BSP PHARMACEUTICALS

ADCs

ADCs

ADCs from Conjugation to Fill-Finish

Injectable formulation: Liquid or Lyophilized vials

ANTIBODY DRUG CONJUGATES (ADCs)

BSP Pharmaceuticals is specialized to support the manufacturing of ADC products from the Conjugation to the Fill-Finish and offers a full and integrated package of services from development to clinical and commercial supply.

DEVELOPMENT Formulation, Process, Analytical methods

SCALE UP/DOWN Process Robustness and Characterization

QUALITY CONTROL Release, Stability, Process comparability testing

MANUFACTURING Clinical and Commercial Supply

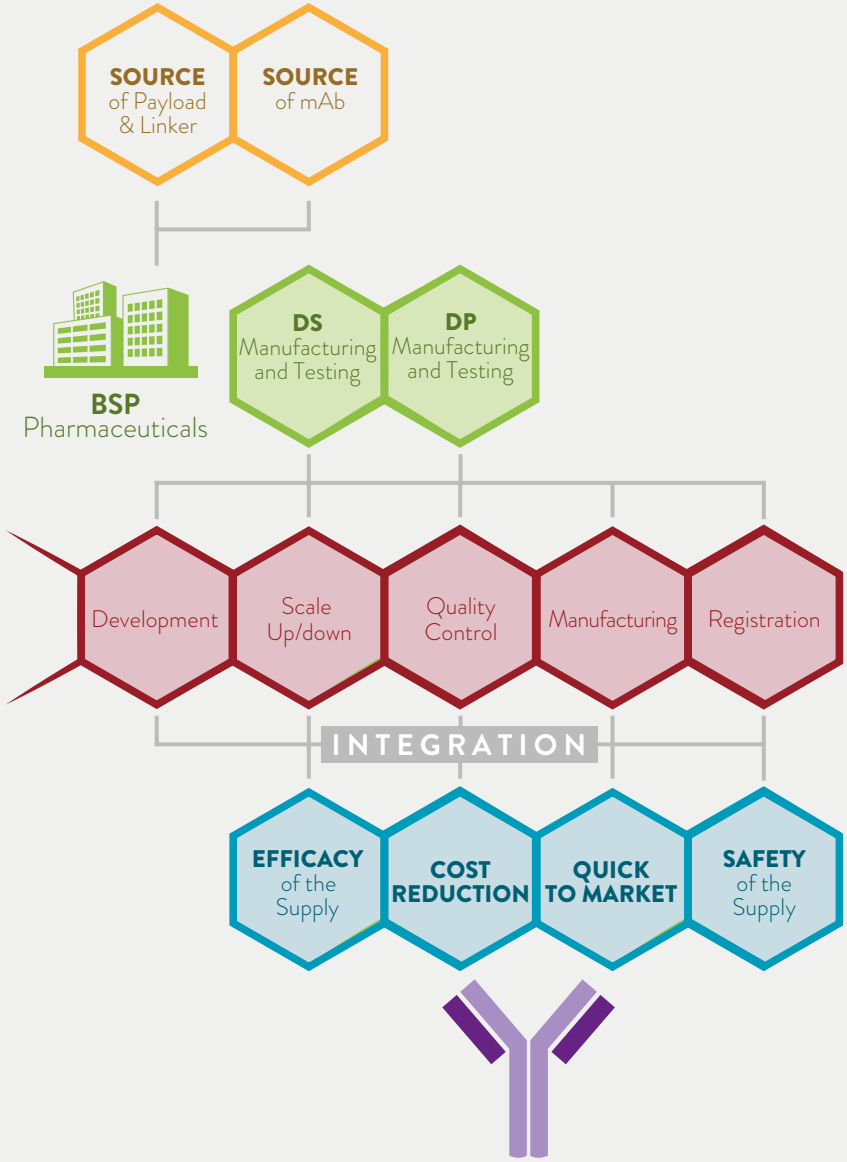
REGISTRATION Regulatory Support for DMF and CMC Preparation

Integration of services in the Supply Chain of ADCs allows the delivery on time of a successful product to the market.

