News

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MOVING ALONG WITH ADCS: A CDMO PERSPECTIVE

Vitor Sousa, Senior Manager of R&D Biological Division at Cerbios, talks about the challenges that a CDMO has to solve while developing a robust and scalable process ready for cGMP production for clinical trials and later on for commercial supply.

"Antibody-drug conjugates (ADCs) for oncology therapies are composed of an antibody chemically conjugated to a highly potent cytotoxic drug through a specific linker molecule.

Currently, ADCs together with gene therapy CAR-Ts represent, in terms of the number of clinical trials, the fastest growing and most promising products in oncology. It is, therefore, not surprising that nearly 40% of antibody-based therapies for cancer therapy in late-stage development are ADCs or similar products. It is worth underlining the diversity of the payloads present in the ADCs in Phase III; two products have a previously approved toxin (MMAE) targeting microtubules, while the remaining have seven new payloads including PBD dimers, duocarmicins, topoisomerase I inhibitors and radionuclides.

The high number of ADCs in late development is followed by more than 100 candidates in Phase I/II and 400 products in discovery that will reach late stages within the next few years, including the arrival of a new type of conjugates with

antibody fragments and polymer conjugates with smaller dimensions and easier tumour penetration.

COMPANY PROFILE

Chimica Oggi - Chemistry Today customer's publication

Moving along with ADCs: a CDMO perspective

Vitor Sousa

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At Cerbios, we are observing progresses in this field, since more than 70% of the ADC development and manufacturing activities are outsourced to CDMOs. The manufacturing process of an ADC poses engineering challenges to CDMOs, which need to cope both with the typical HPAI containment issues, as well as with product protection, while maintaining flexibility to accommodate any process. Moreover, laboratories face the complexity of the analytical methods necessary for the full product characterization of an ADC. Cerbios can combine its long-term experience in HPAI development and manufacturing (including payloads for ADCs, vitamin D derivatives and other antitumor drugs up to SafeBridge category 4) with its knowledge with Biological and Biotechnology products, which both have essential tools for an ADC manufacturer. Additionally, Cerbios is providing together with its partners in the PROVEO, an alliance of an integrated solution covering the full supply chain for a ADCs with payload and mAb, conjugation and fill-finish.
Many monoclonal antibodies initially developed as stand-alone therapies in oncology are now also being evaluated in the conjugated version. In small biotech companies with early development pipelines, it is usually preferred to broaden the panel of candidates among a set of combinations of payloads, linkers and conjugation chemistries generating a panel of ADCs for Proof of Concept experiments. From a CDMO perspective, it is important to have a robust in-house platform to rapidly generate a set of ADCs that meet specific quality criteria and that may provide reliable results for appropriate lead candidate selection.

Regarding safety, during the manufacturing of cytotoxic payloads, protection and containment precautions are implemented in order to protect operators, whereas in the case of ADCs, both operator and product need to be protected. The increase in potency of the new payloads requires the further improvement of the containment measures in order to handle this class of products.
This needs to be accompanied by new analytical techniques with suitable detection limits to assure proper cleaning of both equipment and facilities. Multipurpose manufacturers, in order to overcome the need to develop such analytical techniques, tend to use product-dedicated or single-use equipment where possible. However, some steps, such as payload dissolution still need to be performed using glass equipment. This step usually employs pure solvents, such as DMA or DMSO that is subsequently added to the reaction vessel containing the protein. Therefore, solvent compatibility needs to be addressed appropriately by implementing compatible transfer tubing and avoiding contact between the pure solvent and the film polymer. During the subsequent process steps, where the solvent concentration may reach max 20%, single-use technology may be adequately implemented. In addition, the compatibility of the film and all the components with the payload needs to be evaluated with dedicated studies to detect eventual molecules that may leach or any unwanted adsorption of the payload to the container.
When selecting a CDMO partner for a complex molecule as an ADC and its payload, it is mandatory to take into consideration its flexibility, available know-how, familiarity with different conjugation processes and, very important, its analytical capabilities; scale of capacity remains a parameter to evaluate, but may not be the key factor.

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About Cerbios-Pharma SA

Cerbios is a private company with its headquarters in Lugano, Switzerland, specialized in developing and producing active pharmaceutical ingredients (APIs), both chemical and biological, for its clients around the world. Cerbios is a world leader for some generic products used primarily to treat respiratory, dermatological and oncological diseases.

Cerbios also offers its clients an exclusive service to develop and produce highly active pharmaceutical ingredients (HAPIs) and biological monoclonal antibody tablets, recombinant proteins, conjugated monoclonal antibodies (ADCs) and probiotics for pharmaceutical use.

Cerbios is capable of offering a complete service to develop and register pharmaceutical products, tablets supplied for clinical research phases, the necessary regulatory documentation and subsequent marketing supplies. Cerbios products are marketed around the entire world, primarily in the USA, Japan and Europe.

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