European Biotechnology

Summer 2025

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Lab automation: New modalities

SPECIAL

Finding new leads and modalities automatically

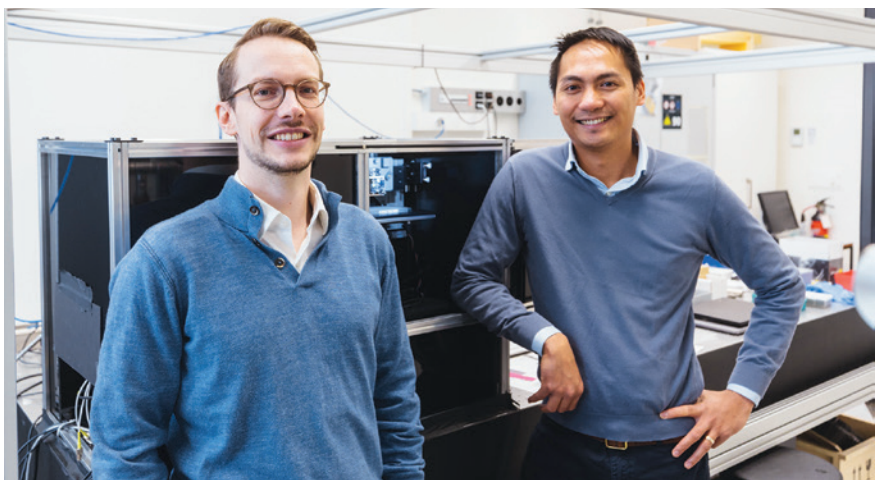
SLAS EUROPE With 25% more visitors (1,700), exhibitors (378) and new product launches (40) than last year, the 6th Annual Meeting of the Society for Laboratory Automation and Screening SLAS Europe 2025 broke all records. Highlights in Hamburg included advances in the automation of CRISPR, toxicity and phenotypic screening in human 3D cell aggregates and the presentation of a completely new protease-resistant and highly specific oral drug class.

Reducing the preclinical attrition rate, faster identification of new drug targets and specific binders with a high therapeutic index were the focus of international technology developers at the 6th SLAS Europe (20–22 May 2025) against a record backdrop. Almost 1,700 visitors (2024: 1,078) and 137 exhibitors (2024: 109) responded to the call of Hamburg-based SLAS President Philip Gribbon (see European Biotechnology 4/2024) to find new partners, talent and technologies and "help shape the future of screening sciences". The Hanseatic city is set to become the new European life sciences automation epicentre "with three further SLAS Europe conferences by 2031", Gribbon told European Biotechnology. Strategically, the local LSN-cluster is expanding relations to the ambitous Scandinavian biotech ecosystem.

New modalities

Inspired by Arthur C. Clarke's Third Law "any sufficiently advanced technology is indistinguishable from magic", ThirdLaw Molecular aims to replace antibodies with oral mid-size drugs that are non-immunogenic, not subject to protease degradation, but exactly match the shape of receptors and intracellular drug targets (see p. 72). At SLAS, the US start-up presented its DNA-encoded library of 4.5 billion Spiroligomer™ molecules for the first time that yielded nanomolar binders in a screening. "We are eager to partner with companies interested in exploring this new modality for their existing targets," senior researcher DJ Bernsteel told European Biotechnology in Hamburg.

A technology conceived in Germany and commercialised in the USA that promises to reduce the side effects of the currently fastest-growing therapy classes of antibody drug conjugates (ADCs), bispecific antibodies and CAR-T cell therapies is presented on p. 73. An allosteric conformational switch can be used to modulate the molecular geometry of (engineered) antibodies and eliminate T-cell hyperactivation independently of the paratope.



ORYL Photonics SA's co-founders Nathan Dupertuis (left) and Orly Tarun. The Lausanne-based start-up won the SLAS Ignite Award for OrylF1 (background), their laser-based light scattering instrument that allows ultrarapid, accurate and cheap high-throughput assessment of drug solubility and aggregation. It is 100 times faster than the previous standard HPLC and that needs 10 times less time than SLS/DLS methods, requires only a hundredth or tenth of the sample volume and preserves the sample material for subsequent kinetic or orthogonal measurements.