THE INTEGRATED SERVICES FOR ADCs

DRUG SUBSTANCE AND DRUG PRODUCT AT ONE SITE

With the aim to facilitate the supply chain of ADCs,
BSP Pharmaceuticals developed, within the same Facility and under the same Quality system, capabilities to handle conjugation and fill/finish, from the early development up to the commercial scale.



EXPERIENCE BSP

DRUG SUBSTANCE AND DRUG PRODUCT AT ONE SITE

THE ADDED VALUE THAT BSP OFFERS IS TO MANAGE THE MOST CRITICAL PHASES OF SUPPLY CHAIN (DRUG SUBSTANCE AND DRUG PRODUCT MANUFACTURING AND TESTING), AT THE SAME SITE , THIS EXPERIENCE GENERATES SOME BENEFITS FROM INTEGRATION:

- Minimize **SHIPMENT** of materials under refrigerated condition

- **DELIVERY** mAb, toxin-linker at one site and receive the Drug Product packed and released

- **ONE** tech transfer, **ONE** site QUALIFICATION

- Drug Substance managed under the **SAME QUALITY SYSTEM** of Drug Product allow a fast release of the Product

- Drug Substance process optimization to **MINIMIZE ADDITIONAL** formulation **WORK** during the Drug Product manufacturing

- **BREAKTHROUGH DRUG DEVELOPMENT PROGRAM** for Drug Substance and Drug Product minimizing post-approval efforts

ADCs CAPABILITIES OVERVIEW

DRUG SUBSTANCE AND DRUG PRODUCT AT ONE SITE

Manufacturing lines, process flow as well as storage capabilities have been specially designed taking into consideration the critical process parameters and the risk factors associated with the handling and production of this class of compounds.

1 | DEVELOPMENT LABORATORY
3 | CONJUGATION SUITES
6 | STERILE SUITES with more than 1800 sqft fully dedicated to production anticancer and cytotoxic drugs

Dedicated Cold Storage Areas for BDS, monoclonal ANTIBODIES, TOXIN AND FINISHED PRODUCT (+2/+8°C; FROM -20°C UP TO -80°C)

Release and Stability Testing (including “Specific Cytotoxicity and Direct Binding)

ADCs DEVELOPMENT CAPABILITIES

DEDICATED LABORATORIES AND SKILLED SCIENTISTS to support formulation, process development and process optimization services

CONJUGATION BATCH SIZE
from 10mg to < 5g (Development scale)

DIAFILTRATION SYSTEM AND CHROMATOGRAPHY SYSTEMS

THERMAL PROFILE characterization, by DSC and cryomicroscope

LYO CYCLE development, optimization, robustness

2 FREEZE-DRYERS of 2.1 and 4.5 sqft installed under isolator

STRONG INTEGRATION between development and cGMP manufacturing

ANALYTICAL METHODS DEVELOPMENT AND OPTIMIZATION to support ADCs manufacturing during early stages

