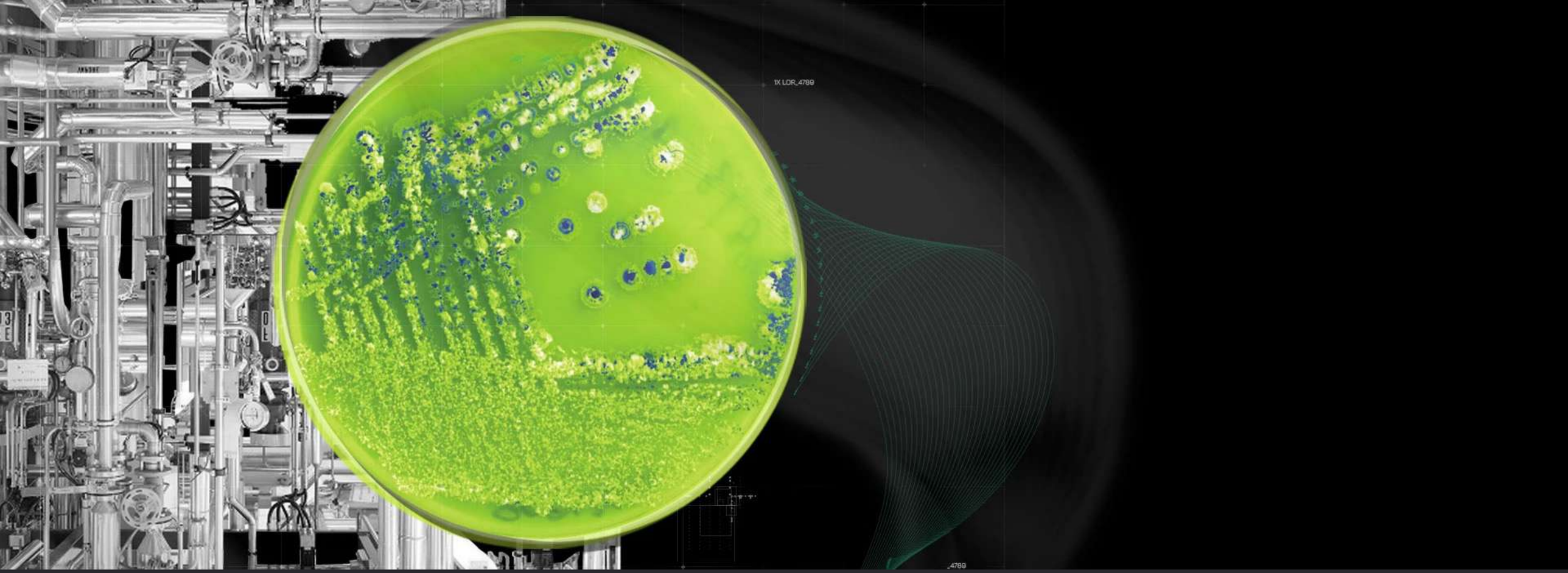


THE INNOVATION PARTNER

CDMO SERVICES

indena®

SCIENCE IS OUR NATURE. SINCE 1921

100+ YEARS

Table of Contents

ABOUT US

Vision and Mission

Our Vision

Indena is committed to developing and producing innovative high-quality ingredients derived from plants for use in pharmaceuticals, nutraceuticals and cosmetics.

This vision drives Indena to extend its excellence to all partners, for the production of highly potent active pharmaceutical ingredients (HPAPIs) and vaccine excipients derived from either fermentative or synthesis processes.

Our Mission

Indena is a long-standing and trusted partner for the cGMP Contract Development and Manufacturing of APIs for new natural solutions that promote health and wellbeing for people around the world.

Indena’s mission is to contribute to the advancement of healthcare by providing fast, safe, effective and sustainable solutions based on natural and synthetic sources to leading pharmaceutical, biotech and startup companies, to achieve product success and guarantee patients a healthier life.

Company History

1920s

The company that will first become Inverni Della Beffa and later Indena is created. The founders' vision sets the **new paradigm in the production of botanical extracts**.

1930s

Quality, scientific insipiration and rigor industrial approach: these are the pillars that allow the company to stand out on the italian market.

1940s

Milan becomes the hub of the company's activity, with **new headquarters and new plant**.

ABOUT US

Company History

1950s

Luigi Della Beffa, son of the founder Biagio Alberto Della Beffa, **joins the company**. Manufacture of finished medicinal products begins, based on the company's own plant derivatives.

1960s

Luigi Della Beffa and his vision: business relations at international level and a **new plant in Settala, a model of innovation**, with cutting-edge facilities and laboratories.

1970s

Inverni Della Beffa develops Indena, INdustrial DErivati NAturali. Pharmaceuticals and Nutraceuticals are the reference market, all over the world.

Company History

1980s

Nutraceuticals become more and more important and scientifically recognized. Indena captures market shares with **multicomponent plant extracts.**

1990s

Research is increasingly a strategic pillar for Indena's leadership. New international plants and commercial branches open, Benedetto and Biagio Della Beffa, both sons of Luigi Della Beffa, join the company.

2000s

Indena develops **Phytosome®, a revolutionary delivery system** to improve absorbption and effectiveness of botanical extracts.