Picture: © OrylPhotonics

Overcoming bottlenecks

In addition, SLAS Europe focused on technologies that enable the automated cultivation of human cells and organoids and their cost-effective phenotypic screening. Chris Oliphant from AstraZeneca plc presented an automated platform for the culture of functional polarised macrophages from iPSCs (induced pluripotent stem cells) and immune-arrayed CRISPR screenings to identify drivers for chronic inflammation in autoimmune disorders. According to Oliphant, AZ investigates factors affecting efferocytosis in cells and organoids – the process where macrophages, engulf and clear apoptotic or dead cells to ensure healthy cell turnover and prevent the release of cellular contents that could trigger inflamma-

tion. As whole-genome CRISPR screening is currently too costly, due to limitations in reagent delivery, cell number limitations, and endpoint complexity, AZ carried out a case study across 186 genes. In the end AZ identified Gene35 as a relevant modulator upholding efferocytosis.

At the beginning of April, Jeffery Truong and colleagues had presented ENVLPE, a new approach (Cell, 10.1016/j.cell.2025.03.015, p. 50) that cuts the cost of CRISPR screens significantly by boosting efficiency. Instead of immunogenic and inefficient lentiviral/AAV vectors, the future company founders used virus-like particles (VLPs) equipped with glycoproteins for organ-specific delivery of CRISPR/Cas cargo. Additionally, only functional ribonucleoproteins (RNPs) consisting of Cas nuclease, guide and editing RNA strands are attached to an aptamer located at the inner VLP surface and are transiently expressed preventing immune reactions.

Organoids vs animals

SLAS Europe also saw numerous new product launches for the expensive and, until now, poorly scalable processes required by drug developers such as AZ for the propagation, passage and differentiation of human iPSCs and organoids. The market is booming because organoids represent a significant step in the evolution to more representative disease modelling. This would significantly increase the preclinical success rate and thus the revenue per drug candidate.

In addition to British Wildcat Laboratory Solutions Ltd., which markets plastic-free 2D lab tube racks from the US company PulpFixin outside the US, Hamburg-based mo:re GmbH received the New Product Award, which SLAS presents for breakthrough innovations. Managing Director Lukas Gaats, who founded mo:re together with David Hackenberger (CTO), plans to make Mo:bot the "gold standard of scaled and automated organoid-based" drug development. Mo:bot integrates artificial intelligence to allow non-specialists to reproducibly mass-produce four organoid types – heart, brain, liver, and pancreas. Another one of the 12 automation start-

Opening of SLAS Europe in Hamburg by SLAS CEO, Vicki Loise

ups supported by SLAS as part of its AveNEW programme and portrayed on European-Biotechnology.com – Acoustofab Ltd (*t1p.de/l3nny*), Instromeda Ltd (*t1p.de/b2nfu*), LifeTaq GmbH (*t1p.de/trm88*), Minos Biosciences SAS (*t1p.de/1zwid*), MyxoTech GmbH (*t1p.de/ku3xl*), Nanovery Ltd (*t1p.de/9vvec*), Nanoworx BV (*t1p.de/sivmj*), NestEgg Labs BV (*t1p.de/3g0p5*), ORYL Photonics SA (*t1p.de/cc561*), Phabioc GmbH (*t1p.de/8ymey*), Third Law Molecular Inc (*t1p.de/z5y71*), and Unicorn Biotechnologies Ltd (*t1p.de/fd2hw*) – also aims to enable the reproducible mass production of 3D organoids: Viennese LifeTaq-Analytics GmbH's Oli-MAT cell cultivation unit, facilitates high-throughput production and scale-up of standardised 3D cultured tissue models for lung, kidney, the gastrointestinal tract, and skin under a controlled oxygen environment.

Another finalist for the SLAS Ignite Award for the most innovative business concept, presented a fully remote-controlled system for cell and organoid handling. EMMET, which was developed by Adam Glen and Jack Reid, automates every step in the cell culture process: from media exchanges and passaging to executing complex differentiation workflows. With onboard autonomous analytical systems and user-defined, machine-driven protocols, Emmet can automate the culture of any cell type, from cell lines to pluripotent stem cells (ESCs/iPSCs). Molecular Devices and Heartbeat.bio gave an update of their AI-powered organoid culture system CellExpress.ai.

Beyond the SLAS award-winning products, there were some fascinating technologies of the future on display: the acoustic levitation technology developed by British company Acoustofab Ltd, for example, replaces all of the pipetting and robotics hardware, tips and consumables that were previously required. A custom-built array of ultrasonic transducers that are precisely controlled to create so-called acoustic holograms levitates the components to be pipetted, sorted, mixed or printed completely contact-free. Another innovation launched by Instromeda Ltd at SLAS Europe is 1/3 the price while requiring 95% less human intervention compared to traditional SPR platforms.

German Ignite Award finalist Phabioc GmbH came up with two innovations reducing process and formulation development cost for complex molecules, such as antibodies or vaccines. Its SpecPlate allows for the dilution-free measurement of absorption spectra in highly concentrated samples while its PermeaPad is a biomimetic barrier for gastrointestinal, oral and mucosal drug permeability studies.

