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In 2018, Solvias achieved excellent business results and gained further momentum on its growth trajectory.

Revenues rose by 22.8% over the previous year to CHF 93.0 million. Profitability improved significantly for the fifth consecutive year driven by the portfolio transformation started in 2015. Solvias generated 64% of its turnover outside of Switzerland, of which 16% in the US, as our international expansion continues.

All business units delivered strong sales growth and profitability improvements in 2018, fueled by greater cross-disciplinary synergies and larger project packages from our customers, in particular with biopharmaceuticals. Sales were also buoyed by increased regulatory scrutiny across the pharmaceutical, biotechnology and medical technology industries, along with the continued trend in higher outsourcing of analytical services and research projects.

Solvias is well-positioned to meet this increased customer demand with a realigned portfolio of services and solutions, expansion into new areas of scientific expertise, and professional project management teams.

In a market where competition for talent is key, the ability of a growing, science-based service organization to recruit many highly qualified people is proof of its attractiveness as an employer. Over the last two years, Solvias has expanded its workforce in France and Switzerland by around 100 employees. In order to onboard effectively, an innovative program was rolled-out in Switzerland, designed to provide a foundational understanding of our company’s culture and the industry’s operating standards to this new generation of talent.

We are confident that Solvias has put in place the right initiatives and measures to provide a solid basis for its future in delivering solutions to help our customers bring safer and better products to the market faster.

Luzi A. von Bidder
Chairman of the Board

Karen J. Huebscher
Chief Executive Officer
the board of directors

Luzi A. von Bidder
President

Christian Leemann
Member

Sandra Neumann
Member

Hansjörg Walther
Member

The Board of Directors is elected every year during the Annual General Meeting.

key figures

EMPLOYEES: 521
284
237

ROW: 64%

SWITZERLAND: 36%

SALES
2018: CHF 93.0 million
2017: CHF 75.7 million

REGIONAL SALES
the executive committee

Karen J. Huebscher  
Chief Executive Officer

Louise Davies  
Chief Financial Officer

Hans Van Nuffel  
Head Conforma & Process Analytical Technology, Head M&A

Elmar Zurbriggen  
Head Biopharma

Danièle Schott  
Head Specialised Expert Analytical Solutions
QUALITY AS A COMMON CULTURE

Solvias is an essential link in the research, development, and manufacturing process for some of the world’s largest pharmaceutical and medical device companies as well as smaller biotechs and contract manufacturing organizations. The solid foundation for that collaboration is our company-wide commitment to quality. It starts with training. Quality is a key component of the Solvias onboarding program in Switzerland, centralized in 2018 to ensure that all new employees share a foundational understanding of our industry’s regulatory practices and systems. New employees in our laboratories undergo a rigorous program with basic training and technical qualification, depending on their type of work. During the year, employees working under GMP conditions take an average of 14 days of training to stay on top of and aligned with evolving regulatory guidelines.

Our Quality Unit for the Solvias Group consists of 20 employees who monitor ongoing processes, prepare for audits/inspections, support colleagues on how to further improve and strive to embed a quality mindset in everything we do. Internal audits are performed to learn from these findings in order to fine-tune our processes. In addition, we are regularly audited by our customers. In 2018, there were 57 customer audits at our site in Kaiseraugst, Switzerland and around 30 at Confarma in Hombourg, France.

PROVEN TRACK RECORD IN REGULATORY INSPECTIONS

Solvias is regularly inspected by the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA) and Swissmedic. The last FDA inspection took place in October 2017; there were no observations. The last Swissmedic inspection was in February 2019.

In 2018, Solvias AG in Kaiseraugst successfully completed ISO recertification and was found to be compliant with ISO 9001:2015. In addition, the scope of our certification was expanded to integrate our production activity in Basel, providing greater transparency for our customers. The resulting Certificate of Compliance confirms our adherence to the standards of good manufacturing practices (GMP) in accordance with the Pharmaceutical Inspection Cooperation Scheme and the directives of the European Commission.

Conforma, our specialized biological analysis unit in Hombourg, France, offers services according to GMP, GLP, ISO 17025, ISO 9001, ISO 14001, and OHSAS 18001 standards. The site is authorized by the French health authority ANSM for compliance to GMP and GLP and accredited by COFRAC for compliance with ISO 17025. Confarma France SAS successfully passed its most recent inspection by the FDA in 2014. In addition, the annual self-identification of Conforma France SAS, as required by the GDUFA, has successfully passed validation and been accepted by the FDA.

While meeting current regulatory requirements, the Solvias group is moving into the future of quality assurance. Our continued roll-out of a paperless quality system with the digital platform MasterControl will enable us to harmonize quality systems across all our sites, help us retrieve crucial information faster, track key performance indicators in quality and offer online training to employees. Importantly, it will help us to better align with the quality systems of our customers.
In 2018, Solvias successfully filled a significant number of positions, representing an increase of 13% of our workforce. This is a solid achievement for a contract research and service company in an area of high competition for qualified resources. The total number of Solvias employees reached over 500 at the end of 2018.