Company History

2010s

Cutting-edge technological innovations are introduced in the Settala plant, for an **advanced CDMO – Contract Development and Manufacturing Organization activity.**

2020s

Innovation and implementation of the most advanced technologies, research on new products and personalized applications, quality and sustainability: this is **Indena’s vision for the next 100 years.**

ABOUT US

Facts and Figures

- **100** years of experience
- **1,000+** employees
- **5** international branches and production sites
- Sales in **80+** countries

- **Same shareholding family** since foundation
- **115+** commercial APIs currently supplied
- Core competence: **research, development** and **manufacturing** of **complex molecules** derived from **natural sources**

Our Locations

Sales offices

R&D centers

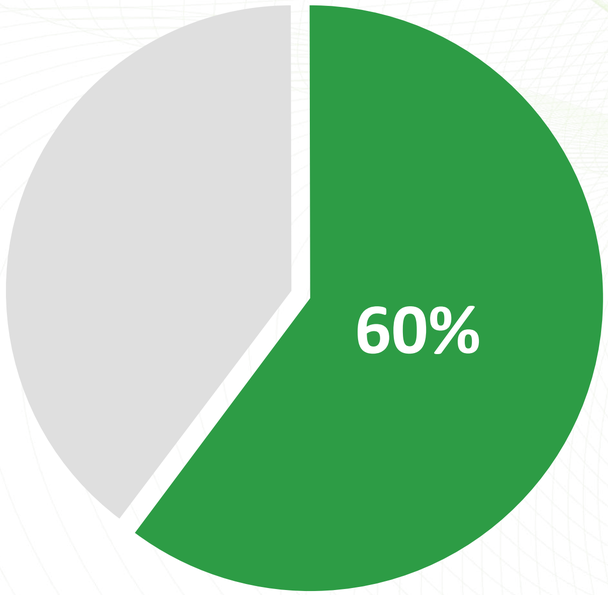
Manufacturing sites

Settala site

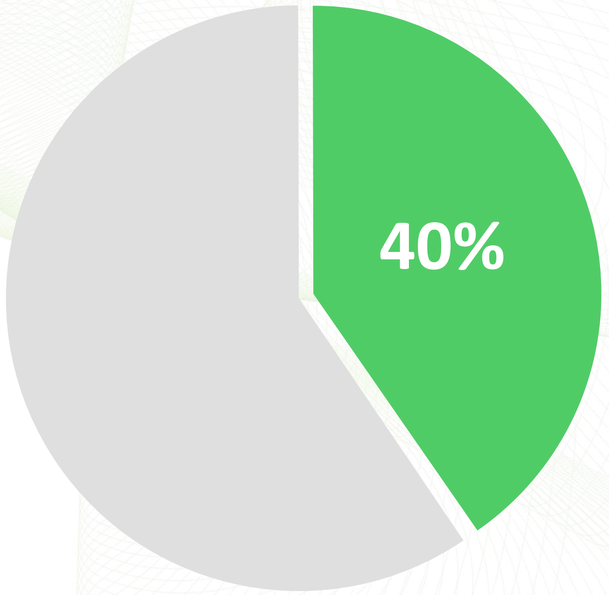
CDMO Overview

Weighted sales turnover 2023 vs CDMO 2023

2023 Group Turnover: €250,000,000 (material + services)



Products from internal development



Products developed in collaboration with partners

CDMO Facts & Figures

Numbers over the last 5 years

CAGR

RFP responses per year

CDMO active projects/products

Projects won

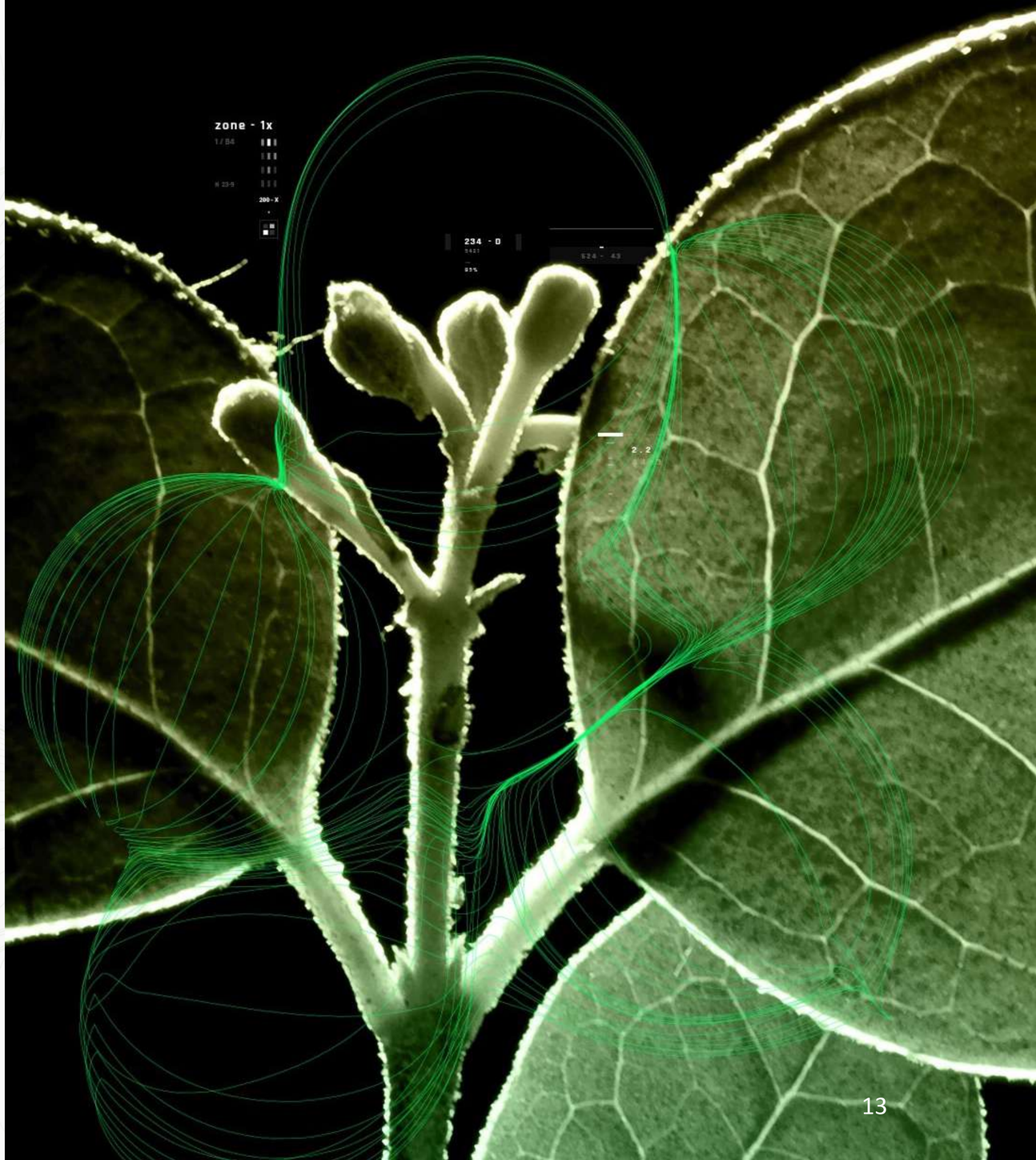
EXPERIENCE AND CAPABILITIES

Research & Development

EXPERIENCE AND CAPABILITIES

Research & Development Services

- Over 100 years of experience in process research and development
- A single state-of-the-art R&D hub to facilitate interactions