BSP
PHARMACEUTICALS

ADCS CONJUGATION CAPABILITIES

CLINICAL AND COMMERCIAL MANUFACTURING

CONJUGATION BATCH SIZE: from 5g to 5kg

MULTIPLE BUFFER VESSELS
up to 10.000 lt capacity

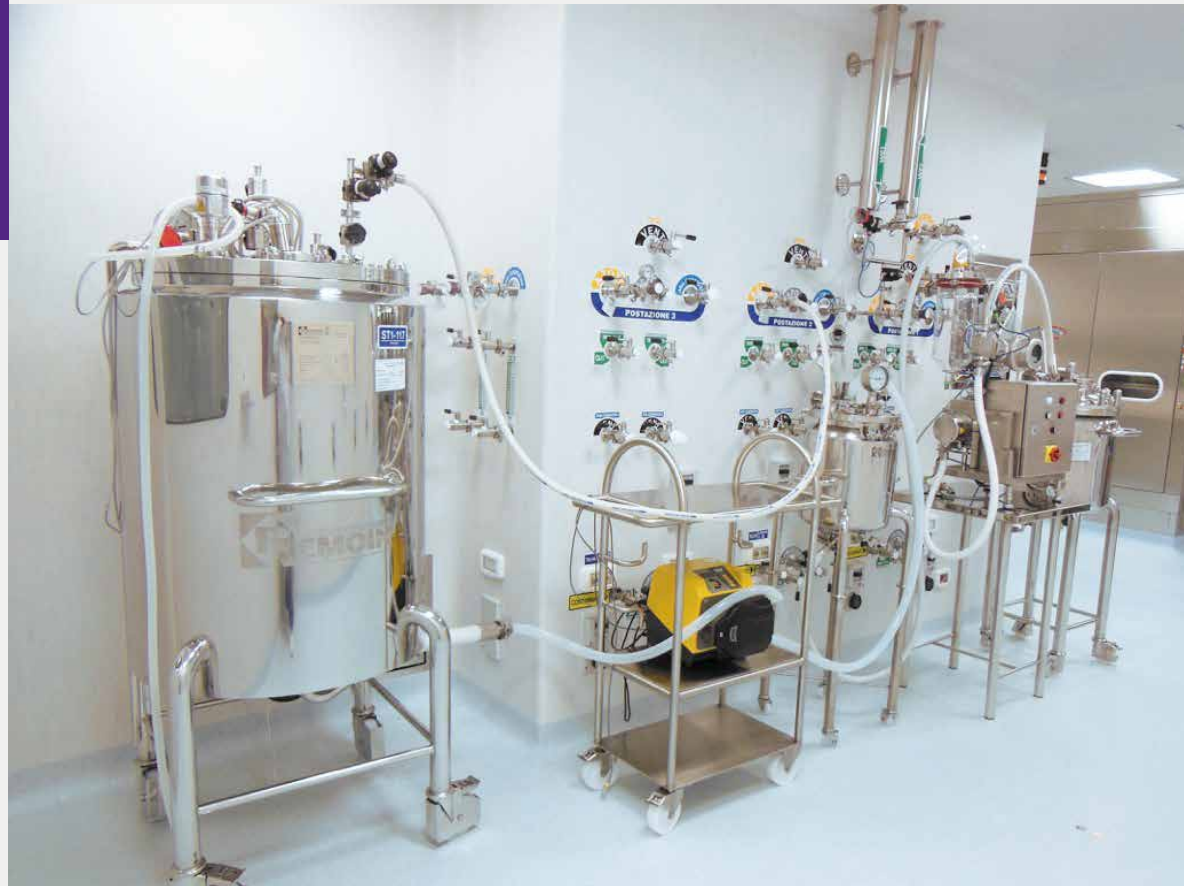
DIAFILTRATION and **CHROMATOGRAPHY SYSTEMS** suitable for development, clinical and commercial scales

