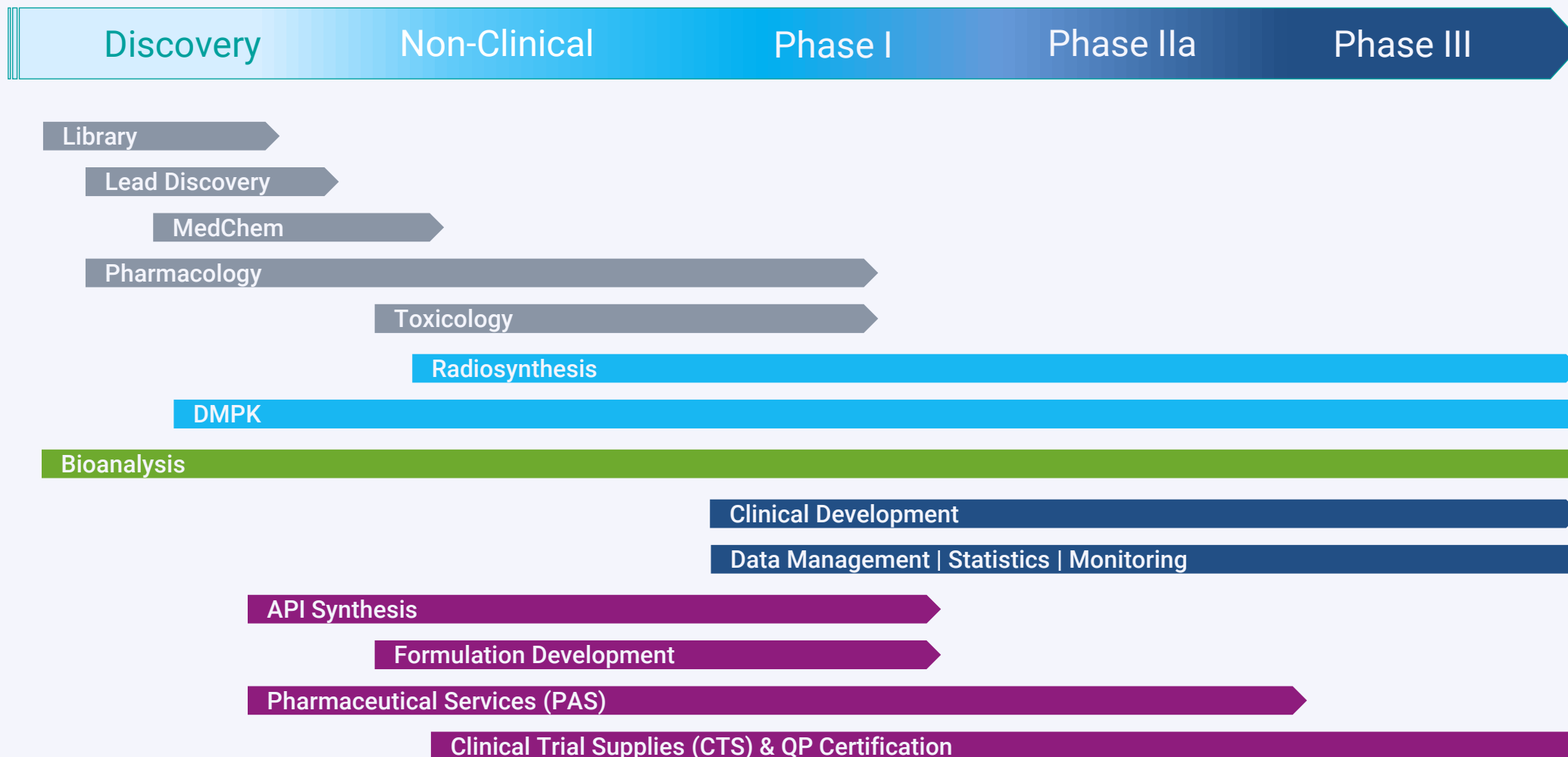


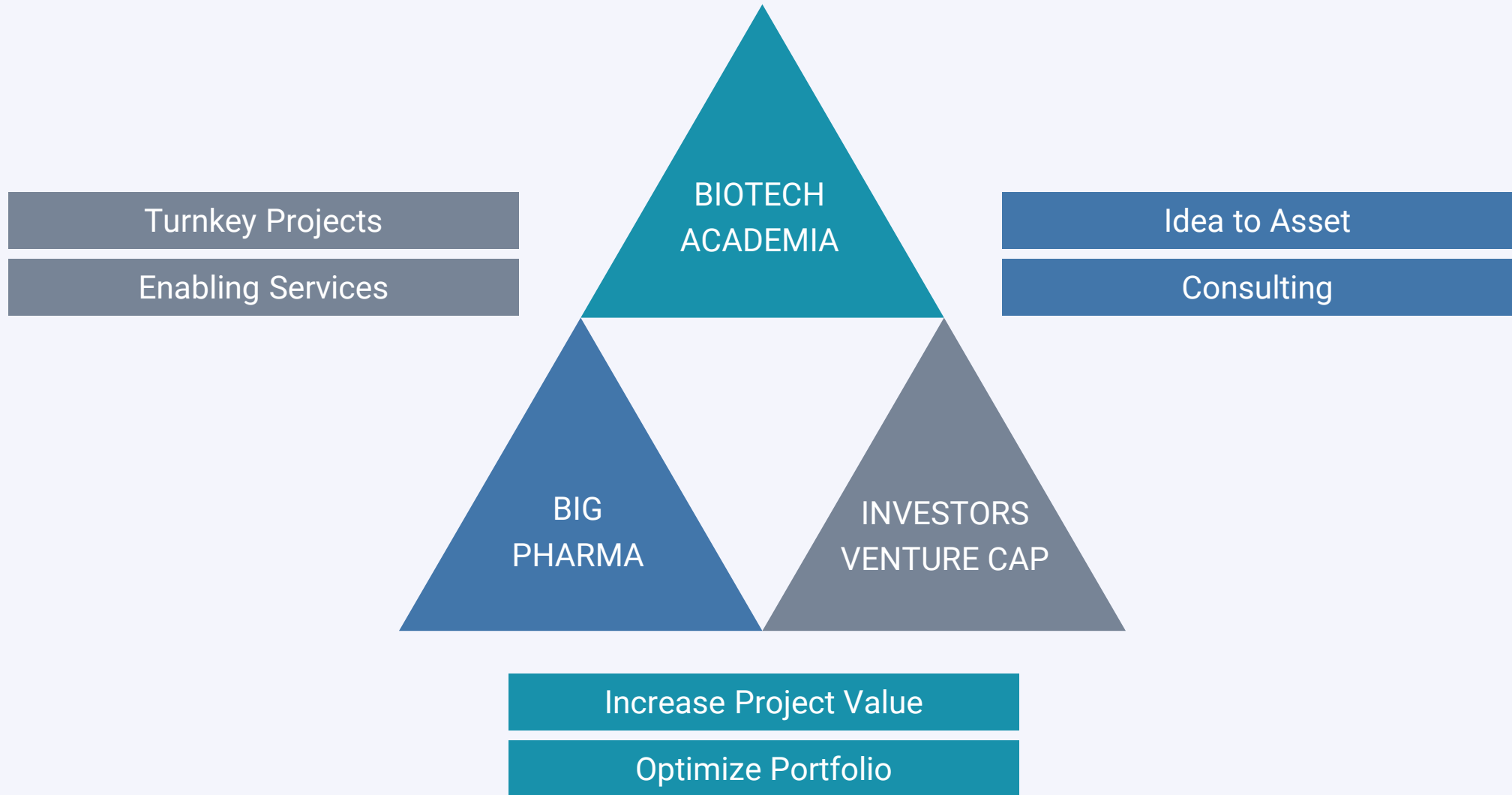
NUVISAN Innovation Campus Berlin

Introduction and Services

W We Are a Fully Integrated “SCIENCE CRO”



W We Increase the Value of Your Project





NUVISAN Sites



Neu-Ulm (GER)

1979

FTE: 260

In-house CPU with 140 beds
Bioanalysis, CTS,
Pharm. Testing, Safety Lab

INAMED | FTE: 20

Phase I & Phase II CRO with
focus on respiratory diseases



Waltrop (GER)

1983 | 2011 NUV

FTE: 26

Pharmaceutical Analysis
incl. large molecules, TDS
and other polymer-based
Drug Delivery Formulations



Munich (GER)

1965 | 2016 as NUV

FTE: 55

In vitro & in vivo DMPK,
Bioanalysis, Metabolite
Profiling and Identification,
Radiosynthesis/ Isotope
Labeling & QWBA



Nice (FRA)

2006 | 2018 as NUV

FTE: 80

API Synthesis under GMP,
Formulation Development,
Manufacturing,
Pharmaceutical Analysis,
CTS & Bioanalysis



Berlin (GER)

1851 | 2020 as ICB

FTE: 400

Lead Discovery,
Medicinal Chemistry,
Pharmacology,
DMPK & Toxicology

NUVISAN

INNOVATION CAMPUS BERLIN (ICB)
The NUVISAN Pre-Clinical Hub
Pharma R&D Excellence



ICB Background

In 2020, Bayer has transferred a significant part of its Berlin-based research unit with around 400 staff to **NUVISAN ICB GmbH**.

