Editorial

The first meeting of the Société de Chimie Thérapeutique (SCT), called Rencontres Internationales de Chimie Thérapeutique (RICT), was organized almost 60 years ago in Lille in 1965. Looking back over those years shows how amazing the evolution of drug discovery has been.

In 1965, drugs were mainly based on small molecules (synthetic or natural) except for small proteins like insulin whose structure had been elucidated in 1951.

The first RICT were mainly devoted to the elucidation of structure-activity relationships. These RICT would today be conceived as single modality-centric meetings. One major evolution has been the extension of the topics to structure-properties relationships in the early stages of the drug discovery process. These gradually involved solubility, permeability, distribution, interaction with metabolic enzymes … that allow to improve the drug-likeness of clinical candidates.

Years later, the structure of more and more "factors" was elucidated (factors designed biologics, whose effect were well documented, but which structure remained unknown). An interesting case being tumor necrosing factor (TNF) and Cachectin (involved in septic shock) that were investigated independently by two groups who discovered when the genes were sequenced that they were chasing the same molecule. The question then arose as to whether they should be included in the topics of the RICT. The answer was that as soon as the structure can be determined and manipulated at the atomic level, these factors, now molecules, fit into the goal of drug discovery chemistry and therefore in the topics of RICT. Eventually, even the boundary between these two modalities became increasingly questionable. For instance, the design of antibody-drug conjugates has benefited of cytotoxins discovery as well as the design of improved chemical linkers.

In recent years there has been an amazing expansion of new modalities such as RNA therapeutics, gene therapy, fusion proteins, none of which could have been developed without chemical tools. Drug discovery has become "modality agnostic". This was clearly illustrated during the recent Covid pandemic where all possible modalities were investigated at an incredible speed. By September 2022, 22 different COVID-19 medicines (6 vaccines and 16 therapeutics) had been approved or authorized by the FDA and the EMA. Although the winners were the two RNA vaccines a modality that had not at that time delivered a commercial drug, the 20 other medicines used more classical modalities such as protease inhibitors, adenovirus and protein vaccines or monoclonal antibodies.

This trend towards modality agnosticity was also true when considering the tools involved in drug discovery. High throughput screening and combinatorial chemistry have opened new path for lead discovery including in targeting protein-protein interactions that were previously considered as "undruggable".

Biorthogonal reactions and chemical biology have added yet another dimension in the molecular aspects of drug discovery and selection. The awarding of the Nobel prize in chemistry to Morten Meldal, Barry Sharpless and Carolyn Bertozzi for the discovery of the

elegant and efficient copper catalyzed or strain-promoted alkyne-azide cycloaddition is another telling example of the importance of chemistry in the discovery of new pharmaceutics, through a better understanding of biology and living organisms. Click-chemistry is becoming a corner stone reaction when probing cells and living organisms. Biologists themselves have seized on this chemistry to answer their biological questions about target function and drug action.

Becoming modality-agnostic, drug discovery now requires from researchers a broad knowledge of (bio)chemistry and structural biology together with molecular pharmacology, pharmacokinetics, and toxicology to name a few of them.

These international meetings, shared in the language of Shakespeare, as was the case for the first time for the RICT Lille in 2007, provide an ideal opportunity to update our knowledge in Drug Discovery chemistry and to better understand how this ever-evolving field contribute to the discovery of new therapies.



Pr André Tartar and Pr Nicolas Willand

Our Scientific Prizes & Awards

Galapagos Award For Drug Discovery Chemistry

Galapagos is a commercial stage biotechnology company specialized in the discovery and development of small molecule medicines with novel modes of action.

In 2022, Galapagos and Société de Chimie Thérapeutique have decided to award a talented team of researchers contributing to a scientific discovery and /or substantial therapeutic innovation. Specific emphasis will be given to the notion of drug discovery chemistry where combined disciplines, among for example molecular modeling, in silico approaches, chemistry, chemical-biology, biology or ADMET can contribute to the achievement of the team's objectives.

This contribution may arise from the any phase of research and the aim of this prize is to nominate a talented team. The "Galapagos Award for integrated medicinal chemistry" (5000 €) is given during the International Conference on Medicinal Chemistry (RICT*), an annual SCT meeting, by a Galapagos company representative and the SCT president.

