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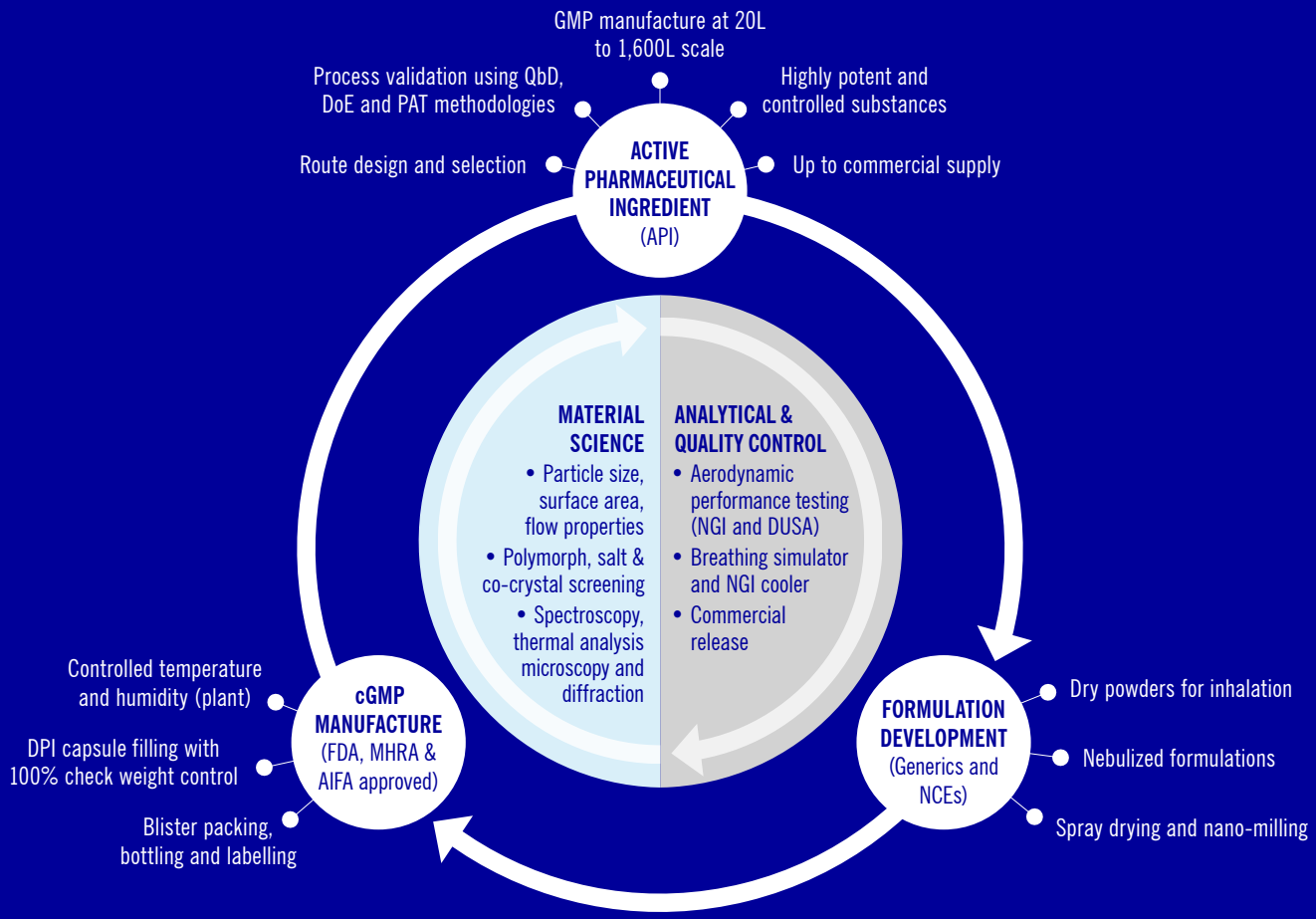
INTEGRATED INHALATION CAPABILITIES

At Evotec, inhaled drug product development is a major part of our integrated CMC portfolio with dedicated cross functional teams working together on your projects – from phase I to late phase clinical studies. Evotec proposes integrated and stand-alone development plans tailored to each project to increase success and save time.



Evotec's inhaled drug product development and manufacture platform supports all stages of clinical development, including commercial release, throughout our cGMP facilities in Italy and the UK. Our programs are supported by a dedicated Inhalation Analytics and Material Sciences team using state of the art equipment to characterise and define the drug product's quality attributes. The integrated approach we apply, alongside our scientific expertise, provides robust and reliable development strategies for challenging pharmaceutical inhaled drug product programs.
For abbreviations used in graphic, please see page 3.