- Over 70 highly qualified and experienced staff members
- Strong communication between cross-functional departments and partners
- Design and development of new routes for targeted molecules
- Integrated Quality-by-Design support since the earliest project stages
- Highly experienced team in synthetic chemistry, natural chemistry and biotechnology
- R&D project management tailored to each project



EXPERIENCE AND CAPABILITIES

Process R&D Services

- Process development of molecules down to OEB class 5 products (20 ng/m^3)
- Technology transfer
- Scale-up activities and GMP manufacturing of HPAPIs
- GMP chromatography on lab scale including TFF for concentration
- Extraction and purification process development of natural molecules
- Toxicological data of starting material, intermediate and final API collection
- IP evaluation
- Particle size engineering via wet milling and spray drying
- Crystallization development and polymorph screening

Analytical R&D Services

Analytical development & Technology transfer

- Analytical method development and optimization
- Related substances carry over
- Related substances/secondary metabolites LC-MS identification, isolation and characterization
- Complex molecular entities structural characterization
- Analytical method verification and validation
- Analytical method transfer
- Support to process transfers, scale-up and validation

Solid state characterization

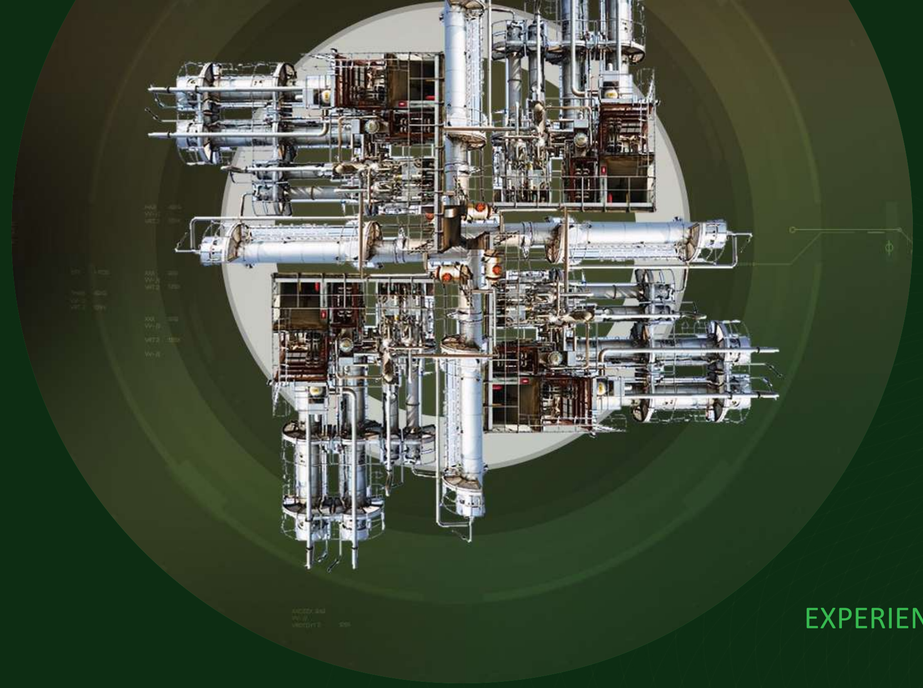
- Polymorph screening and API polymorph characterization
- Particle size distribution and shape
- Hygroscopicity
- Solubility curves