Eligibility: the candidate team should be based in Europe and the members have to accomplish their duty as SCT member by paying their membership by credit card on the SCT website to be eligible.

The "Galapagos Award" jury members select the laureate among the candidates. By accepting the award, the laureate team representative agrees to present a plenary lecture at the next RICT meeting or a SCT (co)-organized event in case RICT meeting cannot take place. Galapagos Award For Drug Discovery Chemistry (sct-asso.fr)

Evotec Prize for Excellence in Molecular Design

Evotec, in partnership with the French Medicinal Chemistry Society SCT, is delighted to invite submissions for the "Prize for Excellence in Molecular Design" to be awarded for the second time to an exceptional young to mid-career scientific research talent from academia or industry. The successful candidate will be selected based on outstanding innovation and applied state-of-the-art molecular design skills that have contributed to a demonstrated advance to drug discovery boundaries. In particular, the assessment panel are keen to recognise "drug hunter" who have demonstrated excellence in drug design resulting in highly informative novel molecules significantly impacting the drug discovery project. Submissions preferably should be the subject of a published (or accepted) scientific article, will cover a "break-through" discovery or innovative technology/method, and may include the application of machine learning and artificial intelligence (AI). Eligibility

Eligibility: The candidate will be a "drug hunter" (medicinal chemist, computational chemist, molecular architect, …) who has demonstrated adventurous and creative qualities to push the boundaries of the industry's current thinking in drug design and data analysis. He or she should clearly demonstrate that he or she has significantly contributed to aspects relevant to excellence in molecular design within discovery research projects. He or she must have published a key article illustrating innovation in molecular design or should demonstrate that such publication is likely to be accepted. He or she should be an "early to mid-career researcher "Evotec Prize for Excellence in Molecular Design (sct-asso.fr)

Our Host : Université de Lille.

Prof. Nicolas WILLAND
Université de Lille - Institut Pasteur de Lille -Inserm, Lille, France
U1177 – Drugs and Molecules for living systems

Prof. Benoit DEPREZ
Université de Lille - Institut Pasteur de Lille -Inserm, Lille, France
U1177 – Drugs and Molecules for living systems

Prof. Rebecca DEPREZ-POULAIN
Université de Lille - Institut Pasteur de Lille -Inserm, Lille, France
U1177 – Drugs and Molecules for living systems

U1177 – "Drugs and Molecules for living systems" research unit

The Lab's mission is to design and study compounds that modulates selected molecular targets in a desired way to treat patients in the fields of infections, immunology and immune-oncology. Our projects engage researchers across physical, chemical and biological sciences to validate *in vivo* new therapeutic targets with drug prototypes and aimaing at bringing drugs candidates to the clinic in area of unmet medical need:

- Developing quantitative pharmacology models and assay (HCS, pharmacokinetics, using cutting-edge imaging and MS), target engagement and ADME-PK,
- Designing the next generation of antibiotics to overcome bacterial resistance to antibiotics that targets TB, as well as Gram+ and Gram- species of concern,
- Inhibiting selected Zn proteases to treat cancer modulate antigen presentation in immunological disorders and accelerate wound healing in Diabetic Foot,
- Developing potent anti-coronavirus candidates.

We seek collaborations with biologists or biophysicists from academia and industry where medicinal chemistry, in vitro pharmacology and pharmacokinetics enable or accelerate the translation of new therapeutic concepts into drug discovery.

We are organized as a sustainable going concern with a maturity- and risk-balanced portfolio of projects, to ensure a continuous production of results (publications, patents). Our researchers are committed to the highest standards of scientific quality and integrity. Our data management system ensures that knowledge is reliably capitalized, enables collaborations between multiple research sites, and downstream valorization. The goal is to produce IP that ca be developed by industry and long term precompetitive assets to the community :

- Leads or drug candidates with data packages,
- High impact papers,
- organic synthesis protocoles and fully described, robust biological models,
- curated databases of biochemical, pharmacodynamic and pharmacokinetic data,
- formatted physical compound libraries (200.000 structures).

Our researchers are faculty members who teach in PharmD and MSc courses in pharmacy, drug discovery, medicinal chemistry, organic chemistry, and R&D strategies.