In hiring new people, we not only look for the best scientific talent but also individuals who embrace our values and behaviors. To this end, Solvias centralized its approach to onboarding new employees in Switzerland with the introduction of an ambitious program in 2018. This one-week program is designed to ensure that each new team member understands the basics of ISO, GMP and Quality, along with our strong customer focus.

Our success is dependent upon highly qualified, engaged people who put their unique skills, experience and expertise to work for Solvias each day. With our central service hub in an area of Europe where the borders of France, Germany and Switzerland meet, our employees share a combination of languages and culture that gives our company a diverse, international touch.

We strive to create an atmosphere where every individual can have an impact and grow both personally and professionally.

A LEARNING ORGANIZATION THAT INVESTS IN ITS PEOPLE

Continuous learning is an important part of who we are. Personal development plans may include specific scientific topics, management training or general courses on improving communication and leadership skills. In addition, all employees involved in projects receive foundational training in project management.

With a professional project management office and ongoing training of dedicated project leaders, Solvias is able to manage complex projects according to internationally recognized standards. Project leaders mobilize internal resources across our different areas of scientific expertise to work in close collaboration with our customers. No matter how great or small the contribution, we enjoy the feeling of shared success in helping our customers achieve their goals.

We continue our intensive company-wide journey to embed Lean culture and continuous improvement at all levels of the organization, from the implementation of shop floor management boards in our labs to the introduction of a paperless system to simplify employee access to HR services such as pension information.

2018 was an intense year of growth for Solvias and we are set to consolidate our progress throughout 2019. As our company’s original founders retire, we will continue to integrate a new generation of qualified people driven by stimulating science, an international culture and dedication to our customers.
Solvias is well-positioned to satisfy our customers’ growing demand for expert analysis of drug products for genotoxic impurities from the manufacturing process as well as extractables and leachables originating from packaging materials and/or devices.
The synthesis of active pharmaceutical ingredients (APIs) and the manufacturing of pharmaceutical products involves the use of reactive chemicals, reagents, solvents, catalysts and other processing aids. As a result of chemical synthesis or subsequent degradation, trace levels of impurities can be found in all drug substances and final drug products. Impurities that are genotoxic or potentially mutagenic represent an area of special concern for drug regulators and the pharmaceutical industry.

Plastics used as single-use materials during the manufacturing process, in pharmaceutical packaging or in delivery systems are a potential source of impurities that can migrate into the final drug product, adversely affecting its quality, efficacy and safe use. Safety assessment of drug products therefore includes identification, toxicological evaluation and quantification of extractables and leachables during design and development of the manufacturing process.

The complex chemistry of potential interactions between compounds and the highly reactive nature of certain substances calls for specialized expertise. Solvias has over 15 years of experience in method development and validation for impurities analysis, with a portfolio of over 100 methods developed. For extractables testing, our proprietary database of 6,000 compounds allows rapid identification down to the ng/mL range. This know-how and expertise are proving invaluable not only for APIs but increasingly with biopharmaceuticals.

Solvias deploys a full range of state-of-the-art technologies: Accurate Mass Orbitrap LC-MS/MS, Liq. Inj. GC-MS/MS, HS-GC-MS/MS, ICP-MS, and ICP-OES. From routine analysis to troubleshooting, customers are ensured of reliable results, flexible capacity and fast turnaround times.

GENOTOXIC IMPURITIES

The International Conference on Harmonisation (ICH) recently updated its guidelines for genotoxic impurities (GTI), those which have been demonstrated to be genotoxic on an appropriate test model, and potential genotoxic impurities (PGI), those which show structural alerts for genotoxicity but have not been tested. Solvias provides analytical services for controlling GTIs in line with ICH guideline M7 (R1) for the assessment and control of DNA-reactive or mutagenic impurities in pharmaceuticals to limit potential carcinogenic risk.

Our expertise spans analytical techniques for structure elucidation and quantification of small molecules, from unknown compounds in release analytics to the development of methods for routine impurities. Solvias’ experts are well versed in handling highly toxic substances that require special safety precautions (e.g. cytotoxic substances). Regardless of the matrix, the genotoxic compound and chemical or physical properties, GTI control relies on careful method selection and years of experience.

EXTRACTABLES AND LEACHABLES

Extractables studies are performed using appropriate solvent systems under controlled conditions simulating the migration expected for the drug product. Extracts are semi-quantitatively evaluated by organic screening methods, capable of identification at ng/mL level. All compounds detected may be toxicologically categorized using the Quantitative Structure-Activity Relationship approach (Q-SAR). Results are used by the drug product manufacturer for safety assessments and for the potentially required subsequent Leachables study design. This study provides accurate quantification of a subset of extractables identified as potential leachables above the Safety Concern Threshold (SCT) using validated methods on drug product stored under controlled conditions for pre-defined periods.