This new CRO center comes with decades of strong and successful pharma R&D expertise.

Comprehensive capabilities and capacities are spanning the entire drug discovery value chain, including

Lead Discovery

Life Science Chemistry

Therapeutic Research

**Preclinical Compound Profiling
(DMPK and Toxicology)**

Bayer, Nuvisan to open small molecule research center

By Jenni Spinner

17-Feb-2020 - Last updated on 17-Feb-2020 at 16:45 GMT



DRUG DISCOVERY

Bayer outsources chemistry R&D to Nuvisan

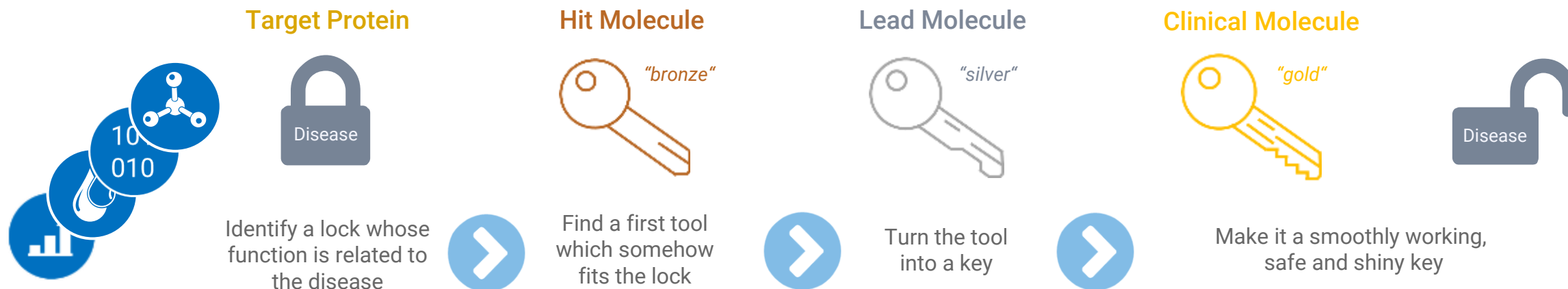
by Rick Mullin

FEBRUARY 15, 2020 | APPEARED IN VOLUME 98, ISSUE 7

Bayer will transfer most of its Berlin-based small-molecule drug research to Nuvisan, a German research services firm with expertise in clinical studies, lab services, and contract manufacturing. Nuvisan will take over a center on Bayer's Berlin campus that employs about 400 researchers focused on activities including lead discovery, medicinal chemistry, and drug metabolism studies. Sanofi entered a similar partnership in 2015 when it transferred its small-molecule site in Toulouse, France, to the services firm Evotec.



F From Target to Clinical Candidate

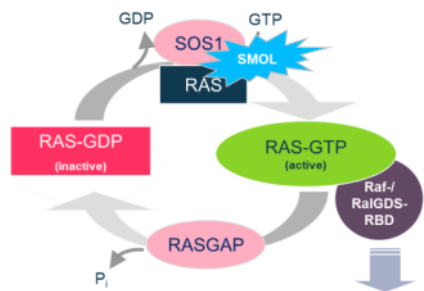


Design | Compute | Synthesize | Measure | Analyze

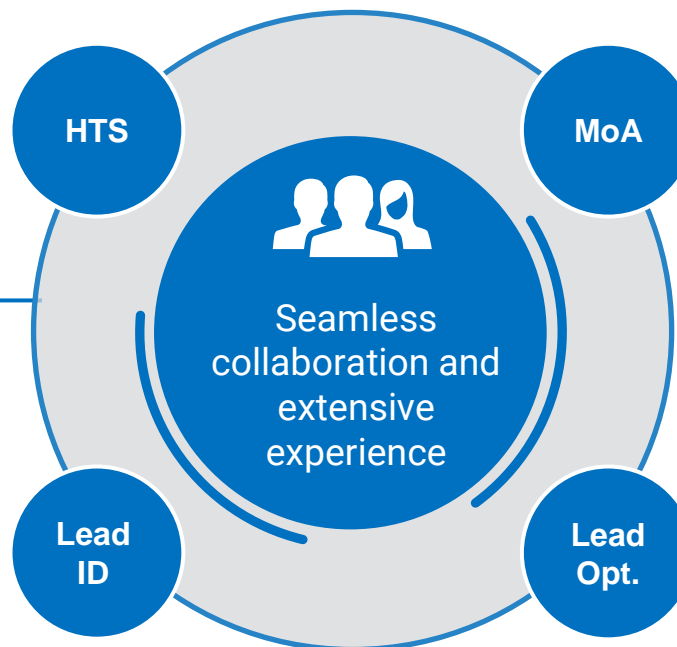
Innovation Enabling Packages for Developing New Medicines

