BSP PHARMACEUTICALS

Development Services

ONE STOP SHOP IN THE SUPPLY CHAIN OF ANTICANCER PRODUCTS

BSP Pharmaceuticals is a Contract Development and Manufacturing Organization focused on production of anticancer and cytotoxic drugs as small molecules and ADC compounds.

BSP Pharmaceuticals provides a full range of integrated services aimed to support the entire life cycle of a product.

From the formulation and process development/optimization, through scale up/scale down studies, we can drive the product to cGMP manufacturing for clinical and commercial needs.

QC laboratories are equipped to run all analytical testing (chemical and microbiological) on raw materials, components, in process controls, release and stability testing.

Internal Regulatory Affairs team to manage data collection and document preparation for DMF and CMC to support filing activities.

DEVELOPMENT
Formulation, Process, Analytical methods

SCALE UP/DOWN
Process Robustness and Characterization

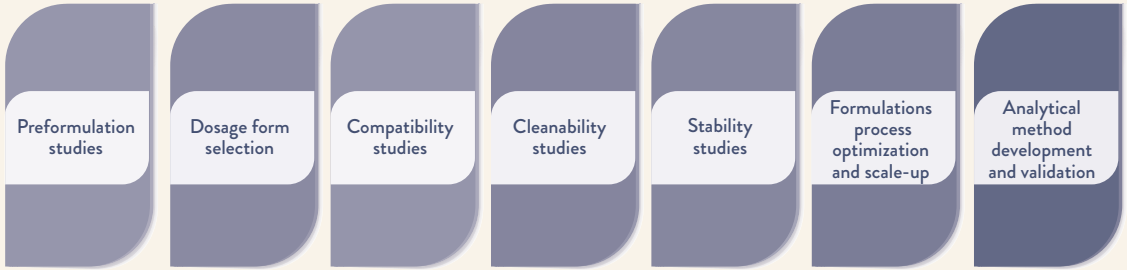
QUALITY CONTROL
Release, Stability, Process comparability testing

MANUFACTURING
Clinical and Commercial Supply

REGISTRATION
Regulatory Support for DMF and CMC Preparation

DEVELOPMENT SERVICES ARE A STRATEGIC BUSINESS FRAME FOR BSP

BSP DEVELOPMENT DEPARTMENTS WORK ON:



The Development Department supports the characterization of anticancer products that has been transferred in the plant, contributing to growth of knowledge of its criticalities for the process and stability aspects.
This department is equipped with all the instruments to project, validate and perform all the chemical tests needed from the pharmacopoeias for analysis and the scale-up of our products.

2 | MAIN LABORATORIES of approximately 3100 sqft completely separated but fully integrated with cGMP Manufacturing areas.

A group of scientists that works in tight connection with manufacturing personnel, represents a unique combination of knowledge, skills and competences that can be make the difference in moving the product quickly to clinic and to the market.
This work mode allows:

- To switch quickly from **development to clinical** and **commercial production**.
- To make the **scale-up** of the product internally without the need to transfer the product elsewhere.
- To **reduce** technical issues and constraints when changing manufacturing scales and batch size.
- To **support cGMP manufacturing** during preliminary tech transfer phase and with the possibility to run customized trials and experiments for trouble-shooting.

CONTAINMENT

To avoid direct exposure of High Potent APIs to the surrounding, specific technical solutions have been applied in the laboratories to respect internal policies and to achieve the same Operational Exposure Limits than the cGMP manufacturing areas.

The use of **ISOLATORS** as primary containment systems , enable full segregation of the Active Ingredients during each step of the process, including **intermediates preparation, material transfer** and **final collection of the product**.

OUR RANGE OF EXPERIENCE INCLUDES:

- **EXCIPIENTS COMPATIBILITY STUDIES**
- **SOLUBILITY STUDIES**
- **FORMULATION DEVELOPMENT AND OPTIMIZATION**
- **CONTAINER/CLOSURE SELECTION**
- **MATERIAL COMPATIBILITY STUDIES**
- **SCALE UP & SCALE DOWN STUDIES**
- **DEVELOPMENT O LIPOSOME AND LIPID BASED FORMULATIONS**
- **CHARACTERIZATION OF THE BULK DRUG SUBSTANCE**
- **ANALYTICAL METHODS DEVELOPMENT AND VALIDATION**
(including HPLC, CE,SEC-MALLS, UV, physical and bioassay methods)
- **STABILITY STUDIES**