Along with expert testing, Solvias provides consulting services for the development of study strategies, choice of targets, and method validation carried out in accordance with FDA/EMEA, BPSA, and PQRI regulations.
Dedication to customers and technological expertise make Solvias the perfect partner for fast and reliable development of analytical solutions to decrease the time required to bring pharmaceutical products to market.
Solvias is uniquely positioned to help our customers meet increasingly strict regulations with a comprehensive range of specialized expert analytical solutions (SEAS), fully aligned with the latest regulatory requirements, GMP and ICH guidelines to ensure patient safety.

Our SEAS team offers a range of services spanning development and validation as well as release tests using methods for elemental analysis, physico-chemical testing, and wet chemistry including titration. We also perform trouble-shooting, e.g. for unknown impurities (including quantification, structure elucidation) at trace level in complex matrices or in the context of particulate contamination of biopharmaceuticals. This is complemented by extractables and leachables services and quantification of genotoxic impurities using coupled analytical methods such as GC/MS/MS and accurate mass high resolution LC/MS/MS (see also feature story pages 10-11).

Our experts provide customized solutions to support the entire life cycle of drug development, from the early preclinical phase to clinical development and commercialization. They develop, validate and execute methods for raw materials, intermediates, active pharmaceutical ingredients (APIs) and drug products, along with packaging and, especially for biopharma, single-use systems.

CUSTOMER-FOCUSED SOLUTIONS WITH A SINGLE POINT OF ACCESS

Our customers benefit from a single point of access to state-of-the-art solutions tailored to the most demanding requirements. By interacting with a network of experts, both within Solvias and through external partners to fill any technology gaps, we ensure a complete package of solutions for customers in the pharmaceutical, biotech, cosmetics, fine chemicals and animal health industries.

Solvias responds to the most demanding regulatory challenges by bringing together a broad scope of analytical techniques with expertise backed by decades of experience in the field. Leveraging complementary techniques for most applications, we are able to offer optimized solutions to respond to our clients’ needs.

Some examples are:

• Application of ion chromatography (HPAEC-PAD) within biopharmaceutical analysis for determination of glycans in complex matrices in addition to other techniques
• Characterization of syringes, e.g. using IR spectrometry for analysis of silicone coating and ICP-MS for determination of tungsten residues
• Occupational hygiene analytics to ensure the safety of customer’s employees
• Solid state studies to ensure the optimal form of drug substance (DS) for development
• ICP-MS applied to metal analysis at the ultra-trace level

Whatever the requirements, our experts in SEAS are dedicated to delivering a solution that is fit for purpose.
Solvias works in close collaboration with innovative, fast-growing biotech companies, major drugmakers and leading contract manufacturers to facilitate faster market access for biopharmaceuticals. We apply our proven expertise to complex analytical challenges around the entire spectrum of monoclonal antibodies, antibody-drug conjugates (ADCs), glycoproteins, PEGylated proteins and peptides, biosimilars and vaccines as well as gene and cell-based therapeutic drugs. We also provide DNA sequencing, cloning, PCR technology and FACS expertise.

Solvias experts understand the need to progress rapidly and cost-effectively at the early stage of drug development. From one central service hub in the Basel area, we provide long-standing expertise not only in physico-chemical and functional analysis, but also in analytical services around raw materials, excipients, extractables and leachables, and trace analysis as well as container closure integrity tests (CCIT).

**SOLVIAS HAS A WEALTH OF EXPERIENCE TO SUPPORT THE CGMP ANALYSIS OF BIOLOGICS AND BIOSIMILARS**

We understand that early assessment of a protein’s stability can be invaluable, even during preclinical development. For drug substances and drug products, all stability aspects can be monitored, including long-term and accelerated stability studies, in-use studies, short-term temperature excursion studies and forced degradation studies according to ICH guidelines Q5C and Q1B. For complex projects, we offer a dedicated team of professional project managers to ensure efficient coordination and communication among all parties.

We support our customers and internal experts with innovation. The service portfolio is continuously expanded, e.g. with new CD instruments for secondary structure determination of proteins, additional UPLC systems, additional mass spectrometer (MS) capacity along with CE-MS, performance of native MS projects, improved data workflows for in-depth protein characterization, as well as particle characterization studies with micro-flow imaging for biopharmaceuticals.
Our expert explains how Solvias supports customers with a range of highly specialized ‘generic’ methods for process validation studies to shorten timelines and minimize costs in bringing new biopharmaceuticals to patients.
Rapid growth in the biopharmaceuticals sector continues to generate increased demand for specialized analytics to ensure the quality and safety of the drug substance and final drug product. Roger Fischler, an analytical chemist with Solvias who leads a dedicated team of experts, explains how we provide optimized solutions to support our customers in this specialized area.