C Case Study 1

Tackling mutant KRAS via the RAS-SOS1 interaction



Drugging the undruggable RAS



High Throughput Screen (HTS) on 3 mio compounds

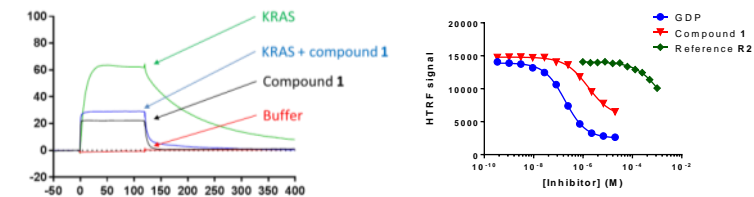
Identify inhibitors of GTP Exchange Factor activity

- ➔ Hitlist with 1814 cpds

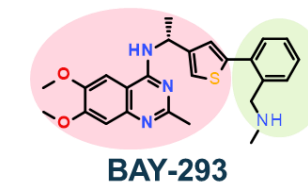
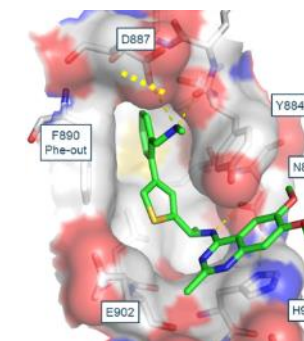
Fragment Approach

Identifying dead-end stabilizers (KRASG12C-SOS1)

- ➔ 42 fragment hits



Extensive screening cascade with biochemical and biophysical assays



Cpd.	Abs. configuration	IC ₅₀ (nM)
BAY-293	(R)	21
BAY-294	(S)	2,340

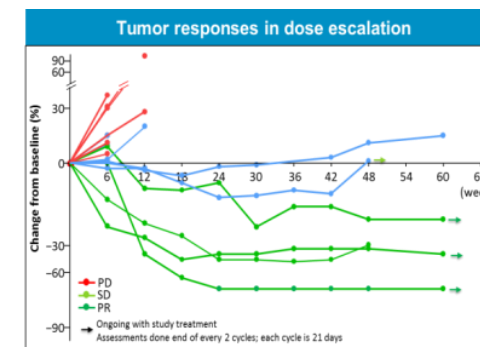
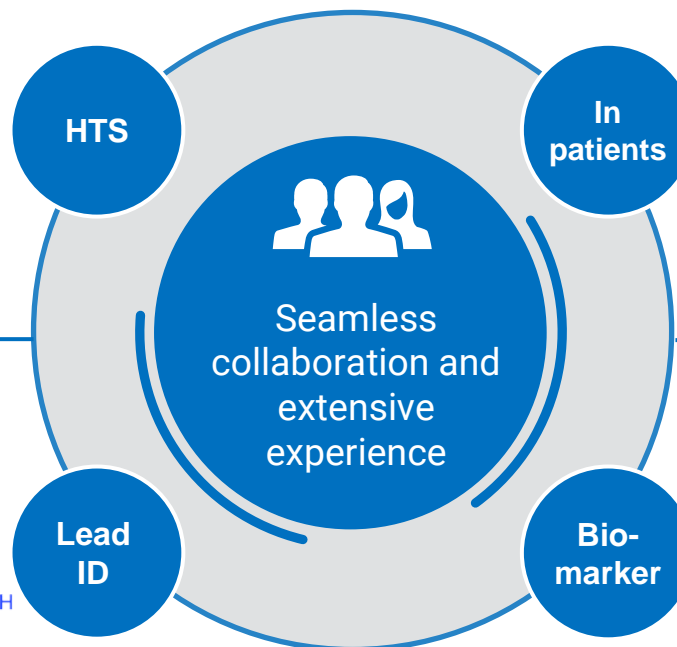
Combination of HTS and fragment hits led to identification of the lead series. MedChem optimization resulted in chemical probe BAY-293.