Early-stage quality control activities (clinical and PPQ batches)

- Analytical release of raw materials and intermediates
- IPC
- Analytical release of APIs
- Reference standard generation, qualification and maintenance

Stability studies

- Preliminary stability evaluation of APIs and intermediates
- API forced degradation studies
- API stability studies according to ICH guidelines



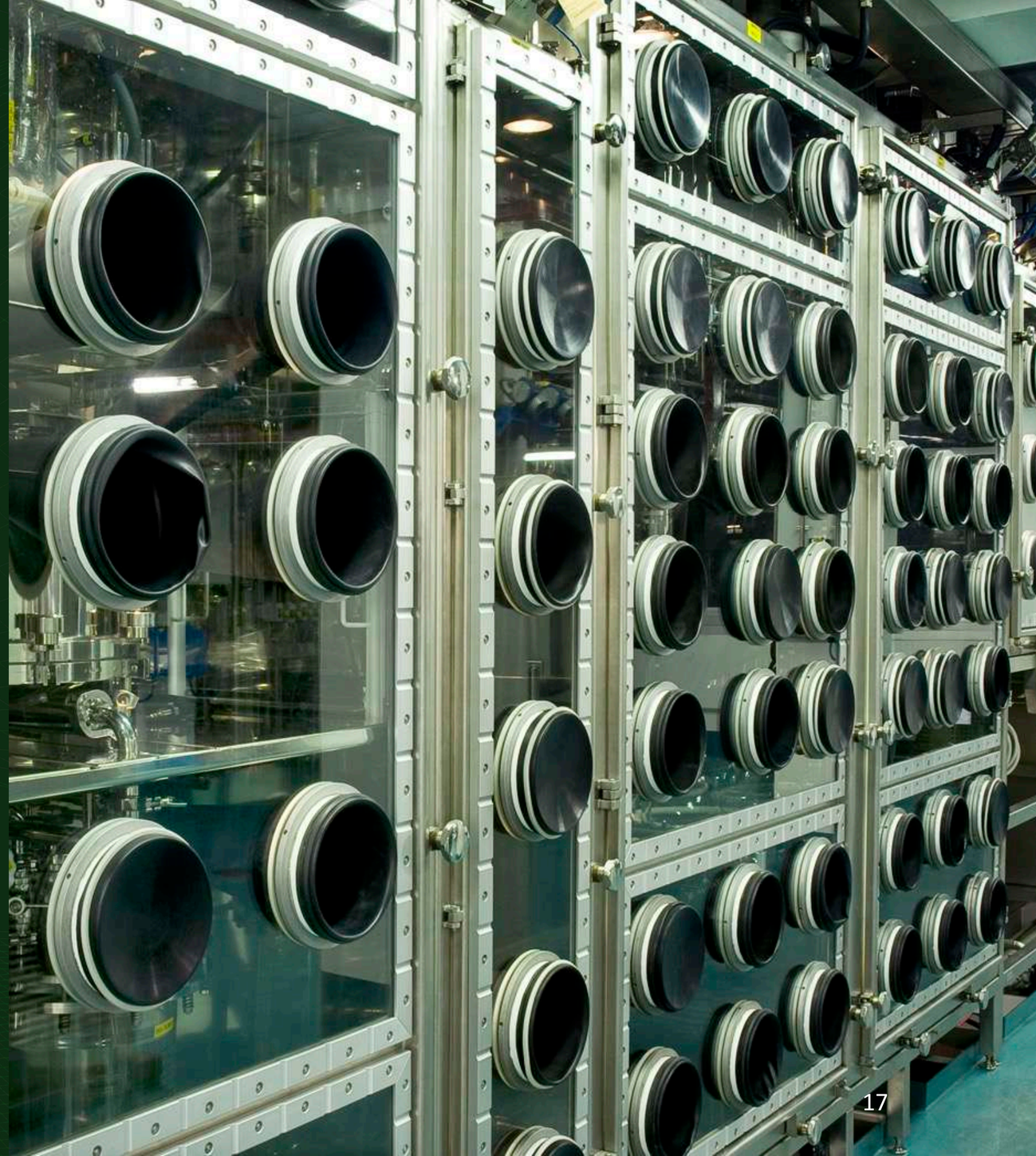
EXPERIENCE AND CAPABILITIES

API Manufacturing Servic

EXPERIENCE AND CAPABILITIES

API Manufacturing

- 7 commercial custom HPAPIs currently manufactured
- 2 PPQ per year, including new HPAPIs handled by a dedicated process validation team
- Tailor-made process validation strategies and flexible approach according to partner requirements
- Fully compliant with ICH Q7, Q8, Q9, Q10 and Q11



EXPERIENCE AND CAPABILITIES

Chemistry capabilities

Kilo Lab Scale

- Alkylations including dimethylsulfate
- Halogenation (Br, Cl, I)
- Amidations (NH3 aqueous, gas)
- Boron chemistry
- Esterifications
- Functional group protections and de-protections
- Homogeneous catalysis and cross coupling
- Hydrazine chemistry
- Hydrogenations
- Nitration
- Organometallic chemistry (alkyl lithium)
- Oxidation (Swern, peroxides, bleach, MnO_2)
- Ozonization (case-by-case evaluation)
- Phosgene surrogates
- Reductions with hydrides
- Thiomethylations
- Thiophosphorylations
- Wittig, Wittig Horner, Peterson reactions