WHAT ARE PROCESS-RELATED RESIDUALS AND WHY ARE THEY IMPORTANT?

A number of chemicals are introduced at various stages of upstream bioprocessing and almost entirely removed during the downstream purification phase. Process-related residuals can remain, however, including any impurities from antibiotics, buffer components, catalysts, anti-foaming or process-enhancing agents. Process validation studies are an essential part of validating the manufacturing process in order to demonstrate the effective removal of these impurities in downstream purification.

At Solvias, the team develops and validates analytical methods to detect and quantify process-related residuals so that customers can be sure their drug substance meets safety guidelines. Our team also interacts with colleagues in the Biopharma department who carry out assays for other process-related impurities, such as host cell proteins and DNA, that may cause adverse reactions in animals and humans.

WHAT SPECIAL CHALLENGES DOES THE ANALYSIS OF SUCH IMPURITIES PRESENT?

We are dealing with relatively low concentrations of small molecules in complex biological matrices. Small molecules can have as few as 20 atoms whereas large molecules have up to 50,000. Depending on the analyte, we must evaluate for interferences from buffers, excipients and protein load. Choosing the best technique can be challenging. It’s often a balance between sensitivity and specificity. Therefore, being able to consult with specialist colleagues in other areas such as mass spec is a great advantage that Solvias can provide through its hub approach and the breadth of services offered.

This kind of work requires a broad set of testing capabilities and a great deal of experience. You need people in the labs who really understand the product and the critical steps in the manufacturing process. You need a team highly skilled in chromatography and also able to do sample preparation.

WHY DEVELOP GENERIC METHODS?

Regulatory guidelines require separate bioprocess steps for each impurity. While specific residuals are unique, the purification and validation steps are identical. Recently, Solvias decided to develop and prevalidate a set of generic methods to provide customers with faster, more economical solutions.

Thanks to decades of experience in this field, we were able to select from a huge palette of methods. Not all analytes have generic methods; in some cases, development of custom methods is key for our customers, which requires additional validation time.

HOW DO YOU APPROACH EACH CASE?

We begin by meeting with our customer to evaluate their requirements, preferably on site. We learn a lot through peer-to-peer contact with our clients, through their experience with the product and the regulatory challenges they face. Based on their sample and matrices, we take into the account various parameters such as the limit of detection (LOD) and limit of quantitation (LOQ).

Throughout the different phases of clinical development, the drug formulation evolves and so we adapt our methods accordingly. We use a range of technologies for method development and validation, the core of which is chromatography: HPLC, GC and GC headspace. We also handle special requests requiring, for example, evaporative light scattering detection or charged aerosol detection.

Our team is expanding in 2019 to meet a growing market demand for support of downstream bioprocesses and generic methods for process-related residuals, along with release analytics, drug substance studies and special cases.
The identification and selection of an optimal solid form can have a significant practical and commercial impact on drugs. Solvias combines decades of experience in this field backed by science and advanced technology. We continuously expand our service offering across the value chain to serve a growing customer base in Europe and the United States.
Solvias has proven expertise in solid state development, from preclinical development through manufacturing of the final drug product. We provide an integrated approach – from systematic salt, co-crystal, and polymorph screening to controlled scale-up of the crystallization process and quality control of drug substance (DS) and drug product (DP) – complemented by a full range of physico-chemical studies.

In a well-designed salt/co-crystal screening process, the optimal solid form is chosen quickly, based on parameters such as solubility, hygroscopicity, crystallinity, chemical stability and suitability for production. Toxicological aspects, as defined in the FDA GRAS list, are the basis for selection of possible counter ions or co-crystal formers as well as the intended application. The aim of a polymorphism program is to identify and characterize new polymorphic forms, hydrates and solvates of a substance, and to understand the relationship between the different solid phases, so that an ideal form can be recommended for development. The Solvias polymorphism screening strategy has been optimized through decades of experience and is tailored to our customers’ needs. The combination of our optimized screening strategies with cutting-edge, high-throughput technology and rapid analysis by x-ray powder diffraction (XRPD) or Raman spectroscopy provides the maximum information with the minimum amount required of the valuable drug substance.

OPTIMIZING OUR EXPERTISE TO MINIMIZE CUSTOMER RISK FROM CRYSTALLIZATION TO COMMERCIAL SCALE

Our crystallization development program leads to robust, reproducible, and scalable crystallization processes that generate the desired crystalline form, size and shape. We collaborate closely to take full advantage of the broad know-how of Solvias Ligands & Specialty Products from process development to commercial scale. The crystallization processes are scaled-up jointly to the kilogram scale and all critical parameters of crystallization downstream processes, such as drying, are defined for large-scale production. Customers are then provided with a data package allowing them to transfer our processes to commercial scale with minimized risk.