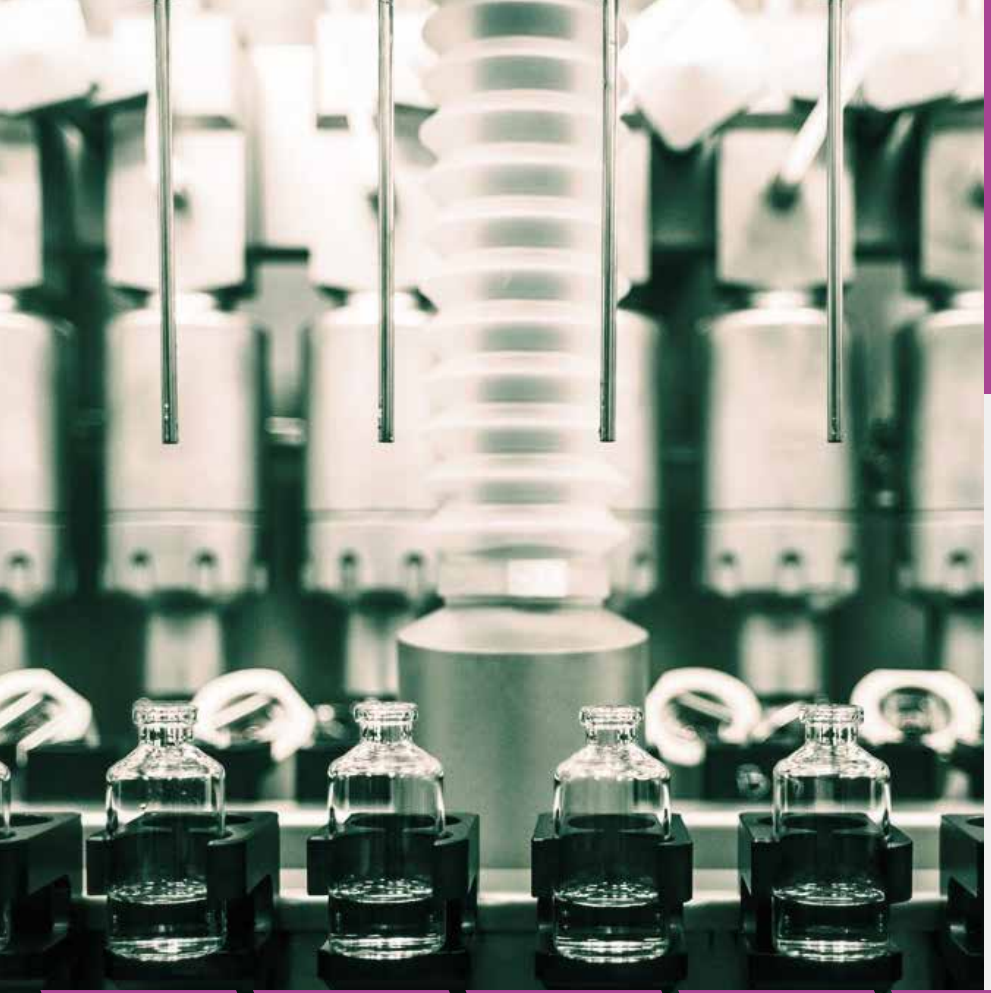
BOTTLING FILLING MACHINE equipped with a peristaltic dosing system to fill BDS in a wide range of primary packaging configurations

MANUFACTURING OPERATIONS
are performed in a "Class C" area

STORAGE @ 2-8°C, frozen conditions (up to -80°C)

DEVELOPMENT	SCALE UP	GMP MANUFACTURING
10mg-5g	1-25 g	25 g - 5 kg





ADCs FILL-FINISH CAPABILITIES

CLINICAL AND COMMERCIAL MANUFACTURING

SIX STERILE MANUFACTURING SUITES equipped to handle liquid and lyophilized vials

FILLING LINES designed to minimize shear stress: possibility to use rotary piston pumps and peristaltic dosing systems

HIGH SPEED FILLING LINE designed to manufacture products with short holding times

CRYOGENIC FREEZE DRYER

ISOLATOR AND CLOSED RABS to have the highest level of sterility assurance and containment

DEDICATED COLD STORAGE AREAS for BDS, mAb, toxin and finish product (+2/+8°C; from -20°C up to -80°C)

DEDICATED AREAS for manual/automatic Thawing activities

TEMPERATURE CONTROL during manufacturing

LOW LEVEL OF RESIDUAL PEROXIDES to prevent protein degradation

DEDICATED PRODUCT CONTACT PARTS (stainless steel, disposable systems) and **SPECIFIC CLEANING PROCEDURES** to avoid contamination/degradation

STERILE 2	STERILE 6	STERILE 1	STERILE 4	STERILE 5	STERILE 3
1x16 sqft	2x65 sqft	2x107 sqft	2x215 sqft	2x215 sqft	2x323 sqft
LYO SURFACE	LYO SURFACE	LYO SURFACE	LYO SURFACE	LYO SURFACE	LYO SURFACE

