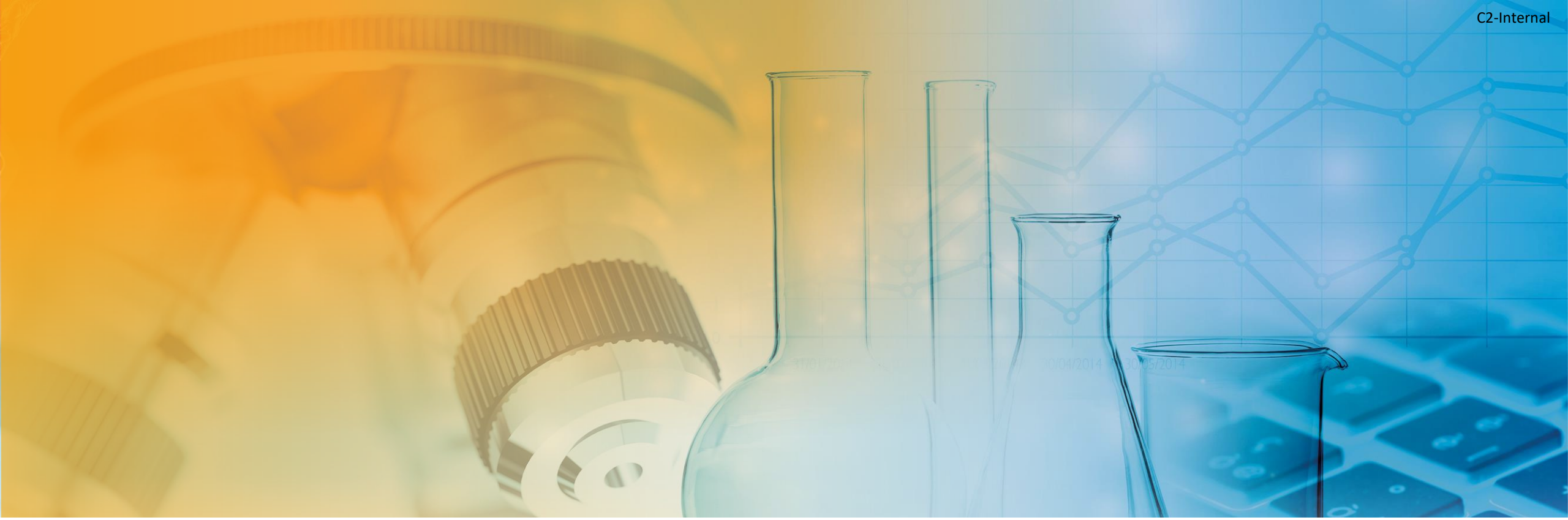

PRAGUE SCIENTIFIC

API Development

PRAGUE SCIENTIFIC

Finding new ways of delivering high-quality and affordable medicines

- Our team of more **than 200 experts** utilize the most advanced science, using state-of the-art equipment at our modern facilities in **Prague/CZ** and **Ankleshwar/IN**.
- We go further for the people we serve, by developing **value-added medicines** that innovate around established products, enhancing the patient experience in order to support improved outcomes.
- To the clients we perform the full scope of services. **From API and Formulation development to Drug product registration**.