C Case Study 2

ATR kinase inhibitor BAY 1895433

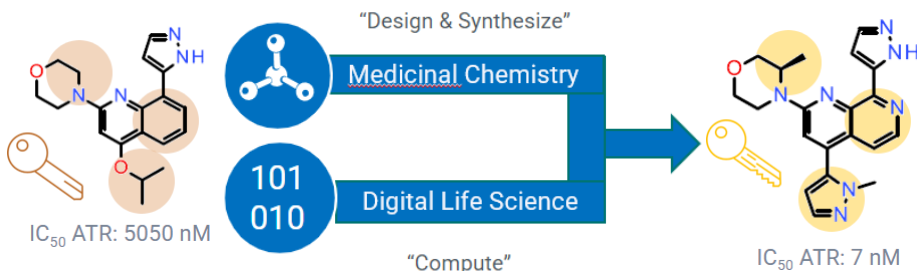
Lead identification and optimization using uHTS (activity plus ligand displacement)
Structure-based design

ATR Inhibitors from bench to bedside

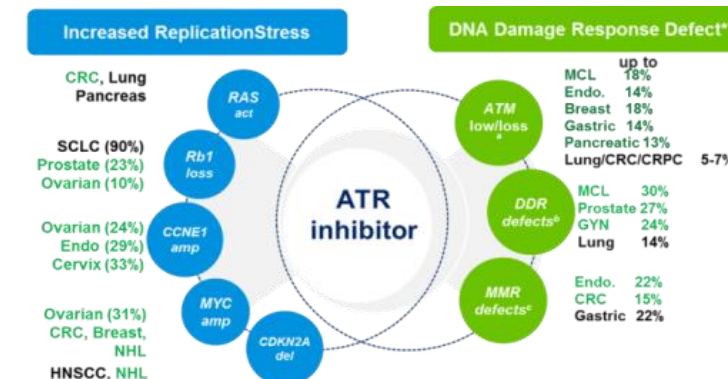


BAY 1895344 shows a dose-proportional increase of exposure, a manageable safety profile and encouraging clinical activity in heavily pre-treated patients with different histologies and DDR defects, including ATM aberrations