Quality control of DS and DP with respect to solid form composition is critical for product quality and safety. Depending on product and application, the team develops and validates methods from simple identity tests to sophisticated quantitative and limit tests of crystalline or amorphous fractions. Routine QC testing under cGMP can also be provided.

For more than 10 years, Solvias has supported the enforcement of intellectual property rights of its customers. The combination of high data quality and state-of-the-art equipment with highly skilled experts guarantees best possible results from investigations of samples that potentially infringe upon existing solid-state patents.
Release testing parameters typically address:

- **IDENTITY**
  identifications of ions and functional groups, chromatographic methods: HPLC, TLC and GC, spectroscopic methods: IR, UV

- **STRENGTH AND PURITY**
  chromatographic methods: HPLC, UHPLC, HPTLC and GC, titration

- **QUALITY**
  physico-chemical properties, water content, aerodynamic particle sizing (e.g. NGI for inhalers), galenical tests for all dosage forms, hydrolytic resistance of glass

- **SAFETY**
  limit tests of heavy metals and ions, residual solvents by GC

- **POTENCY**
  enzymatic activities

Regularly performed testing includes:

- Long-term stability studies according to ICH guidelines
- Ongoing and follow-up stability studies
- Comparability studies
- Stress tests, forced degradation
- Photostability testing according to ICH guidelines
- In-use tests, freeze-thaw cycles
- Excipient/API compatibility
- Interaction studies with primary packaging
- Stability protocols, reports and interim reports
- Stability indicated method development
- Identification of unknown/new impurities at following conditions: 25°C/60%R.H., 30°C/65%R.H., 40°C/75%R.H., 30°C/75%R.H., 5°C, 50°C or 60°C, -20°C, ≤-60°C, and so on.
Confarma is a fully-owned affiliate of the Solvias group specializing in functional and biological analysis. Based in France, this business unit expands our access to key European markets with a highly complementary and growing customer base in the pharma, biotech, medtech and cosmetic industries.
Our highly specialized analytical services span microbiology, cellular biology, virology, toxicology and molecular biology, with particular expertise in sterile products and environmental analysis. We work according to GMP, cGMP (FDA), GLP and ISO 17025 standards. Operating from a specialist facility in Alsace, France, we offer expert services in the following areas:

**MICROBIOLOGY**
- TESTING FOR STERILE PRODUCTS
  - rapid sterility test, sterility test, bioburden, mycoplasma detection
- TESTING FOR NON-STERILE PRODUCTS
  - microbial limit test (MLT), challenge test
- ENVIRONMENTAL TESTING
  - water analyses, mapping, microbiological identification, disinfectants
- SPECIALIZED STUDIES
  - antibiotics, integrity testing, alternative methods

**BIOLOGY, TOXICOLOGY AND CELLULAR BIOLOGY**
- ENDOTOXIN AND PYROGEN TESTING
  - monocyte activation test (MAT) *(in vitro pyrogen test)*
- CELL BIOASSAYS
  - characterization
- IN VITRO ASSAYS
  - cytotoxicity, genotoxicity, ames test, ELISA, proteins
- BIOCOMPATIBILITY
  - all *in vitro* and *in vivo* studies according to ISO 10993 and USP guidelines (<87> and <88>)

**VIROLOGY**
- VIRUS DETECTION
- VIRUS ACTIVITY MEASUREMENTS
- VIRUS IDENTIFICATION BY DNA SEQUENCING

**CHEMISTRY**
- TESTING FOR STERILE PRODUCTS
  - particle size determination
- TESTING FOR HERBAL PRODUCTS
  - pesticides
- ENVIRONMENTAL TESTING
  - cleaning validation, total organic carbon, total hydrocarbons
unleashing the potential of gene therapy

Gene therapy holds huge potential to treat and even cure many diseases, especially those due to defective genes. However, gene therapy presents many technical challenges that must be overcome in the research lab before it becomes a practical approach to treating disease. Solvias is applying the skills of our highly trained analytical experts on cross-functional gene therapy projects that may unleash this untapped potential.

Solvias has been active in assuring the safety of advanced therapy medicinal products (ATMPs) for years, with a range of tests including analysis of sterility, mycoplasma and absence of pyrogens. This has required adaptation of well-known analytical methods to the new products, including development of specific protocols, e.g. for mycoplasma detection by polymerase chain reaction (PCR) in solutions containing a highly concentrated cellular background. Methods like the monocyte activation test for detection of fever-inducing contaminants were adapted to cell suspensions, and solutions found to bring testing from the centralized lab to the site where patients await their treatment.