EXPERIENCE AND CAPABILITIES

Chemistry capabilities

Pilot Scale

- Alkylations
- Halogenation (Br, Cl, I)
- Amidations (NH3 aqueous, gas)
- Boron chemistry
- Esterifications
- Functional group protections and de-protections
- Homogeneous catalysis & cross coupling
- Hydrazine chemistry
- Hydrogenations
- Mercaptanes chemistry
- Nitration
- Chlorosulfonic acid chemistry
- Oxidation (Swern, peroxides, bleach, MnO_2)
- Reductions with hydrides
- Wittig, Wittig Horner, Peterson reactions

API Manufacturing Services

- GMP manufacturing:
  - Starting Materials
  - Intermediates
- GMP manufacturing of synthetic, fermentative and natural HPAPIs (with OEL as low as 20 ng/m^3) *(early/late clinical phase, commercial phase)*
- GMP manufacturing of synthetic, fermentative and natural HPAPIs (OEL 800-1,000 ng/m^3) *(early/late clinical phase, commercial phase)*
- GMP manufacturing of synthetic, fermentative and natural APIs and intermediates (OEL 10 mcg/m^3) *(early/late clinical phase, small-scale commercial batches)*
- GMP spray drying of molecules down to OEB class 3, 10 mcg/m^3

EXPERIENCE AND CAPABILITIES

Regulatory Affairs Services

- Development of regulatory strategies for a fast and successful submission (AIFA, FDA, PMDA, KFDA, ANVISA, SWISS MEDIC)
- Full regulatory support for product and process development, from pre-clinical phase to commercialization
- Regulatory input for validation activities and stability studies
- Preparation of CMC sections (DMFs) for INDs, NDAs, ANDAs

INDENA'S EXPERTISE

HPAPI Services

- 18 HPAPIs developed in the last 5 years
- Capability to handle molecules with OEL as low as 20 ng/m^3 (OEB class 5)
- Comprehensive HPAPI development and manufacturing capabilities, on scales from grams to hundreds of kilos for OEB class 3 molecules
- 20-year track record for safe operations in developing and manufacturing HPAPIs
- Handling and manufacturing of even the highest potent products, including warheads and payloads for ADC

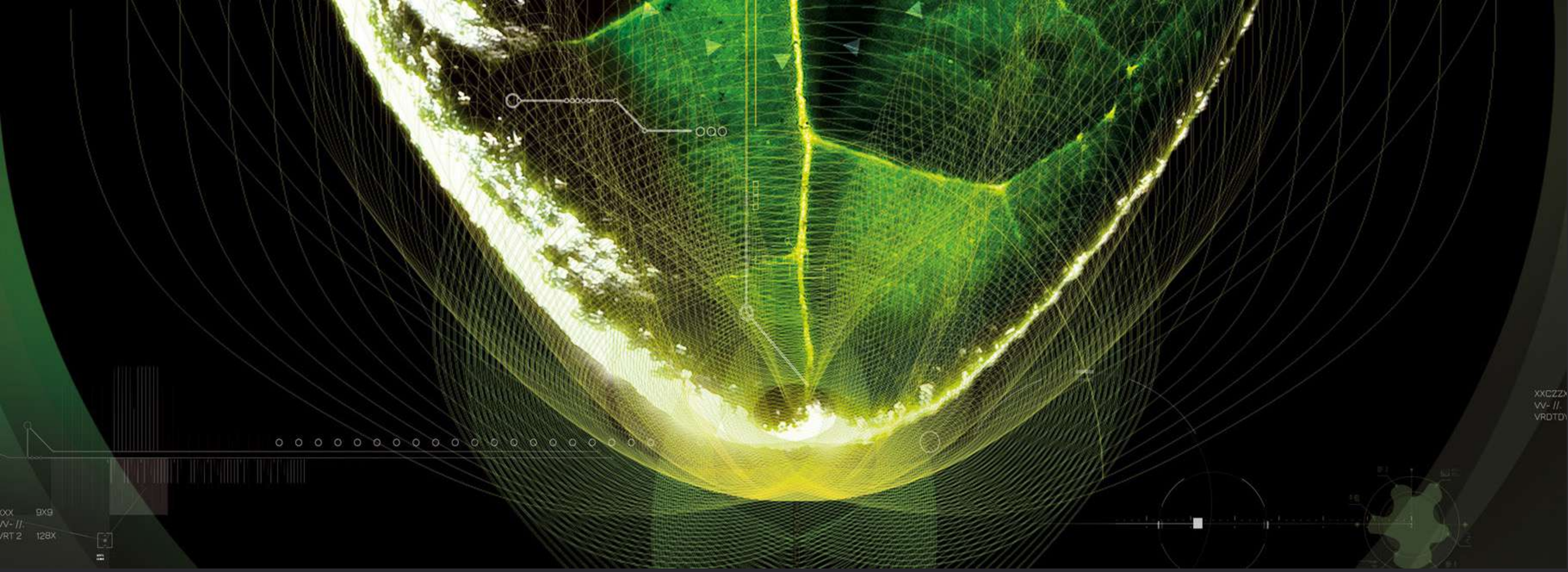
HPAPI Capabilities

Dept	Reactors (L)	Temperature Range (°C)	Potency (OEL ng/m³)	OEB class
LK2	2 x 28	-60 to +160	20	OEB 5
	2 x 65	-50 to +160	20	OEB 5
LK1	1 x 22 + 1 x 65	-20 to +150	150	OEB 5
P10	1 x 35 + 1 x 60	-15 to +120	150	OEB 5
	1 x 35 + 1 x 60	-15 to +120	150	OEB 5
	1 x 20 + 1 x 35	-15 to +120	150	OEB 5
P7	4 x 60	-15 to +120	800	OEB 5
	2 x 60	-15 to +120	800	OEB 5
P7	2 x 350	-15 to +120	1,000	OEB 4