The next SLAS Europe conference will take place in Vienna from 19 to 21 May 2026. Hamburg will host SLAS Europe in 2027, 2029 and 2031. ■

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Picture: © SLAS

Spiroligomer™ molecules: advancing drug design

PLATFORM Thirdlaw Molecular Inc (Blue Bell, Pennsylvania) focuses on platforms that utilise novel Spiroligomer™ molecules, which possess fused-ring structures with multiple R-groups. Screening a DNA-encoded library consisting of 4.5 billion members has found nanomolar binders. The new platform has been presented at SLAS Europe 2025 in Hamburg.

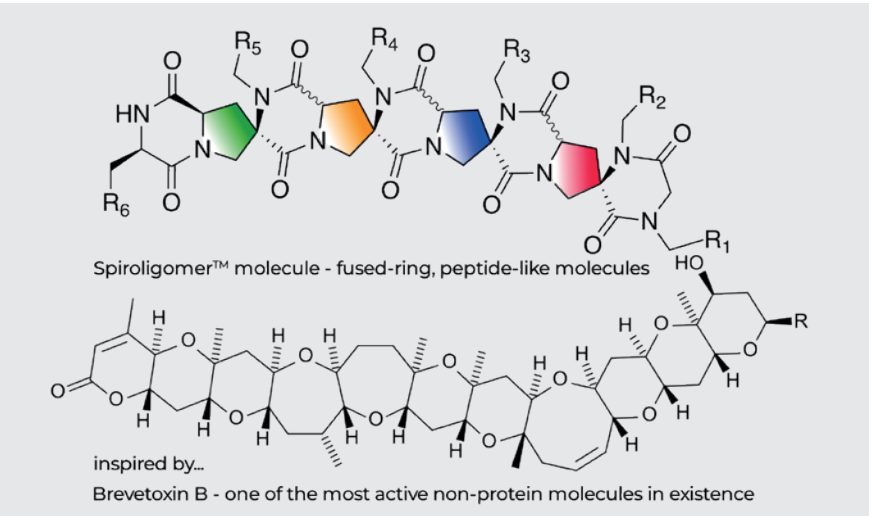
In drug discovery, compounds are classified as either small molecules or biologics. Small molecules, defined by Lipinski's "rule of 5," weigh under 500 Daltons and are optimised for bioavailability. However, they mainly bind to small protein pockets, limiting their scope and increasing off-target effects. Biologics, such as antibodies, interact more specifically with large protein surfaces, avoiding many off-target interactions. However, they require injection and are prone to degradation.

A new drug class

At ThirdLaw Molecular, we have developed Spiroligomer™ molecules, a novel therapeutic class in this intermediate size range. They are very different from, and complementary to, the recently popular cyclic and stapled peptides (500-3000 Da)–where both seek to combine the benefits of small molecules and antibodies.

Spiroligomer™ molecules are built from cyclic monomers connected into fused-ring, ladder-like frameworks with multiple stereocenters. Their rigid, protease-resistant backbones differ from the flexible structures of peptides. Embedded stereocenters allow precise 3D configurations and placement of functional groups. ThirdLaw Molecular's synthetic platform also enables rapid incorporation of thousands of non-natural amino acids or R-groups.

As described above, the structure of Spiroligomer™ molecules makes them unique; however, a critical question remains: how do these structural changes result in superior pharmaceuticals? In a chloroalkane penetration assay, ten of 11 random Spiroligomer™ tetramers showed cell permeability; eight entered cells within 20 minutes via passive diffusion. This is significant: 85–90% of human proteins are intracellular, yet most approved small-molecule drugs target only a small subset (~850). Spiroligomer™ molecules bind to grooves found in all proteins, including "undruggable" intracellular targets. They also demonstrate oral bioavailability without special formulation – something peptides generally lack.



Spiroligmers drafted by Affinity Designer

In collaboration with X-Chem Technologies, ThirdLaw Molecular has created a 4.5-billion-member DNA-Encoded Library (DEL) of Spiroligomer™ macromolecules. These can mimic monoclonal antibodies in protein binding but are about 1/30th the size, with the potential for oral delivery. Screens against extracellular targets (validated by antibodies but lacking small-molecule drugs) have already produced nanomolar binders. Functional validation is underway.

A second DEL of cell-permeable Spiroligomer™ molecules is in development for Q3/25. This library will focus on intracellular proteins currently inaccessible to traditional drug types.