Now Solvias is breaking new ground with the evaluation of treatment efficiency, working on the technical transfer and validation of selected analytical tests for the characterization of patient-derived cellular gene therapy drug products. These emerging therapies obtained from the patient’s own genetically modified cells may soon offer a potential cure for severe inherited disorders.

LEADING EXPERTISE IN PCR COMBINED WITH CELL-BASED BIOASSAYS

Extensive capability in PCR technology has enabled the scientists in our molecular biology labs to adapt and quickly acquire additional expertise, for example in fluorescence activated cell sorting.

“From a technical point of view, the analytics are well established at Solvias. Our real-time or Q-PCR work, for example, to determine identity and transduction efficiency typically involves a three-room concept to avoid any risk of false positives from cross-contamination,” explains Dr. Renato Tarchini, Senior Scientist.

When cells are withdrawn from the patient and genetically modified to produce the drug product, it is essential to ensure the efficacy of the therapy in a timely manner before reintroducing the cells to the patient.

Dr. Anja Fritsch, Head of R&D at Confarma, Solvias’ biological analysis center, explains the critical role of cell-based bioassays: “This is really cutting-edge science and it’s very exciting. If you’re correcting a genetic defect in cells, you have to show that the new cells actually perform their physiological function better than before. One of the challenges is developing methods that haven’t been used in a GMP context, with instruments that haven’t been qualified in that environment, so creative solutions must be found to ensure data integrity and other regulatory considerations.”

The project team deploys a step-wise approach, collaborating as a team between Solvias group sites in France and Switzerland.

Dr. Katsiaryna Tarasava, Project Leader: “In addition to the excellent work from our operational teams in the labs, we need close collaboration between our scientists and good communication with our customers to troubleshoot and implement the best solutions. Thanks to this approach, projects are running smoothly and we are able to perform gene therapy analytics under GMP using fully validated methods.”

Solvias will continue to expand these activities in order to support a growing customer demand for such specialized techniques and ultimately help transform medical practice in multiple disease areas.
Our catalysis technology and ligands unit provides a full range of services to support customers in the field of homogeneous and heterogeneous catalysis. With in-depth expertise and specialized infrastructure, Solvias can tackle the most demanding projects in the pharmaceutical, agrochemical, fragrance, material and chemical industries. Our innovative products include a world-leading library of over 700 ligands while our R&D efforts span collaborations with leading universities and external scientists.
Solvias has an outstanding track record in the successful implementation of catalysis technology as well as the production of ligands and other specialty products. Flexible high-throughput experimentation (HTE) arrangements, using the Symyx workflow based on dedicated 96-well plates, allow the team to identify optimal catalysts and conditions for customers’ reactions and substrates. Solvias uses the HTE platform to find leads for asymmetric transformation, C-X coupling, heterogeneous hydrogenation and miscellaneous catalytic reactions that can be adapted to HTE protocols. Leads obtained from HTE projects can be seamlessly optimized and developed by Solvias experts, culminating in a technology transfer to the client or kg scale-up in Solvias laboratories.

Separation of racemic mixtures by the formation and crystallization of diastereomeric salts (chiral resolution) is an important technology in the pharmaceutical industry. Solvias offers HTE-assisted evaluations using a large variety of chiral acids and bases. Applying this methodology, Solvias has successfully resolved a large number of chiral customer compounds. Close interaction with the Solvias solid state department allows for further in-depth analyses towards scalable processes.

**ONE OF THE LARGEST PROPRIETARY LIGAND PORTFOLIOS FOR CATALYTIC TRANSFORMATIONS**

Based on in-house development and licensing, Solvias has built one of the largest proprietary ligand portfolios in the world to further support our customers’ catalytic transformations. The portfolio consists of a variety of families of chiral phosphine ligands for stereoselective catalytic reactions, achiral phosphines and catalysts – including the new Nickel-Josiphos catalysts – that can be utilized for C-X coupling (e.g. the cataCXium ligand families) as well as chiral phosphoric acid catalysts for use in organocatalytic transformations. All ligands and catalysts in the Solvias portfolio are readily available for commercial-scale applications and are sold IP included. Their performance (quality, chemical stability, ease of handling, safety) and supply chain meet all applicable pharmaceutical industry requirements.

Solvias also has longstanding experience in the field of heterogeneous catalysis and is able to develop highly chemoselective processes, including those for very complex and demanding molecules. An example of our expertise in heterogeneous catalytic hydrogenation is the successful application of the Solvias amine monomethylation technology for an improved synthesis of an API-intermediate, in which we developed a superior lab procedure and successfully demonstrated it on a kilogram scale.