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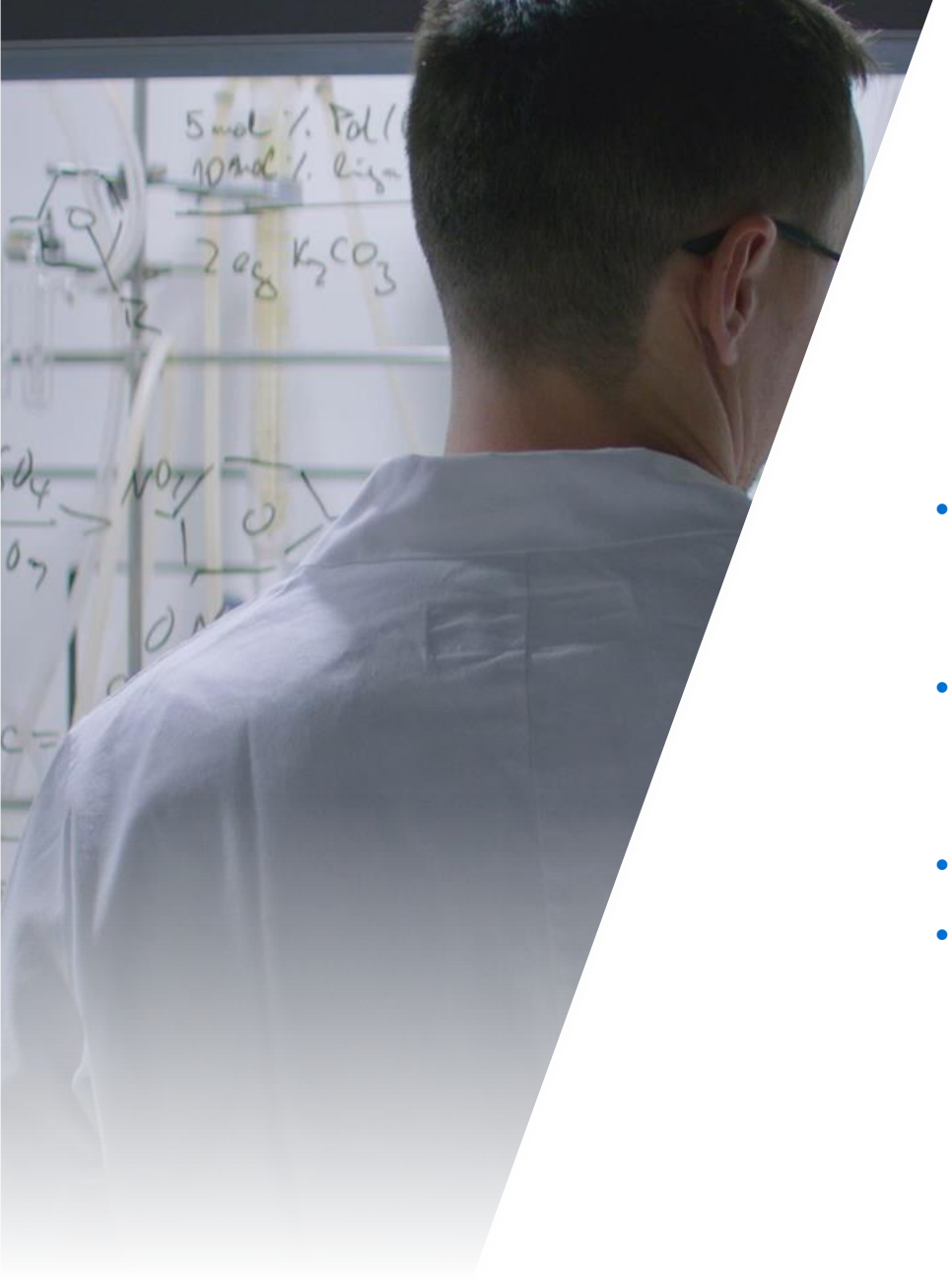

API Development

Route Scouting Services, Prague & Ankleshwar

- **Literature search** to establish current state of the art routes, as well as to identify synthetic routes options including designing novel routes.
- **Laboratory assessment and optimization** on small scale to select the most promising synthetic route incl. preparation of standards of impurities.
- **Synthesis of oligonucleotides**
- **Intellectual Property** often protected by patents.

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API Development

Process Development, Prague & Ankleshwar

- **Optimization of chemical reactions parameters** utilizing DoE and QbD principles (e. g. COGM, yield, cycle time, quality etc.)
- **Verification** of the process on the scale
- **Selection of raw material suppliers**
- Designing scale-up and scale-down models

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API Development

GMP operations in Kilolab Prague and Pilot Plant Ankleshwar

- Process validation of **Development APIs** for clinical trials.
- Manufacturing of **Commercial APIs**
- **Equipment available:** Reactors 25-2500L, Autoclaves 20-630L, Isolation and Drying Units, Sieving and Milling equipment.
- Pilot **Spray drier** will be installed in 2023.
- **Full scale Production Plant** in Ankleshwar is ready to supply commercial quantities of APIs.
- The facilities comply with **cGMP and HSE** requirements
- **50+ CEP**, ASMF and US DMF were developed, compiled, and used for DP registrations.