In summary, ThirdLaw Molecular's Spiroligomer™ molecules combine the size benefits of peptides with critical advantages: passive cell permeability, protease resistance, tunable 3D conformations, and R-group modularity. These features support a new generation of orally available, selective therapeutics for extracellular and intracellular targets. ■

Remote controls for immunotherapies

ANTIBODY ENGINEERING Mabswitch Inc's platform technology enables the remote and repeated regulation of antibody affinity in various immunotherapeutic applications. This makes it possible to actively and individually mitigate adverse effects, increase specificity and maintain efficacy by improving immune fitness and persistence.

› Dr Yemi Onakunle, CEO, Mabswitch Inc., Los Angeles, USA

Mabswitch is developing ON/OFF control switches for antibodies using our Universal Allosteric linker and Switch Module for Antibodies (UNASMA™) technology that facilitates the regulation of virtually any antibody's affinity for its target under physiological conditions. We achieve this by inserting a calmodulin-derived allosteric modulator domain as a linker between the variable domains of an antibody scFv, replacing the standard (G4S)n linker. This allosteric-linker switch is activated by a small molecular ligand, modulating antigen affinity through conformational changes in the antibody's binding site, which are triggered by the interaction of the ligand with the allosteric-linker. The fully human allosteric modulator domain ensures low immunogenicity and is compatible with virtually any scFv.

Why regulate antibodies?

Many cancer immunotherapies face significant challenges, including triggering harmful side effects due to broad immune activation or losing effectiveness over time. Our innovative approach enables precise control over when and where immune cells are activated, enhancing the safety and efficacy of treatments, by:

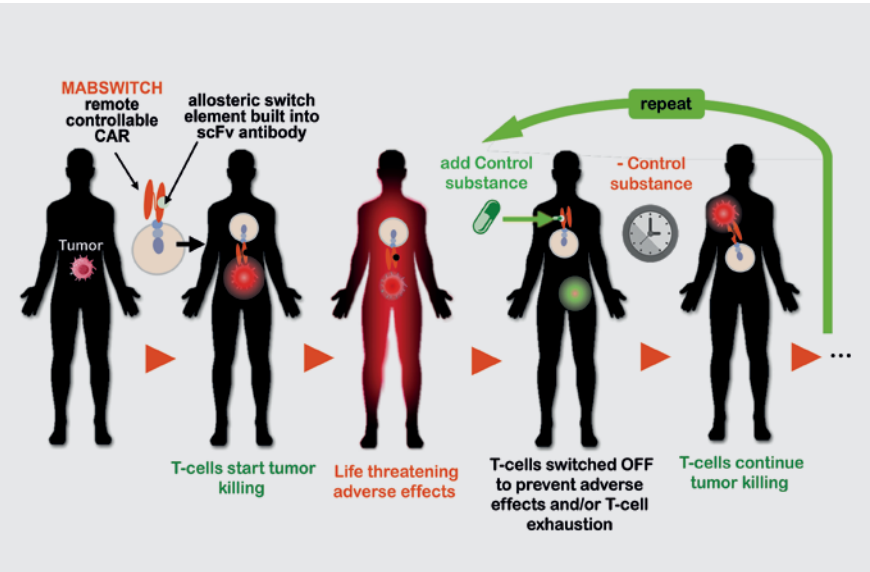
- Activating only at the tumor site to avoid harming healthy tissues.
- Providing precise, on-demand control to limit side effects.
- Reducing immune system burnout by improving its fitness and persistence.

Our technology addresses key limitations of conventional immunotherapies, and leading pharmaceutical companies like AbbVie, BMS, and Amgen have taken notice, awarding us Golden Tickets that provided laboratory resources to validate the technology. Additionally, Mabswitch secured NIH grants to validate UNASMA™ in two groundbreaking applications: remote-controlled CAR-T therapy and mild elution immunoaffinity ligands.

But there is more: our award-winning remote-controlled antibody platform is not just for cancer, but broadly applicable to most antibody-based therapies, and could even enable first in class products in fields not yet accessible to therapeutic antibodies. It could revolutionise treatments for:

- Autoimmune diseases (like arthritis, multiple sclerosis, and lupus).
- Metabolic disorders (including diabetes and obesity).
- Blood and neurological diseases.
- Other next-generation therapies, such as CAR-T cell treatments and antibody-drug conjugates.

Mabswitch develops breakthrough cancer immunotherapies, but also offers to engineer our affinity switch into your antibody for application as remotely controllable ADC, CAR, TCE or other antibody-based products. ■



Mabswitch application example: "Time-resolved / repeatable ligand-controlled T-cell activation"

Picture: © Mabswitch Inc