Technological expansion: ongoing activities

HPAPIs:

- **New R&D labs for HPAPI projects.** 14 work places for 11 synthetic chemists and 3 analysts. All the experimental activities related to HPAPI will be transferred in LK2 building. To be completed by March 2024.



War-heads and payloads for ADCs

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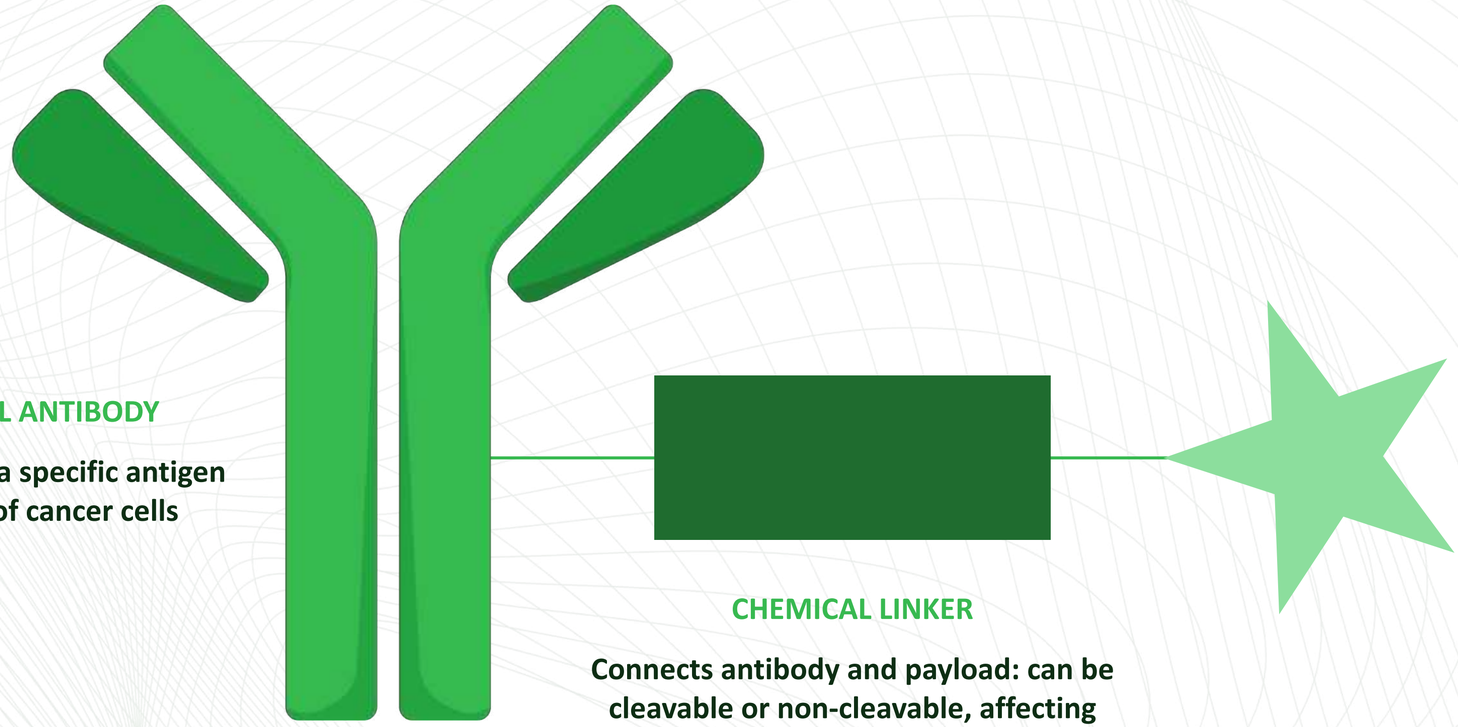
100+ YEARS

Antibody Drug Conjugate (ADC)



MONOCLONAL ANTIBODY

Selectively targets a specific antigen on the surface of cancer cells

CHEMICAL LINKER

Connects antibody and payload: can be cleavable or non-cleavable, affecting stability, efficiency and bioavailability of the ADC

PAYLOAD

Cytotoxic compound with high potency

ADCs payloads & linkers

- Handling of HPAPI (OEL < 20 ng/m3). SMEPAC test at <1 ng/m3 on-going
- Chromatographic purification (including prep. HPLC)
- Lyophilization (lab scale, Production of Clinical Phase batches)
- Fermentation for backward integration

INDENA'S EXPERTISE

Chromatography Services

- More than 100 years of industrial experience in complex molecule chromatography
- Conventional chromatography capacity (up to 7,700-L columns)
- HPAPI chromatography capacity
- Dedicated cross-functional technical team with vast experience

Achiral separation:

- Direct phase
- Reverse phase
- Ion exchange
- Hydrophilic interaction

Chiral separation:

- Preparative HPLC

Supporting activities:

- Extraction and evaporation
- Analytics

Chromatographic Capabilities

Dept	Columns	Potency (OEL ng/m^3)	Comments
LK2	20 L	20	HPAPI
LK1	Preparative HPLC (11-cm d.)	150	
	60 L	150	
P10	2 x 120 L	150	
P7	2 x 130L	800	
	1 x 400 L	800	
P7	6 x 2500 L	1,000	
	1 x 3300 L	1,000	
	6 x 7700 L	1,000	Standard
Pilot	Preparative HPLC (11-cm d.)	1,000	
	2 x 100 L		
	1 x 600 L		
	1 x 2,000 L		

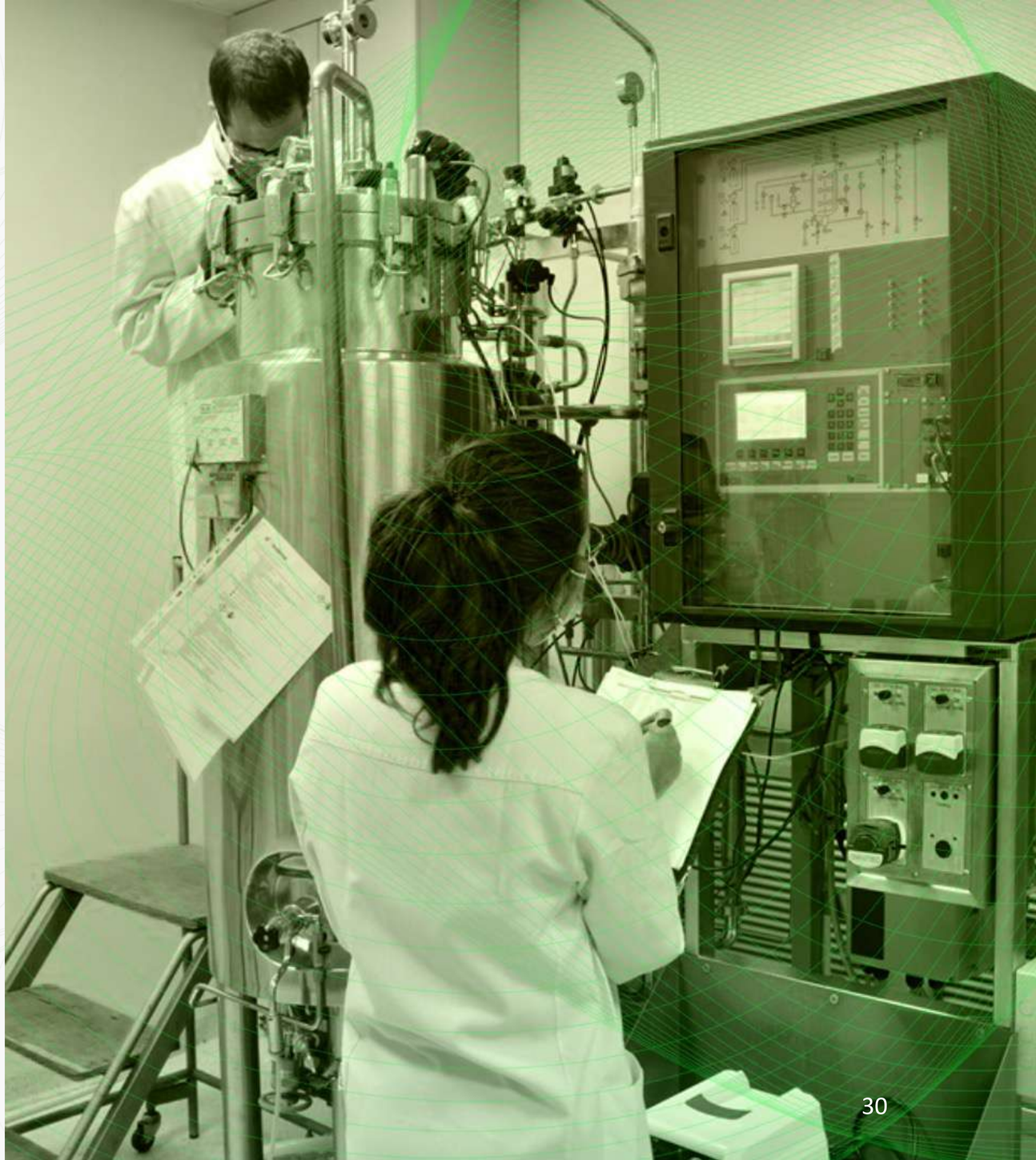
INDENA'S EXPERTISE

Fermentation Services

- Dedicated biotech cross-functional team with vast experience
- Lab and pilot-scale fermentation capabilities to support scale-up activities
- In-house industrial multipurpose fermentation plant
- Fermentation broth downstream capabilities for HPAPIs

Fermentation experience for:

- GMP microbial fermentation – bacteria, yeasts and fungi
- Living cell-based bio-transformations – bacteria, yeasts and fungi
- Risk group class 2 microorganisms
- HPAPIs



Fermentation Capabilities

Department	Fermenters	Activities
Biotech Lab	5 L	Familiarization
	10 L	
	100 L	Scale-up
P9	150 L	Manufacturing
	2 x 1,000 L	
	2 x 1,000 L	
	1 x 20,000 L	