Prof. Patricia MELNYK
Inserm - Université de Lille, Lille, France

Pr Patricia Melnyk is the responsible of “Brain Biology & Chemistry” (BBC) team. BBC is a multidisciplinary team gathering biologists, biochemists, chemists, spectroscopists and hospital neurologists in the “Lille Neuroscience & Cognition” research center (U1172, University of Lille, INSERM, CHU Lille). Our objective is to propose therapeutic solutions for the treatment of neurodegenerative diseases, by identifying targets, designing and developing new molecules active on common hallmarks of these diseases. The BBC expertise covers all the drug discovery process from biology to drug development. To face the lack of disease-modiying compounds for these diseases, we develop multiple strategies : first a target directed approach with the protein-protein interaction modulators (LRRK2/phosphatases, YAP/TEAD, …) and enzymes inhibitors (ACSL4, …), secondly a multi-target compounds, and then a phenotypic approach and the search for new targets and biomarkersAfter target study and validation, screening tests are implemented and compounds tested to identify hits. Molecular modelling and medicinal chemistry allow their optimization from hits to lead. Pharmacological studies and ADME Tox are performed to characterize them as drug candidates. From our team, one compound is in the market and one compound is ending clinical phase 2.

Dr Priscille BRODIN
Inserm - Université de Lille, Lille, France

Dr Priscille Brodin is head of the team « Chemical Genomics of Intracellular Mycobacteria (CGIM) » at the center for infection and Immunity of Lille. The team projects focus on Tuberculosis (TB). TB is an infectious disease caused by Mycobacterium tuberculosis (Mtb) that results in millions of

deaths annually worldwide and an increased incidence of reported drug-resistant cases. New drugs as well as novel drug targets are urgently needed. In order to realize radical advances in TB drug discovery, a better understanding of Mtb persistence and latency are necessary. In particular, this requires detailed elucidation of the mechanisms by which host cells control intracellular replication upon infection by pathogenic mycobacteria.

The team's overall objective is to better understand TB pathogenesis to develop powerful strategies with enhanced efficacy, which allow the host to minimize or eradicate colonization by Mtb. The comprehensive picture of the molecular interactions between Mtb effectors and host cell proteins is necessary to generate the molecular tools for the development of antivirulence compounds that affect specific host pathways.

OUR ACTIVITIES

The French Medicinal Chemistry Society (Société de Chimie Thérapeutique, SCT) was founded in 1966 with the aim to disseminate scientific results and promote interdisciplinary knowledge in the major pharmaceutical R&D domains, covering the whole spectrum of chemical sciences that support drug discovery and development, from target identification to drug registration, with a focus on drug discovery and selection.

The SCT is also involved in advancing medicinal chemistry & chemical biology by initiating cooperation, networking, providing training and coaching, and rewarding scientific excellence. The SCT is interested in fostering scientific contacts between industrial and academic research groups, between medicinal chemistry and chemical biology related associations, both on national and international levels. The SCT is an active member of the European Federation of Medicinal Chemistry.

Since inception, SCT has been organising the "Rencontres Internationales de Chimie Thérapeutique - International Conference on Medicinal Chemistry", the RICT, a yearly international congress devoted to drug discovery or chemical biology. The RICT gather between 400 and 600 participants and around 20 internationally recognized speakers from Europe, Asia and North-America to present outstanding results in every aspect of innovative drug discovery. Every other year, a RICT are open to chemical biology. In 2022, SCT has organised and hosted the XXVII EFMC International Symposium on Medicinal Chemistry on behalf of the European Federation for Medicinal Chemistry and Chemical Biology (EFMC). In 2023, SCT is organizing RICT -devoted to drug discovery and selection- in Lille. In 2024, SCT will hold a RICT -on drug discovery and chemical biology- in Bordeaux.

The SCT pays special attention to the young scientists and students' community, as they will ensure the future endeavours in drug discovery. Each year, special scientific days (Journées des Jeunes Chercheurs, Young Researcher Fellows Meeting, JJC-YRFM) are organized for PhD students and postdocs to present their work through oral presentations or posters. The YRFM provides unique occasion for attendees to present their work, exchange with peers and meet representatives of pharmaceutical companies, small biotechs and start-ups. In these meetings, students can also benefit from coaching for CV improvement and simulation of job interviews with senior employees of pharma companies.