MedChem & Digital



Biomarker Strategy

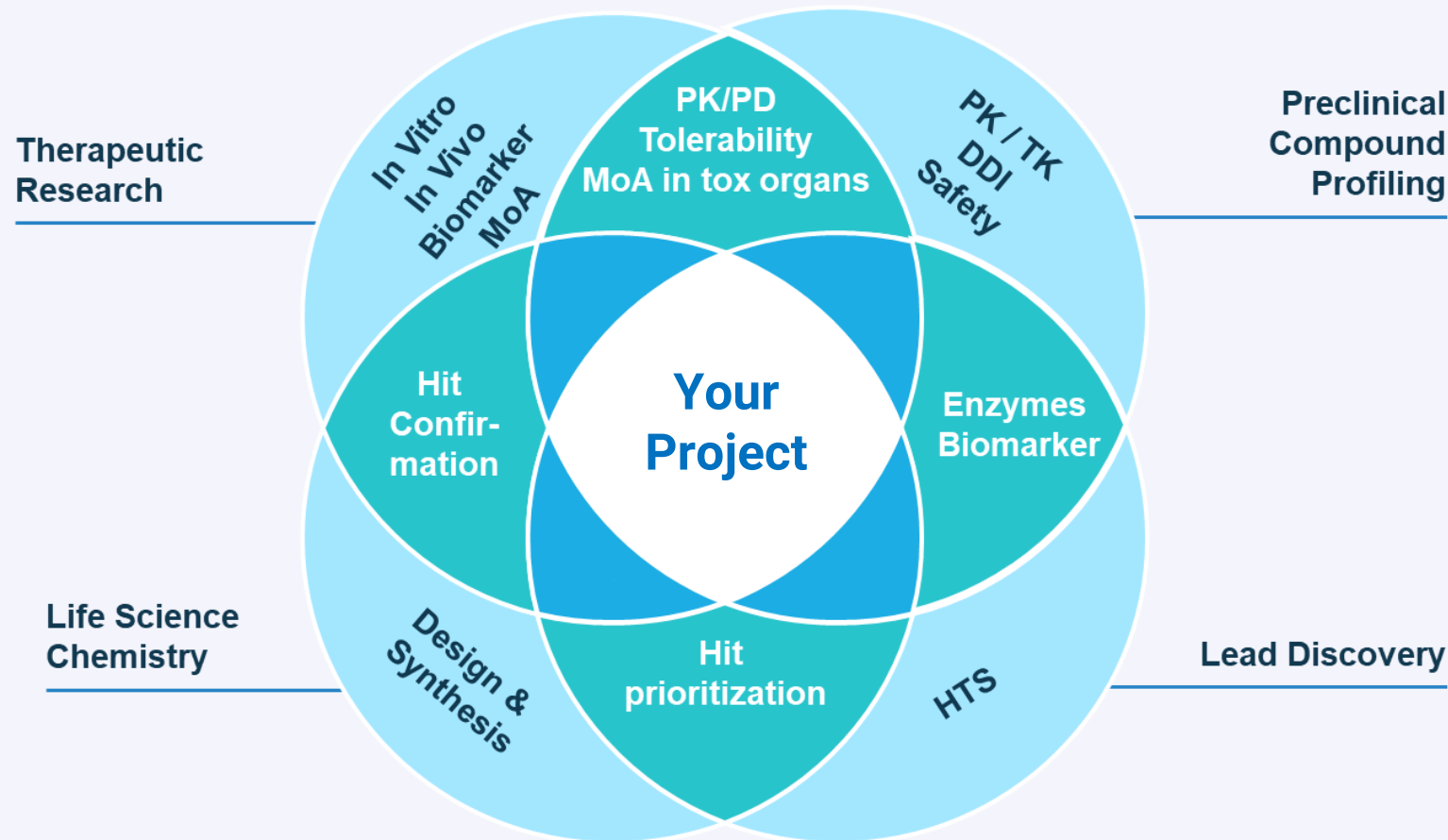


Durable responses or prolonged stable disease (>1 yr) were observed in patients with a variety of cancers and ATM / BRCA1 DDR defect.



Drug Discovery Under One Roof

Close collaboration between all necessary functions



HTS: High-Throughput Screening | MoA: Mode of Action | PK/PD: Pharmacokinetics/Pharmacodynamics | DDI: Drug-Drug Interaction

Fully integrated turnkey projects | Subprojects | Individual questions

L Lead Discovery

Finding the right molecule and studying it in detail - transforming ideas into assets

Screening

Assay development, lead identification and lead optimization support with a broad technology and target biology base

Providing access to 3 mio well characterized compounds

High-throughput compound testing (up to 750.000 experiments per day)

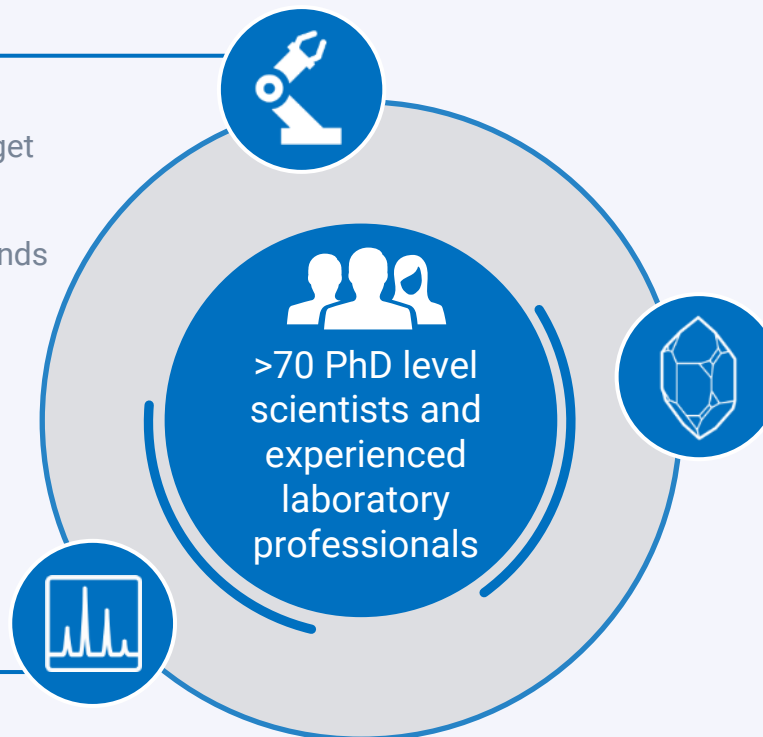
Best-in-class high content screening (HCA) platform

Protein Technologies

High quality tool protein production to enable assay development, protein structure determination and biophysics analysis

Extensive biophysics platform

Fragment screening platform



Structural Biology

Structural Biology with focus on X-ray structure determination including fragment screening