Explore the wide application range of our modular ligand families on the LIGANDS & CATALYSTS INFORMATION PLATFORM [https://ligands.solvias.com](https://ligands.solvias.com)
Solvias brings together the experience, resources and expertise required to meet the most demanding requirements for custom synthesis and manufacturing of active pharmaceutical ingredients (APIs). We serve a diverse range of customers, from small startups and biotech companies up to large multinationals. In addition to a GMP kilo laboratory, we also offer synthesis according to ISO 9001 standards for non-pharma applications, TOX-batches or early steps of API synthesis. Working closely with colleagues in analytical services, the team of globally recognized experts in catalysis and solid state as well as analytical services, we are able to cover all aspects of modern early phase development.

Professional support can be offered in early preclinical to clinical development by delivering gram to kilogram quantities of APIs. This includes the development of robust, scalable syntheses and purification steps into fully GMP-compliant processes and transferring customer processes to our GMP kilo labs. In our ISO laboratories, we offer small-scale synthesis up to kilo scale of high-quality fine chemicals for research and development, including the synthesis of lead analogs, scaffolds, building blocks, metabolites, reference standard, impurities, degradation products and fine chemicals for technical applications, e.g. electronic materials.

FROM SCALABLE SYNTHESES TO FULLY GMP-COMPLIANT PROCESSES

Our state-of-the-art kilo lab is well equipped to handle a wide range of chemistry on scale under virtually unlimited reaction conditions. This includes cryogenic (–80 °C), high temperature (250 °C), hazardous and high-pressure chemistry (up to 300 bar). The chemical development experts at Solvias can rapidly develop scalable, robust and cost-effective chemical processes and optimize reaction conditions for complex, often chiral molecules. Our expertise in process R&D is evidenced by the launch of numerous production processes for Solvias customers. Newly designed processes can be readily transferred to our kilo lab in the form of a proof-of-concept study, or for scale-up and delivery of material to support preclinical studies. We also have long-term experience in transferring processes to custom manufacturing partners.

One example of a successful project in 2018 was the supply of API for clinical trials which was developed from scratch by route scouting, process R&D, scale-up and GMP production. The project included GMP- and ICH-compliant analytical services, stability studies and documentation. Another success story was the production of a GMP starting material for commercial API production. The sequence comprised a homogeneous asymmetric hydrogenation using one of our ligands, followed by a heterogeneous hydrogenation demonstrating deep expertise in developing production processes using catalytic transformations.
new biological entities (NBEs) and biosimilars

Harnessing our extensive expertise in biopharmaceuticals to help bring biologics to market faster

As biological therapies continue to transform the treatment paradigm for many diseases, demand for bioanalytics supporting both NBEs and biosimilars is growing. Solvias serves a wide range of customers from major pharmaceutical companies to innovative biotechnology experts working in a virtual or outsourced structure. Whatever the business model, customers are looking for expert support in conducting complex projects from the earliest stages of development to commercialization.

The development and manufacturing of biologic medicinal products to prevent or treat disease is a complex process requiring a comprehensive set of analytical tools and project management skills. From precise protein characterization according to ICH Q6B to protein analysis for comparability, Solvias applies extensive expertise in biopharmaceuticals to help our customers bring their new biological entities (NBEs) and biosimilars to market faster.

Since 2016, a dedicated team of experts has been working on the development of an NBE for a neurovascular disorder. Biopharma Customer Project Leader Christina Engels shares her enthusiasm for leading a multidisciplinary project team while closely collaborating with the customer: “It is extremely motivating to see our project moving ahead with the anticipated filing of a New Biologics Application with the FDA in 2019. Analysis is the core strength of Solvias, but this achievement shows that we are able to support the entire process, from setting up and validating methods through to release analytics for commercial batches. Our objective is to support our customers by offering our scientific and technological expertise and by continually making our processes more effective, with faster turnaround times.”

BRINGING THE HIGHEST SCIENTIFIC STANDARDS TO BIOSIMILAR COMPARABILITY STUDIES

Solvias has more than a decade of experience in the highly competitive market for biosimilars, also known as follow-on biologics. Regulatory approval is based on the totality of data demonstrating similarity between the biosimilar and the originator, including quality characteristics, biological activity, safety and efficacy. Hence, analytical testing is at the heart of a biosimilar’s success. In addition, speed-to-market represents a strategic commercial advantage for the customer.

Solvias brings together comprehensive capabilities and experience in protein analysis to meet the specific challenges of bringing biosimilar drugs to the market in a timely manner. Erhard Bappert, Solvias Senior Customer Project Leader, explains: “In order to characterize the originator product, samples from a great variety of different batches are required. Solvias can apply a broad range of analytical methods that are required for the originator material characterization and comparability, especially those of our highly skilled mass spectroscopy team. Solvias makes sure that the analysis with a broad range of methods is prioritized to save time in the clone selection process and allow the client to enter the market earlier. Finally, we always bear in mind the importance of automation in facilitating data exchange and method transfer to our customer.”