To reinforce its mission of advancing medicinal chemistry / chemical biology a new series of Webinars organized or co-organized by SCT have been launched this year. In 2022, the webinars were devoted to "Covalent molecular probes", and "Nucleos(t)ides as antiviral drugs : past, present and future".

A specific series of webinars is devoted to excellence in education in the field of medicinal chemistry and drug discovery, co-organized by AFECT and AECOP, the national associations of faculty members respectively in medicinal chemistry and organic chemistry. In this context, SCT awards the **Wermuth Prize** to a team devoted to innovation and excellence in medchem teaching.

With Galapagos, the SCT awards the **"Galapagos Award For Drug Discovery Chemistry"** to a talented team of researchers contributing to a scientific discovery and /or substantial therapeutic innovation. Specific emphasis is given to the notion of drug discovery chemistry where combined disciplines, among for example molecular modeling, in silico approaches, chemistry, chemical-biology, biology or ADMET can contribute to the achievement of the team's objectives. This contribution may arise from the any phase of research and the aim of this prize is to nominate a talented team.

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In recent years, the SCT continued its transformation to better meet the expectations of researchers, academic and industrial partners. In 2015 a **'Business Development Unit'** was created under the guidance of Dr Pascal George to build interactions with SMEs, CROs and Biotechs and deal with their specific needs (consulting, coaching, due diligences). The Business Development Unit counts 5 members to-date, all recognized for their expertise in different domains of drug discovery and/or business development and has set in place quite a number of contacts with SMEs, SATTs, incubators, etc …

Our communication team publishes and updates the ongoing activities on our web-site and social Networks, in order to draw interest from the scientific community seeking to network and exchange, to encourage subscriptions and increase visibility of the SCT within the European Federation of Medicinal Chemistry**. Since May 2023 SCT is proud to publish a monthly Newsletter**.

For inscription and for more information on our activities and events please feel free to visit our website www.sct-asso.fr.

OUR LOCAL SPONSORS

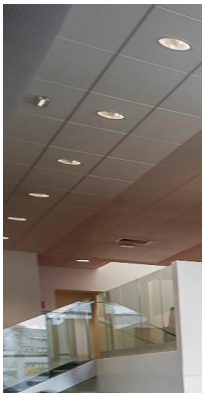
The University of Lille *a reference in transitions*

Located at the crossroads of Europe, the **University of Lille** is a member of the French Excellence Programme and affirm his openness to the world through our international partnerships. With more than **80,000 students**, the University of Lille covers all fields of study across **fifteen faculties, institutes and schools**.

From very early on, our university chose stand out on the issue of the transitions facing our society, whether technological, economic, health-related , social or environmental, and to participate fully in the public debate, especially with regard to the UN sustainable development goals (SDGs).

Four scientific and educational themes have been identified as key to meeting these challenges: **precision human health**, **science for a changing planet**, **human-friendly digital world**, and **changing cultures, societies and practices**. All of our actions contribute to our ability to attract high quality teacher-researchers and students to our high-level graduate programmes: multidisciplinary research-based academic programmes for MA and PhD students taught entirely in English.

This dynamic relies on partners from the private sector, local government authorities, our scientific partners (**Lille University Hospital**, **Inserm**, **Inria**, **CNRS**, **Institut Pasteur de Lille**) and the Euroregion through robust cross-border partnerships with **KULeuven**, **Ghent University** and the **University of Kent**.



To further enhance our appeal, we provide dedicated services for incoming mobility in order to guarantee a high quality welcome for new international students and researchers.

In January 2022, the Ecole Nationale Superieure des Arts et Industries Textiles (Ensait), the Ecole Superieure de Journalisme de Lille (ESJ Lille), the Ecole Nationale Superieure d'Achitecture et de Paysage de Lille (Ensapl), Sciences Po Lille and the University of Lille joined together to create a new public institution.

With the support of national and European funding, the University is perfectly positioned to promote its home territory and develop its academic and research offer for the benefit of all stakeholders and with the goal of training young people for tomorrow's professions against an international backdrop.