INDENA'S EXPERTISE

Spray Drying Services

- Experience in spray drying since the 2000s
- 5 spray drying systems for APIs over 2 sites
- Spray drying capacity up to 93,000 kg/year
- Spray drying activities with **class 2 organic solvents**
- Strong analytical support for spray drying activities

Spray Drying Capabilities

Department	SD brand	Evaporation capacity	Activities
Laboratory	Buchi		Familiarization and SD parameters set up
	Procept 4M8trix		
P11	Gea PSD2	13 kg/h of water	Manufacturing
	Lurgi	35 kg/h of water	

KEY STRENGTHS

Quality Management & Audit History

Quality accreditations

- ISO 9001:2000
- ISO 14001
- ISO 45001
- ISO 22000
- C-TPAT Validated (US Customs & Border Protection)
- KNOWN COSIGNOR – Certification (ENAC, Italian Civil Aviation Authority)
- Authorized Economic Operator - Full (AEOF) - Certification (EU)

Settala Inspection History

Agency	Date	Reason
FDA	25-29 July, 2016	Routinary inspection
MFDS	Feb 27-March 3, 2017	Specific drug product inspection
AIFA	12-16 June, 2017	Routinary inspection
AIFA	8-10 May, 2018	New department and new API authorization
MFDS	19-21 November, 2018	Specific drug product inspection
Italian MoH	27 November, 2018	Routinary inspection
FDA	28-31 October, 2019	New API authorization
AIFA	22-26 November, 2021	Routinary inspection
AIFA	27-29 April, 2022	Routinary inspection
AIFA	17-19 October , 2023	Routinary inspection

KEY STRENGTHS

Sustainability

KEY STRENGTHS

Sustainability

Indena’s most important actions for energy saving

All the electric engines in the different plants are **energy efficient**:

- small engines are IE3 class*
- big engines are IE4 class*

** The highest level of efficiency for the category, according to European law CE 640/2009*

All machines (i.e. compressors or chillers) are **constantly monitored to verify their efficiency** and replaced with more performing versions if necessary.

Inverters (electrical devices which convert direct current into alternating current) **reduce energy waste**: at the moment, electric engines equipped with inverters use 1/8 of the energy compared to those without.

Continuous improvement of energy efficiency of buildings, in plants and headquarters, leads to **higher performance through the rationalization of energy use and flows**:

- Coatings on our buildings in plants
- Insulated roofs, doors and windows
- Low-consumption light bulbs
- Sensors to regulate when lights switch on and off

KEY STRENGTHS

Renewable Energy

Indena is equipping all of its sites with state-of-the-art photovoltaic panels.

- The panels already installed at Settala currently produce 220,000 kWh per year.
- By the end of 2022, the yearly capacity of the panels will be:
    - **@Settala** 1,600,000 kWh
    - **@Tours** 200,000 kWh
    - **@Palestro** 1,000,000 kWh
    - **@Milan** 113 kWh
- By the end of 2023, additional photovoltaic panels in Settala will produce 2,100,000 kWh per year.

The total energy self-production from renewables thus will go from 2,913,000 kWh per year in 2022 to 5,013,000 kWh in 2023.

Energy Self-production and CO_2 reduction @Indena plants

Infrastructure	kWh produced per year	CO_2 reduction
Cogeneration plant	16,566,000	2,500 Tons
Turbine on boiler for steam production	600,000	277 Tons
Photovoltaic panels (end of 2022)	2,913,000	1,340 Tons
Photovoltaic panels (installed by end of 2023)	2,100,000	1,000 Tons
Total	22,179,000	**5,117 Tons**

OUR GOAL: 67% OF ENERGY SELF-PRODUCED BY 2023,

OF WHICH 23% FROM RENEWABLE SOURCES

EcoVadis Rating

- **What is EcoVadis?** EcoVadis operates as an evidence-based online platform, providing sustainability ratings and allowing companies to assess the ESG performance
of their global suppliers. It considers a range of CSR issues, grouped into 4 categories:

- Environment, Labor & Human Rights, Ethics and Sustainable Procurement.

- Last August 2023, Indena has achieved an EcoVadis **Bronze medal** rating for sustainability and is in the top 29% of companies rated by EcoVadis in the Manufacture of basic pharmaceutical products and pharmaceutical preparations industry

KEY STRENGTHS

Why Choose Indena?

KEY STRENGTHS

Indena’s Key Strengths

PARTNERSHIP

Collaborate to win

Transparency in communication

PEOPLE

Highly experienced staff, fully committed to supporting projects and Client needs

RELIABILITY

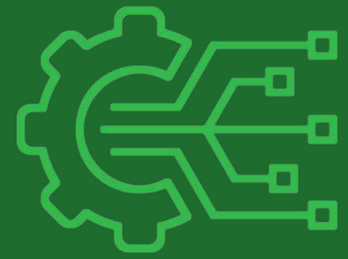
Solid track record of successful custom development activities

On-time developments and deliverables

REACTIVITY AND FLEXIBILITY

Committed to start a new CDMO project within max 90 days

Development schedule adapted according to partner requirements



TECHNOLOGY

State-of-the-art equipment

Continuous investmentent in new technologies

indena®

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100+ YEARS

Contact: cdmo@indena.com

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