LYOPHILIZATION CYCLE DEVELOPMENT AND OPTIMIZATION THROUGH THE FOLLOWING STEPS:

• Thermal analysis by **Differential Scanning Cromatography** (DSC) to obtain information on the critical temperatures of the Bulk Drug Solution as melting temperature and glass transition temperature
• Cryomicroscopy or **Freeze Dry Microscopy** (FDM) studies to support the information gained from DSC analysis and to investigate the behavior of the Bulk Drug Solution. With FDM lyophilization conditions can be simulated in a drop of solution, to estimate the critical temperature of the formulation in micro scale.
• **2 Small scale lyophilizer** with a total capacity of 0.20 sqft (2 shelves) and 0.45 sqft (3 shelves) to run a complete lyo cycle and verify all the critical process parameters. Sample thief systems on board enable vials collection during the primary and secondary drying without the need of interrupting the cycle. Thermocouples probes to monitor product's temperature during the cycle.

INJECTABLES LIQUID & LYOPHILIZED

We have full development capability for small molecules and ADCs in liquid and lyophilized injectable dosage forms.

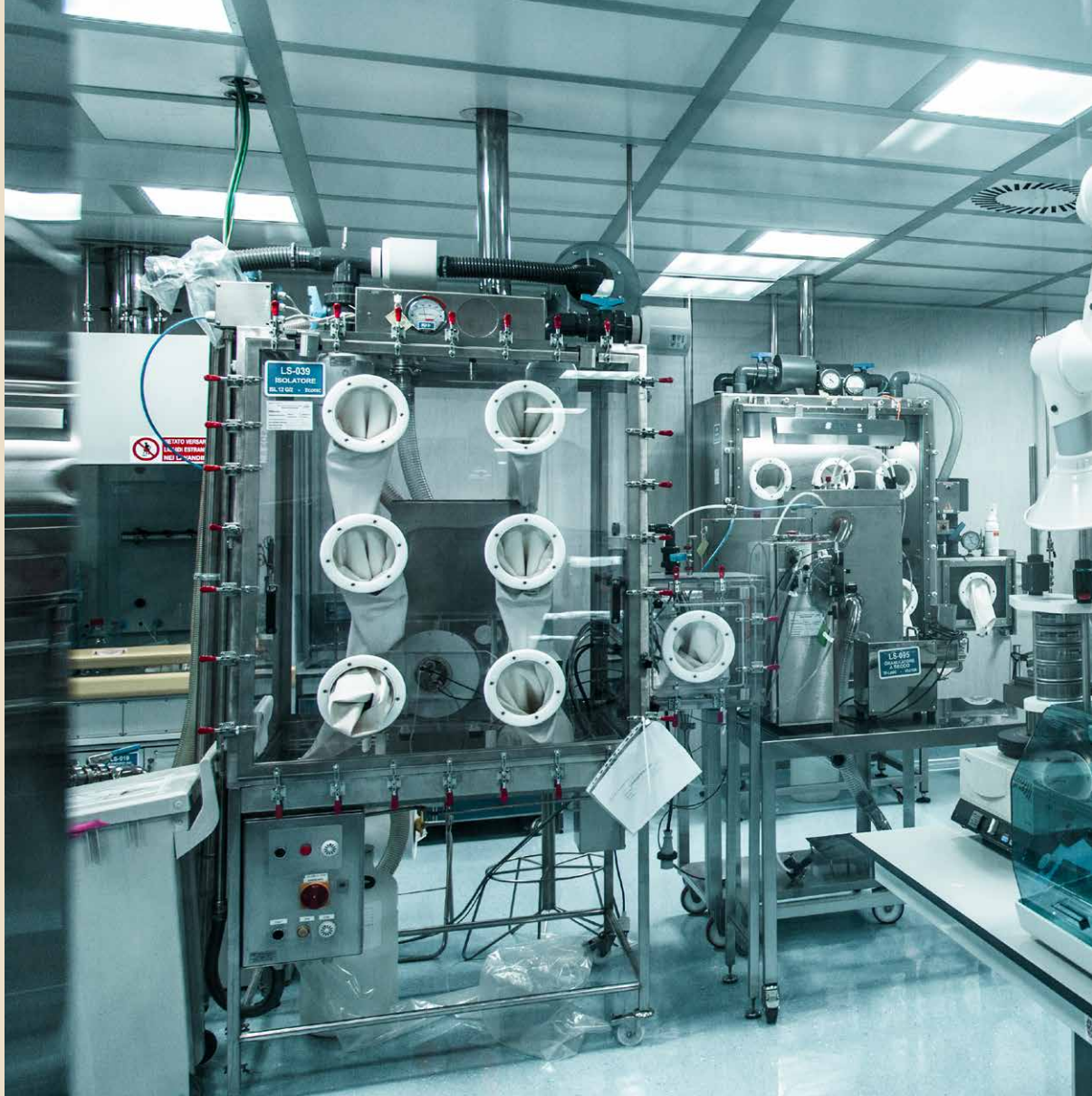
CONJUGATION & FILL-FINISH OF ADCs

With a **fully integrated system** that can support manufacturing of ADCs from Bulk Drug Substance (BDS) to Drug Product (DP) **in the same site**, BSP has developed specific capabilities to strategically manage the criticality of this class of compounds. The need of reducing the time-to-market and the possibility to receive a **BREAKTHROUGH DESIGNATION** or FAST TRACK APPROVAL pathway from the Regulatory Agencies, have deeply changed the clinical life cycle of these therapeutic entities.
BSP Development Team for ADCs has the goal of generating a robust and deeply characterized process to support scale up to cGMP manufacturing and the production for Clinical Studies.

The development work is focused on each step of the conjugation process and includes:

- Optimization of mAb preparation and **Conjugation Reaction** parameters.
- Development and optimization of **Diafiltration/Purification** steps.
- Characterization of **Tangential Flow Filtration** parameters.
- Development and optimization of **Chromatography** step.
- Development and optimization of **Final Formulation**.
- **Mixing studies** for Intermediates and Final Formulation.
- Characterization of **storage condition**.
- **Freeze/Thaw** studies.
- **Stability** studies for BDS and DP.

ORAL SOLIDS