Université de Lille

80,000
Students

7,700
Staff

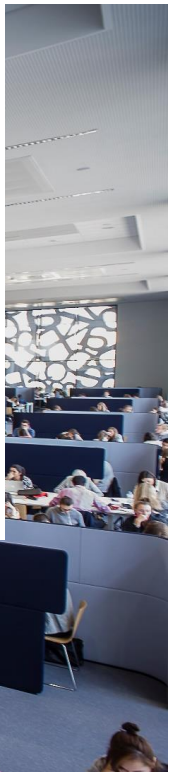
8,000
International students

153
Different nationalities

24
Campuses

64
Research units

For more information



Alzprotect | THERAPEUTIC SOLUTIONS FOR NEURODEGENERATION

A CLINICAL-STAGE BIOTECH COMPANY SPECIALIZED IN NEURODEGENERATION AND TAUOPATHIES

Alzprotect is a French clinical-stage Biopharmaceutical company, founded in 2007 We are, developing AZP2006 (INN: ezeprogind®), a proprietary, first-in-class oral small molecule for the treatment of Progressive Supranuclear Palsy (PSP), an orphan disease with large unmet medical need. Besides PSP, the company is actively investigating other therapeutic areas such as Alzheimer's and Parkinson's diseases. Encouraging preclinical results open the door for additional clinical trials those larger fields.

Mode of Action

AZP2006 is a small molecule with unique mode of action that confers an innovative therapeutic solution for the treatment of neurodegeneration through Progranulin release modulation. In a nutshell, AZP2006 increases the level of "usable" progranulin in the neuron, that degenerating brains tend to lose.

Progranulin is a secreted pleiotropic growth factor. It expresses primarily in mature neurons and microglia. It physically interacts with prosaposin to regulate neurite outgrowth, neurons inflammation and survival (*Callizot et al. Sci. Rep. 2021*).

AZP2006 addresses neurodegenerative conditions by combining pleiotropic effects. It targets lysosomes and binds to prosaposin. Prosaposin modulates Progranulin role in maintaining proper lysosomal function and is involved in progranulin secretion by stabilizing the prosaposin-progranulin complex. AZP2006 is seen to enhance lysosomal homeostasis, which in turn will allow neuroprotection and prevent microglial inflammation. AZP2006 also increases secreted progranulin availability, activates the Wingless Integrated (Wnt) pathway, enhances synaptogenesis and reduces Tau hyperphosphorylation by inhibiting GSK3beta

Promising clinical data

After promising preclinical studies and responses in animal neurodegeneration models, AZP2006 has completed three phase 1 studies in human (SAD, MAD, food effect) and more recently a Phase 2a clinical trial in PSP showing promising results:

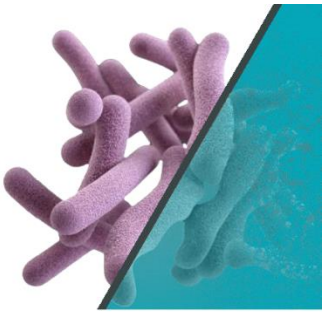
- Excellent safety profile without serious reported adverse event,
- Significant increase of progranulin level in plasma, confirming target engagement,
- Effective maintenance of progranulin level in cerebrospinal fluid (CSF) after 3-month treatment,
- First signs of slowing down evolution or stabilization of the disease evolution reflected by PSP-Rating (PSP-RS gait and total scoring) after 3-months treatment and after the follow-up period.

Based on these positive results, an open label extension trial (6-month treatment) is starting in France. A Phase 2/3 clinical trial with an adaptive design is being planned. This multicenter, randomized, double-blind, placebo-controlled study with an open-label extension, should pave the way to potential early market authorization thanks to its potential for pivotal results.

For further information, please contact Dr Philippe Verwaerde, CEO (p.verwaerde@alzprotect.com).