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- **Formulation development of dry powders and liquids designed to meet a quality target product profile (QTPP) with consideration of final commercial process**
- **Inhaled analytics: Dedicated laboratories for testing Dry Powder Inhalers (DPI), Pressurized Metered Dose inhalers (pMDI), nasal sprays, nebulizers and soft mist for all stages of development up to and including commercial release**
- **API: Chemical development and manufacturing services enabling industry leading API route design and process development services up to and including commercial supply**
- **Material science: Best-in-class laboratories for physical properties analysis and API solid form selection and crystallization development**
- **cGMP manufacture: Dedicated inhaled production pilot plant clean room status ISO7, Grade C. Environmental controls and material handling up to and including OEB5 ($<1\,\mu g/m^3$)**
- **Quality assurance: FDA, MHRA and AIFA approved facilities**

It is widely recognized that the development of inhaled products are extremely challenging and therefore by having all the different groups involved in the project situated in the same Evotec building in Verona Italy is a huge advantage.

FORMULATION

Our team has extensive experience in developing, optimizing and scaling up dry powder inhaled and liquid and suspension formulations from first in human studies up to phase III. The QTPP is considered from the very start in order to reduce the frictions in inhaled products development to enable robust GMP manufacturing. We apply the Particle Engineering concept through spray-drying and nanotechnology. Developing NCEs and generic products (505j submission) using our platform of technologies includes high shear and low shear powder blending along with capsule filling equipment (volumetric and gravimetric).

ANALYTICAL AND QUALITY CONTROL

Our experts have significant experience in the aerodynamic performance testing (NGI and DUSA) of inhaled products including the reverse engineering of multiple generic DPI products, *in-vitro* equivalence studies, inhaler device selection and verification testing. All performance testing is performed inside cabinets with controlled temperature and humidity. We take a structured, straight forward and reliable approach for method development and validation based on Quality by Design (QbD) principles in a fully validated GxP environment. Data is recorded, evaluated and reported using a fully validated GMP Laboratory Information Management System (LIMS) and electronically controlled (barcode) sample management system. Our QC laboratories are equipped with HPLC, UPLC, LCMS, GCMS, automated and manual dissolution and KF instruments; performance testing is carried out with NGIs with optional NGI cooler, DUSA and Breathing Simulators. We provide full ICH stability storage testing capabilities.

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API

Our API teams possess a pharmaceutical development mindset using a risk based approach to establish critical process parameters and robust processes to develop optimise and manufacture small molecule APIs. Activities include polymorph, salt and co-crystal screens, and the design of superior crystal engineering strategies and crystallisation processes.

Our FDA, MHRA & AIFA approved GMP labs and pilot plants offer the flexibility to manufacture a wide range of APIs (including potent and controlled substances) at various scales (volumes ranging from 20L to 1600L), supporting both non-GMP and GMP API manufacturing from pre-clinical to commercial.

MATERIAL SCIENCE

Our scientists have expertise in using our state-of-the-art technologies to support integrated inhaled projects including micromeritics (particle size, surface area, DVS, pycnometry, powder rheology, wettability), spectroscopy (FTIR, Raman, NMR), X-Ray Diffraction (XRPD, including non-ambient and 2D), SAXS, thermal analysis (DSC, TGA, TGA-IR), microscopy (PLM, ESEM+EDX). Studies specific for inhaled projects include assessment of micronization and storage conditions on amorphous formation and particle agglomeration, specific surface area relationship to particle size and surface morphology, and rheology for cohesive powders.

cGMP MANUFACTURE

Our pilot plant has a dedicated area for the manufacture of inhaled products with ISO 7 classified facilities (equivalent to Grade C) with suitability for highly potent compounds up to OEB5 (<1µg/m³). The environmental conditions can be controlled within the manufacturing area (often a requirement for inhaled products). Batches up to a scale of 100k units have been completed for DPI capsules with 100% check weight control. Packaging includes bottling and blister packing.

QUALITY ASSURANCE

The independent Quality Assurance unit oversees GMP activities to ensure compliance and provide both customer and regulatory audit support. Evotec also has a long-established relationship with a preferred partner that can bring specialist advice on regulatory aspects.

Abbreviations used: QbD – Quality by Design; **DoE – Design of Experiment; PAT** – Process Analytical Technology; **ICH** – International Council for Harmonisation; **ASAP** – Accelerated Stability Assessment Program; **NGI** – Next Generation Impactor; **DUSA** – Dosage Unit Sampling Apparatus; **NCE** – New Chemical Entity

Contact us to find out how our integrated CMC approach and cross functional teams can support your orally inhaled drug product development and manufacturing projects. Please contact us at info@evotec.com or visit www.evotec.com