NMR methods for fragment screening

High-throughput workbench enabling multi-target crystallization

CryoEM in collaboration with external partners



Library, Data & Digital Life Sciences

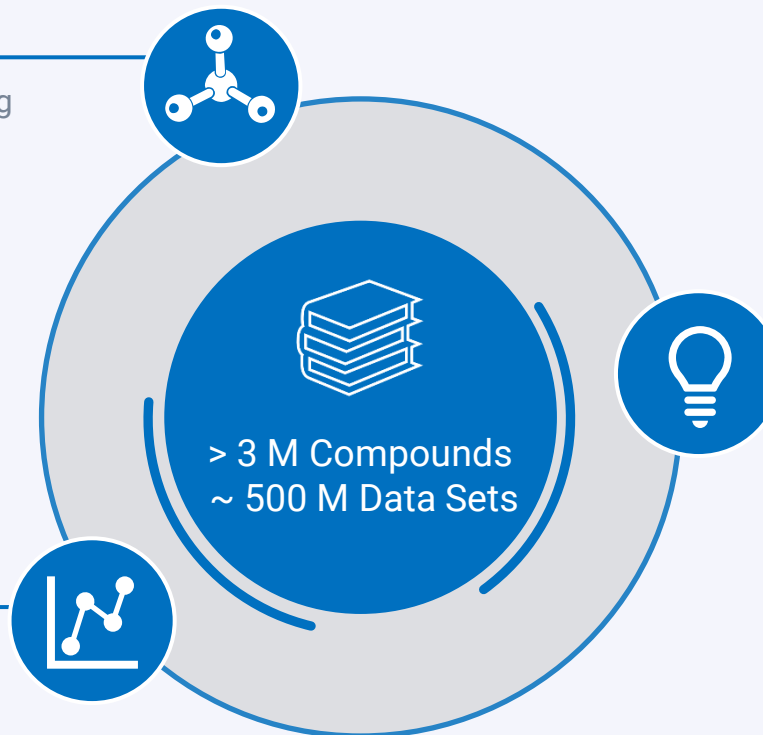
Taking informed decisions based on comprehensive libraries and data sets

Compound Library

- 3 million test compounds for HTS and follow-up testing
- High chemical diversity
- High level of proprietary compounds
- Built on Bayer's and Schering's pharma legacy

Life Science Data Base

- In vitro and in vivo data connected to 3 million library compounds (~ 500 million data sets)
- HTS data
- Chemical data, PhysChem data
- PK and pharmacological data



Digital Life Sciences

- Bioinformatics
- Computational chemistry
- Data scientists
- Virtual Screens & Data Mining
- Data-driven decisions

L Life Science Chemistry

Designing the right molecule for a specific disease - from library to new chemical matter

Design and Synthesis: Medicinal Chemistry

Decades of **expertise** in SMOL MedChem from lead finding to clinical compound

Hit compound assessment & modification

Multi-parameter molecule enhancement (lead finding & lead optimization)

Design & synthesis of high-quality test compounds & chemical probes

New modalities (e.g., PROTACs)

Computational Chemistry

Modelling

Virtual screens (target-based, ligand-based)

Data Mining & analysis

ADME models

Access to Life Science Data Base (LSDB)



Microbiological Chemistry, Upscaling and Special Technologies

Reactors up to ~100 L

Fast Metabolite synthesis, biotransformation, protein production

Late-stage diversification

New chemical methodology (e.g., photochemistry)

Purification, Analytics and PhysChem

~ 10,000 substance purifications per year (normal phase & reverse phase)

Chiral Separations

NMR, LC-MS, optical methods, structure elucidation

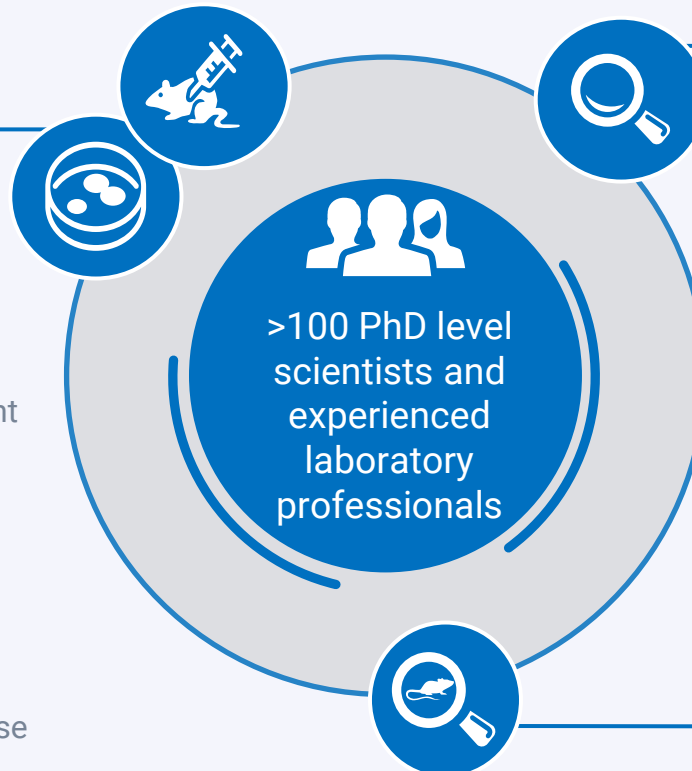
Solubility, lipophilicity and stability

T Therapeutic Research

Empowering translation to the clinic

In Vitro & In Vivo Characterization of Compounds

- Functional genomics (CRISPR/Cas9)
- Expression analyses (NGS, SCS)
- Pathway analyses
- Mode of Action studies
- Broad set of cellular methods / assay development
- Diverse set of disease models (established & customized)
- Tumor models (CDx, incl. orthotopic)
- Small animal imaging capabilities
- Radiation capabilities
- IND enabling activities, e.g. human efficacious dose prediction; PK-driver of efficacy; potential target organs of side effects