BSP can support development of **conventional** oral dosage forms as **tablets, hard capsules** and **multiparticulate/granules** with preformulation, formulation and process screening and optimization studies for immediate release, controlled release and solubility enabling formulations (i.e. self emulsifying systems approach).
BSP can also work on **non conventional** capabilities such as **hard gelatin capsules filled with liquid** or semisolid **lipid-based formulations** and **organic based formulations**. BSP can work on existing formulation and/or processes coming from Customers or start from the Customer target product profile. Using **state of the art** laboratory scale equipment the most common technologies can be applied to generate all the critical information for a **robust scale-up** to cGMP Manufacturing department.

Among others:

- **WET GRANULATION, DRY GRANULATION, DIRECT COMPRESSION, FILM COATING CAN BE CONDUCTED, MATCHING LAYOUT AND WORKING PRINCIPLE OF PRODUCTION FACILITY EQUIPMENT AND ALLOWING COLLECTING PROCESS PARAMETERS SUITABLE FOR SCALE-UP ACTIVITIES**
- **HIGH SHEAR GRANULATOR, FLUID BED GRANULATOR, ROTOGRANULATOR**
- **ROLLER COMPACTOR**
- **FREE FALL BLENDER**
- **SINGLE PUNCH TABLET PRESS WITH FORCE MEASUREMENT CAPACITY**
- **PERFORATED PAN COATER**
- **HARD CAPSULES POWDER FILLING**
- **HARD CAPSULES LIQUID FILLING**
- **FULL SET OF TECHNOLOGICAL CONTROLS EQUIPMENT IS AVAILABLE FOR CHARACTERIZATION OF INTERMEDIATE AND FINISHED PRODUCTS AND DOSAGE FORMS**

ANALITYCAL SERVICES

All the main conventional analytical instruments are available in the Development Laboratories to support formulation and process development and optimization.

Full set of analytical techniques includes:

- UV-visible and fluorimetric spectrophotometry
- Gas Chromatography (Head space sampling)
- Liquid chromatography (HPLC and UHPLC - RP, SEC, HIC, HILIC, IEX)
- Dynamic light scattering
- Osmometry
- Instrumental densimetry
- Karl Fisher titration
- Conductivity measure
- Differential scanning calorimetry
- Total Organic Carbon determination
- Solid dosage form in vitro dissolution test (USP I and USP II)

They are applied in wide range Development activities:

- Characterization of intermediate and finished products
- Stability Studies
- Development/optimization of specific product analytical methods
- Transfer of Customer's analytical methods
- Support of method robustness and method validation
- Development of specific cleaning methods

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RELIBILITY, QUALITY, DEVELOPMENT