BIOVERSYS

Saving Lives in Resistant Times



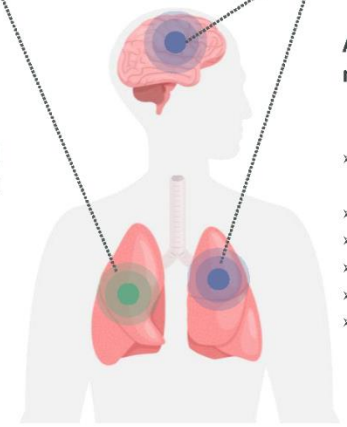
BioVersys AG is a privately owned Swiss pharmaceutical company focused on research and development of novel solutions addressing the most dangerous and increasingly resistant bacteria. We develop life-changing novel antibacterial therapies for patients with unmet medical needs. Our IP protected portfolio consists of two clinical and a number of preclinical & discovery programs, with distinct modes of action and potent efficacy against high priority pathogens.

HIGHEST PRIORITY PATHOGENS World Health Organization CDC

BV100 — FDA QIDP

Against carbapenem-resistant *Acinetobacter baumannii* (CRAB)

- Strong efficacy due to proprietary and patent protected (2039+) formulation
- Phase 1 trials completed
- Phase 2 trial in progress
- Clear target positioning in clinical practice
- FDA QIDP Designation[1]



BVL-GSK098 — FDA QIDP

Against tuberculosis in the brain (TB meningitis) and the lungs

- Largest infectious disease killer, 1.5 m deaths/year
- Phase 1 trials completed
- Phase 2 trial in progress
- Partnership with GlaxoSmithKline (GSK)
- Eligible for FDA PRV (~ 100 mUSD)[2]
- FDA QIDP Designation[1]

BV200 – Anti-virulent from TRIC-Platform

- Atopic dermatitis program
- Next program to enter Phase 1
- High value market
- Pneumonia program: CARB-X $ >3 million funded

BV Discovery – In-house platform technologies

- Discovery and Lead Optimization programs
- Undisclosed targets
- Addressing high priority & emerging pathogens

[1] QIDP– Qualified infectious disease product - confers priority review by FDA and fast-track designation, and additional 5 years' market exclusivity
[2] PRV – Priority Review Voucher, estimated market value ~ 100 mUSD

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Institut Pasteur de Lille

Vivre mieux plus longtemps

Accelerating research and taking action *to live better and longer*

As an international research center based in Hauts-de-France, the Institut Pasteur de Lille is a private, non-profit foundation recognised as a public utility since 1898, dedicated to research and prevention. This makes it unique in the world. More than half of our funding comes from the generosity of private donors, individuals and businesses.

TWO PRIORITIES : INFECTIOUS DESEASES AND DEGENERATIVE DISEASES

The Institut Pasteur de Lille has set two priorities:

INFECTIOUS DISEASES, in the context of emerging epidemic risks and antibiotic resistance, through the innovative INTHREPIDE program. The purpose of this program is to identify new therapeutic principles against emerging viral infections and infections caused by multi-resistant bacteria by bringing together a critical mass of scientists who complement and synergize all the necessary expertise.

DEGENERATIVE DISEASES related to lifestyle, longer lifespan, and environmental changes:

- Diabetes and its complications
- Cardiovascular and respiratory diseases
- Neurodegenerative diseases
- Senescence, fibrosis, and cancer

These two approaches are strongly interconnected at the scientific and methodological levels, as both are related to the functioning and aging of innate and adaptive immunity and the microbiota. They are also associated with effective prevention methods.

A campus open to the world

As an open campus, we welcome nearly 50,000 visitors every year for health check-ups, vaccination, or to follow a prevention program with our Longevity Health Pathway, a real health coaching tool.
Focused on business, our center of expertise in microbiological safety and toxicology supports industries on health issues by testing their products.
With 800 employees on campus, representing more than 33 different nationalities, we perpetuate the Pasteurian spirit by putting science at the service of everyone's health.

OUR 34 RESEARCH TEAMS WORK DAY TO DAY TO UNDERSTAND AND FIGHT THESE DISEASES, SLOW DOWN THEIR DEVELOPMENT, IMAGINE THE TREATMENTS OF TOMORROW, AND CHANGE BEHAVIORS.

800 PROFESSIONNALS

8 RESEARCH UNITS

33 DIFFERENT NATIONALITIES ON CAMPUS

13 TECHNOLOGICAL PLATFORMS

50000 SQUARE METERS OF LABORATORY

Institut Pasteur de Lille
Vivre mieux plus longtemps

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