Strong Research Expertise in a Broad Spectrum of Diseases

- Basic up to IND-enabling translational research
- Repurposing & life cycle management of compounds
- Broad indication spectrum:
 - Cancer
 - Dermatitis, Psoriasis & Wound Healing
 - Overactive Bladder & Neuropathic Pain
 - Peritonitis
 - Arthritis & Bowel Disease
 - Liver fibrosis & Steatohepatitis
 - Stroke & Cardiovascular Diseases
 - Women's & men's health

Translation Research & Biomarker Strategy

- Biomarker technologies (IHC, RNAScope, blood-based assays)
- Identification and characterization of selection/stratification and pharmacodynamic biomarker
- Characterization of patients/ indications which most likely benefit from treatment
- In vitro & in vivo mechanistic PK/PD assessment to support human starting dose prediction

P Preclinical Compound Profiling

Providing guidance regarding PK, DDI potential and tolerability for compound selection

In Vitro Assay Platform

Comprehensive in vitro ADMET assay panel incl. 2D culture and genotoxicity assays

High-throughput in vitro assays (CYP inh, CLint, Caco2)

In vitro panel suited for IND-enabling PK characterization

DDI profiling (victim & perpetrator) and assessment on metabolizing enzymes in the project context

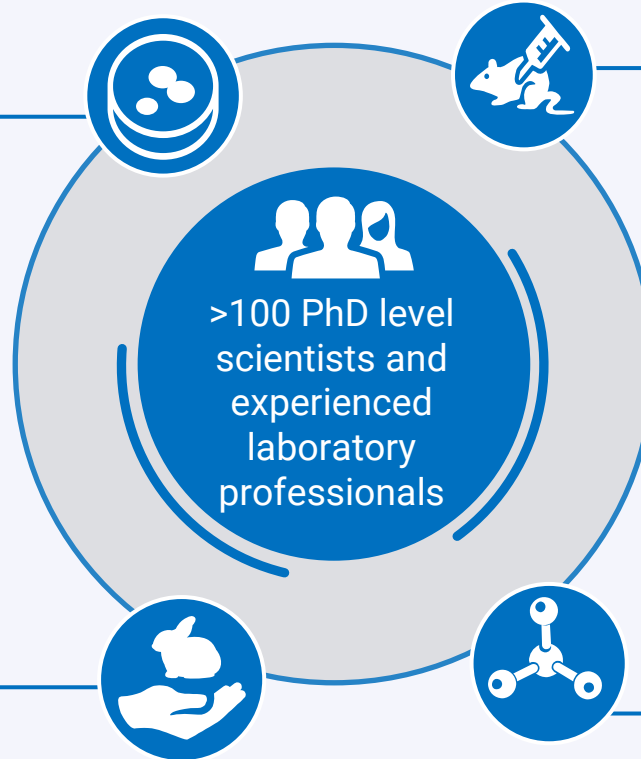
Animal Management & Infrastructure Services

Husbandry for all relevant laboratory animal species (rodents, rabbits, minipigs)

Automated cage cleaning, supply organization and disposal services

Animal welfare and supervision of legal compliance

Animal care services



In Vivo Profiling & Toxicology

Profound expertise in in vivo rodent PK, tolerability studies & MNT testing

Single cmp and cassette dosing, different admin routes incl. basic compound formulation

Special PK studies in rodents (e.g. BDC, GIT, portal, lymph, femoralis administration)

Dose range finder studies (2-4W) in rodents

Necropsy, advanced histopathology, clinical chemistry incl. hematology & endogenous biomarkers

Structure & Sample Analytics

Metabolite ID, structure elucidation & confirmation in various matrices

Quantification of compounds, metabolites & endogenous biomarkers in accordance with bioanalytical standards

Broad Experience using high-res. HPLC MSⁿ devices

Strong expertise in Mass Spectrometry Imaging (MSI)



Our Approach to Advance Your Project

All relevant technologies and competences combined in one team



Seamless transition of projects along the drug discovery value chain
 Quick turnaround times through close colocalization
 Unified data and compound handling standards



Fully integrated **drug discovery team along the value chain and beyond**
 Programs or part of programs to be handled by one partner
Integrated or selected services out of one hand



High caliber drug discovery team available to drive challenging programs
 Long term drug discovery experience and knowledge in one integrated team
 High end technology and competence portfolio to deliver on challenging tasks



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NUVISAN ICB Extended Leadership Team 2020