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API Development

Solid Form Devepment, Prague

- **Screening and process development of crystalline forms** (polymorphs, hydrates, solvates, salts, cocrystals)
- **Screening and process development of amorphous forms** (amorphous APIs, co-amorphs and solid solutions by precipitation, HME or spray-drying)
- **Particle size modification, API solubility increase systems**
- API documentation – DMF writing: **CEP**, **ASMF**, **DMF** compilation and filing
- Experienced team of **PhD chemists** with **>100 patents**

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API Development

Solid Form Selection, Prague

- Along with the solid form development we perform the range of experiments to **select the most appropriate solid form** with respect to its stability and bioavailability:
- **Physical stability** investigation under exposure to elevated temperatures and humidity
- **Chemical stability** investigation under exposure to elevated temperatures and humidity
- **Hygroscopicity** determination
- **Specific surface** and surface properties measurement
- Detailed **particle morphology** description
- **Rheological and flowability** properties

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API Development

Success Strory of Solid form Development

DASATINIB

Safer therapy due too alternative solid form allowed development of value-added drug product (gastric) pH indipendent

AGOMELATINE COCRYSTAL

The first ever and innovative co-crystal discovered and patent protected

SACUBITRIL SODIUM

Shorter manufacturing time thanks to optimization in crystalization process

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Oligonucleotides API Technology

Synthesis, Purification, Analysis, Characterization, Prague

Akta OP 100 Synthesizer:

- Currently available syntheses scales:
  - approx. 42 µmol (1,2 ml column) and 247 µmol (6,3 ml column)
- Higher scales are technically also possible
- Eight amidite positions available

Preparative Akta Pure 150 LC:

- HiScale 26 column CaptoImpRes (IEX), separations of 1 to 2 g of crude oligo at maximum
- Desalting by SE chromatography
- Purified products as ammonium salts
- Lyophilization available

Analytical Shimadzu HPLC System :

- Analyses of crude and purified fractions by IP RP HPLC or SAX HPLC

Characterization:

- IP RP HPLC or SAX HPLC
- 31P NMR measurement possible
- LR LCMS possible

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Nitrosamines

- Identification of **nitrosamine-formation pathways** and sources of nitrosable and nitrosating species.
- Specific **know-how to fight nitrosamines** gained on 30+ APIs and Drug products (pH influence, antioxidants, scavengers, pre-treatment of excipients and solvents to minimize nitrite content, exposure to NOx/air)
- Know-how **IP protected**, e.g. low-nitrosamines Metformin (WO2022079287A1).
- **Nitrosamine-free API and drug product development** and reformulation
- Synthesis and analytical characterization of **nitrosamine standards**
- Confirmatory **nitrosamine testing on the ppb/ppm level** (analytical methods development and validation)
- Coordination and evaluation of additional **toxicological tests such as AMES**
- Preparation of **nitrosamine risk assessment reports**

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Analytical Development

Our team of **80 highly skilled analytical chemists** can offer the following services:

- Analytical **method development**
- Analytical **method validation**
- Specification setting
- Analytical method transfers
- **Stability and Stress testing**
- **Reference standard characterization** by MS, NMR, IR
- **Solid state NMR Analysis**, Polymorph Characterization and Purity
- Preparation of CMC part of ASMF

PRAGUE SCIENTIFIC

Project Management

Guide You to success

- All projects are governed by **Project Managers,** planning, coordinating, and executing projects according to specific requirements from early evaluation to completion, often **involving transfers across sites** and continents
- Emphasis is placed on creating and maintaining **project milestones and the project schedule**. The end goal is to complete the project on time and within **budget**

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