Whether for NBEs or biosimilars, dedicated project management and efficient coordination across Solvias group sites makes the difference in achieving key drug development milestones on time and on budget. By designing flexible and customized programs for each customer’s unique requirements, our project leaders are able to optimize the process to meet critical timelines for regulatory submissions. Ultimately, this helps our customers bring safer and better products to market faster.
The continued success of our process analytical technology (PAT) illustrates the value of a highly qualified team able to serve customers producing in harsh surroundings. Our products range from robust fiber optic probes to high-performance analyzers for toxic environments. We offer the competitive edge of experience and the ability to customize products and services to the most demanding requirements.

Our innovative solutions in process analytical technology (PAT) enable our customers to monitor, understand and optimize chemical reactions and pharmaceutical processes under the most demanding conditions.

Solvias offers a wide variety of probes that operate in transmission, transflection, reflection and ATR equipment for online and inline analysis of liquids, gases and solids in laboratories and production plants. In addition to our wide range of standard fiber optic sapphire probes, we also work closely with customers to develop specialized immersion probes or flow cells, such as those designed for use in high-pressure and high-temperature applications or in highly corrosive environments.

Our extremely robust fiberoptic probes are designed to the highest fiber optic standards of performance in NIR and UV-VIS spectroscopy. Inline process photometers (multi-purpose analyzers) are connected with fiber optic probes designed for Ex-zones 0 and 1, and the photometer is located in a control room. A single spectrometer can be coupled with several fiber optic probes for transmission, reflection, transflection and ATR applications via standard SMA connectors or other common standards.

Solvias also produces high-performance analyzers for continuous monitoring of highly toxic or carcinogenic substances in the air or in the workplace. Based on GC technology, these monitors offer a high level of selectivity and sensitivity, as well as low detection limits, combined with high reliability.

Our PAT team provides efficient project support for customer-specific solutions for the life science, chemical and petrochemical industries. Our services include consulting, feasibility studies, installation and qualification of the equipment and the training of operators.
In 2019, Solvias is celebrating 20 years of passion for putting science at the heart of serving our customers. We are driven by respect, responsibility and reliability. We listen and stay connected with our customers as we follow regulatory changes and technological developments to maintain and develop long-term partnerships built on mutual trust and engagement. This will not change.

Our future success also depends on connected innovation, a unique approach to connecting our expertise to our customers’ purpose.

One example is the Solvias Innovation Board, being expanded in 2019 to integrate perspectives from across the organization. This participative approach to brainstorming ideas, from the concept phase all the way up to implementation and commercialization, has been successful in developing our MAT kit, a CCIT instrument for spores, the rapid sterility test, and rubber oligomers as reference standards. Our intention is to more fully harness the power of this innovation engine going forward.

The increasing focus on stem cell solutions and our early interaction with cell and gene therapy companies will drive new demand, along with the continued importance of biological analyses and our comprehensive biopharmaceutical analytical solution packages. Analytical method development across our two main pillars in small and large molecules will support our customers’ growing needs for physico-chemical analytics and characterization, along with biological analysis, functional and bioassay components. New investments in state-of-the-art equipment to expand and enhance our mass spectrometry capabilities (GC/MS, LC/MS) will ensure that our customers continue to benefit from the most sensitive instrumentation.

Following a period of intense growth for our company, we will focus and invest in key support functions at Solvias to facilitate internal processes and better serve our customers. In the next two to three years, Solvias will increase investments to upgrade our financial and information systems and processes, while also transforming customer services to adapt to evolving needs. We will sustain business momentum by leveraging our newly expanded teams, project management organization and realigned portfolio. Most importantly, we will strengthen cross-disciplinary collaboration internally and externally so as to fully leverage the rich knowledge in our different areas of scientific expertise.

At the same time, we will take further steps in our Lean Transformation to prepare for the future, continuously improve our efficiency and effectiveness and as a result drive an ongoing improvement of our financial performance metrics.

The convergence of technologies and industries is continuing to dynamically shape our market place. Software development, improvements in artificial intelligence and data management are providing platforms for new possibilities in medical devices, pharmaceutical development and new therapeutic approaches. Diagnostic companies, clinical CROs, CMOs and analytical service companies are moving closer together to serve one purpose: to help bring safer and better products to the market faster. Scale and size are not the only drivers of success in this rapidly evolving market environment, but consolidation is picking up in pace as these industry segments grow closer. Solvias will play a part in shaping our market.

To this end, Solvias has become more entrepreneurial, customer-focused and dynamic. As our business continues to grow and our organizational transformation matures, we will be exploring new opportunities for expansion to further secure our strong position and sustainable growth for the future.
CELEBRATING

Collaborative expertise.
Connected innovation.

1999 – 2019

Celebrating 20 years of success in connecting scientific solutions to people.

solvias