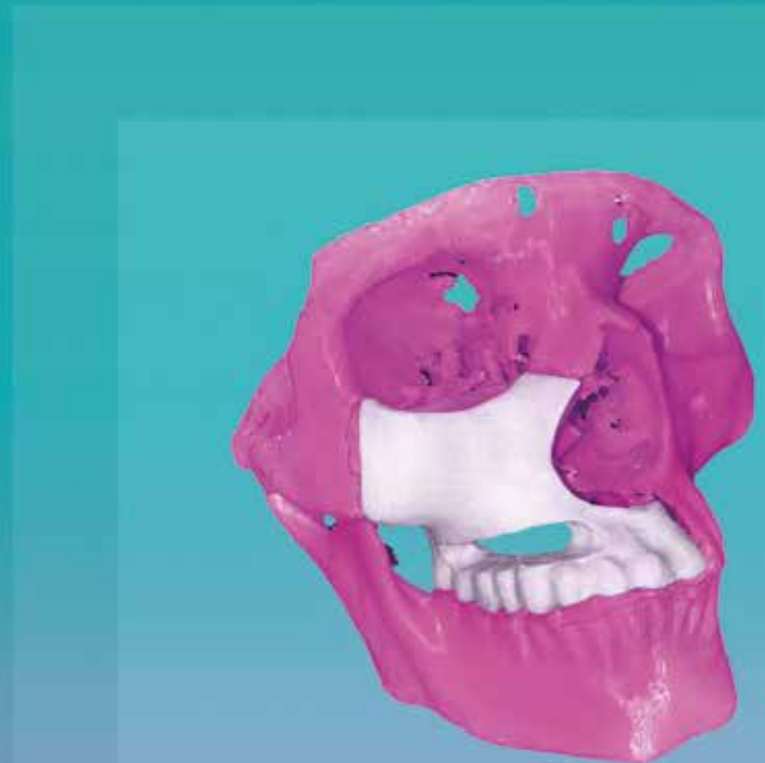
His wife, Sara, has seen the joy that these prostheses give to patients: "You see them light up because now they have the opportunity to do what they love to do, and they tell Mike, 'You have changed my life'." In the 2018 Winter Paralympics, all nine athletes who made it onto the podium in one of the snowboarding events – winning a total of 11 medals between them – were using BioDapt equipment. Today, the company's Moto Knee can be used for snowboarding, skiing, cycling, motocross, driving all-terrain vehicles, strength training, horse-riding and watersports. And the list is continuing to grow as BioDapt's research and development progresses.

SEEING BEYOND APPEARANCES WITH **DAMAE MEDICAL**

Skin cancer is the most common form of cancer, and exists in two forms: carcinoma and melanoma, with the latter being the most serious. Late diagnosis reduces the chance of survival, and every year more than 10,000 people die of skin cancer in Europe. The incidence of melanoma in the general population has been rising for several decades: since 1945 it has doubled every 10 years. DAMAE Medical helps diagnose skin cancer at an early stage and in real time. The company has developed a new portable imaging device that allows non-invasive 3D imaging of cutaneous tissue. Just placing the device on the skin allows it to generate real-time images very similar to traditional histological images. The portable device uses a patented approach that combines optical coherence tomography (OCT) and reflectance confocal microscopy (RCM), called LC-OCT (Line-field Confocal OCT). This French startup has been supported by Dassault Systèmes' **3D**EXPERIENCE Lab program since November 2019.







LUCID IMPLANTS AND **3D**EXPERIENCE

LUCID Implants uses the **3D**EXPERIENCE platform to design personalized implants and carry out immersive surgical planning. The platform is also used for the cloud quality management system, particularly for the in situ monitoring of machines, data capture and part traceability, and for inventory and logistics management, sales management and financial reporting. LUCID Implants has been supported by the **3D**EXPERIENCE Lab program since March 2020.

No two individuals have the same facial anatomy

LUCID Implants is an Indian medical technology company that provides personalized surgical solutions. Its teams design, develop, manufacture and sell craniomaxillofacial and neurosurgical implants that are custom-made and individually fitted to adapt precisely to each patient's specific anatomy. LUCID's complete solution includes virtual planning for 3D presurgical simulations, personalized anatomical models for evidence-based simulated assessments, patient-specific preoperative surgical guides to ensure absolute precision and customized implants for a perfect fit.

No two individuals have the same facial anatomy, whereas all conventional implants are mass-produced. Often, the surgeon tries to adjust the patient to the product rather than the other way around. In traditional facial reconstruction procedures, the practitioner must choose a commercially available implant, such as titanium mesh, or harvest an autologous bone graft taken from the patient's own body with a size and shape that the surgeon thinks will work best for the patient. These solutions lead to problems such as increased risk, poor aesthetics and low patient quality of life. LUCID's personalized solutions also allow full control over the surgical procedure and the value chain, minimizing tissue damage, the length of hospital stays and the cost of care.

REPAIRING **A CHILD'S HEART**

Dr. David Hoganson, a cardiovascular surgeon at Boston Children's Hospital, was born with a congenital heart defect that required cutting edge open heart surgery. After working several years as an engineer, he pursued cardiovascular surgery before further specializing in pediatric cardiac surgery. As a surgeon, he does innovative work with newborn babies and children with congenital heart disease, often adapting procedures intended for use in adults. In particular, Dr. Hoganson developed revolutionary transplantation therapies and lung tissue engineering protocols.

Further he has pioneered the use of a patient's virtual twin to model complex cardiac configurations prior to treatment, allowing the surgical team to simulate various surgical scenarios in silico. For example, Dr. Hoganson's team can simulate how blood flow will change depending on different repair or reconstruction approaches, helping them select the most effective surgical option. In complex cases, synthetic patches can be designed and tested on the virtual twin to precisely match the patient's morphology and ensure optimal outcomes. He is also revolutionizing the patient experience by combining virtual twins and virtual reality to help patients and their families better understand the condition and participate in the treatment plan.

By combining his personal experience, engineering background and medical training, Dr. Hoganson is creating new possibilities for complex treatments, giving hope to many families whose children may now thrive when otherwise they might not even survive.