ANALYTICAL SERVICES

IN ADDITION TO CONVENTIONAL ANALYTICAL TESTING AND INSTRUMENT, ANALYTICAL CAPABILITIES HAVE BEEN DEVELOPED TO SUPPORT ADCS MANUFACTURING

- METHODS DEVELOPMENT & OPTIMIZATION
- METHODS VALIDATION & TRANSFER
- CLEANABILITY & COMPATIBILITY STUDIES
- FREEZE-THAW STUDIES
- STABILITY & PHOTOSTABILITY STUDIES

SUPPORT
FORMULATION/ PROCESS DEVELOPMENT

DEVELOP
OPTIMIZE
VALIDATE
AND TRANSFER
ANALYTICAL
METHODS

CHARACTERIZE
PRODUCT
STABILITY
PROFILE

PROCESS
COMPARABILITY
TESTING

ANALYTICAL CAPABILITIES

TO PROVIDE
THE FULL RELEASE
AND STABILITY TESTING

MOLECULAR WEIGHT OR SIZE:
SEC-HPLC, Bioanalyzer (under reducing and /or non-reducing conditions) and other appropriate techniques.

POTENCY ASSAYS:
Ligand binding, ELISA, Monoclonal antibody assays, Binding assays (microplate reader, CE and other appropriate techniques).

ISOFORM PATTERN:
by isoelectric focusing (iCE280) or other appropriate techniques.

EXTINCTION COEFFICIENT:
by UV/visible spectrophotometry.

ELECTROPHORETIC:
patterns data on identity, homogeneity and purity by polyacrylamide gel.

ELECTROPHORESIS:
(bioanalyzer), Imaged Capillary Isoelettric Focusing (iCIEF), Western-blot, capillary electrophoresis (CE system), SDS-PAGE, Isoelettric Focusing (IEF)

LIQUID CHROMATOGRAPHIC PATTERNS:
size exclusion chromatography, reverse-phase liquid chromatography, ion-exchange liquid chromatography, affinity chromatography.

SPECIFIC CYTOTOXICITY

mAb AND FREE TOXIN IDENTIFICATION:
by LC/MS/MS.

WHY BSP IS THE PARTNER

INTEGRATION IN THE SUPPLY CHAIN OF ADCs: FROM CONJUGATION TO FILL-FINISH, FROM DEVELOPMENT TO COMMERCIAL THROUGH CLINICAL TRIAL MANUFACTURING AT THE SAME SITE
MOST OF THE **PLAYERS** IN ADCS ARE OUR **PARTNER**

BSP PHARMACEUTICALS

HEADQUARTER AND MANUFACTURING PLANT

BSP PHARMACEUTICALS S.p.A.
Via Appia km 65,561
04013 Latina Scalo - Italy

Phone +39 0773 822 1
Mail info@bsppharmaceuticals.com

COMMERCIAL BRANCH

BSP USA Inc.
100, Overlook Center Suite 200
08540 Princeton, NJ - USA

Phone +1 609 375 2700
Mail info@bsppharmaceuticals.com

FOR TECHNICAL INQUIRIES AND TO REQUEST A QUOTATION

Mail business.development@bsppharmaceuticals.com

bsppharmaceuticals.com

6th WORLD adc AWARDS 2019
BEST CONTRACT MANUFACTURING (CMO) PROVIDER

5th WORLD adc AWARDS 2018
4th WORLD adc AWARDS 2017
3rd WORLD adc AWARDS 2016
WORLD adc AWARDS 2015

CMO
LEADERSHIP AWARDS 2019
CAPABILITIES, EXPERTISE, RELIBILITY, SERVICE
LEADERSHIP AWARDS 2018
CAPABILITIES, COMPATIBILITIES, EXPERTISE
RELIBILITY, QUALITY, DEVELOPMENT