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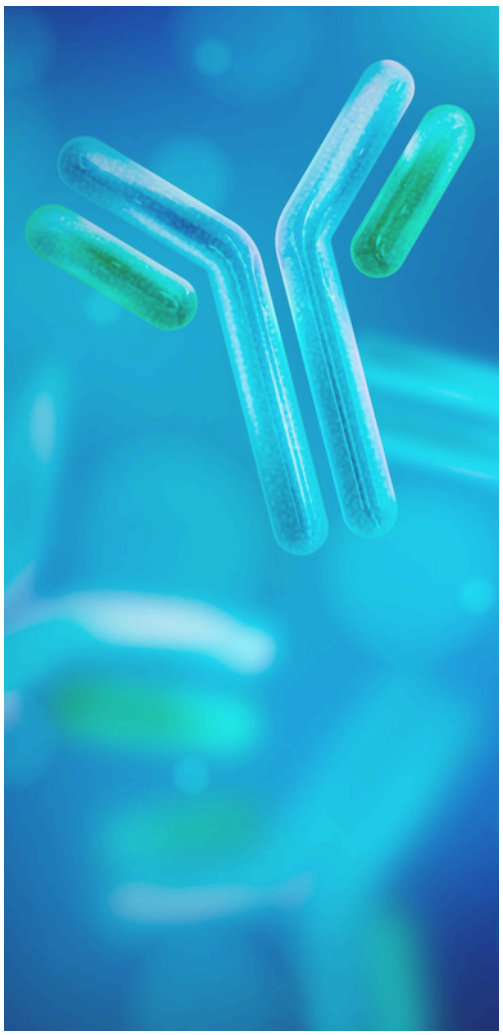
Bispecific Antibodies: Navigating From Design To Market Success



Each bispecific antibody design should be unique. The design of bispecific antibodies (BsAbs) should not be limited to only one format but rather should be determined based on their individual characteristics. Currently, there are over 100 different formats for BsAbs, aiming to address pairing errors and avoid patent infringement. In addition to these considerations, the design of BsAb formats requires a more comprehensive assessment. Factors influencing BsAb format design include half-life, mechanism of action (MoA), target characteristics, and considerations for issues arising during the manufacturing process such as yield, impurities, and conformational stability. A common challenge in BsAb development is low yield and poor stability.

Therefore, a holistic evaluation is necessary in the format screening process that strikes a balance between functionality and scalability. In the early stages of BsAb development, prioritizing format selection involves simultaneous consideration of expression levels, functionality, and preliminary expression profiles, along with aggregation tendencies. One of the most commonly asked questions is: "Which BsAb format is the best?" Unfortunately, there is no standardized answer. Each stage requires specific assessments to address the unique challenges associated with BsAb development, and there is no one-size-fits-all answer to determine the best format.

Stages of BsAb Development

The focus of BsAb development varies at different stages, with distinct evaluation criteria:

I. Format Screening: yield, BsAb integrity, monomer ratio, biological functionality, stability testing

II. Expressing Clone Screening: yield, integrity, monomer ratio

III. Upstream Development: productivity, quality

IV. Downstream Development: recovery rate, purity

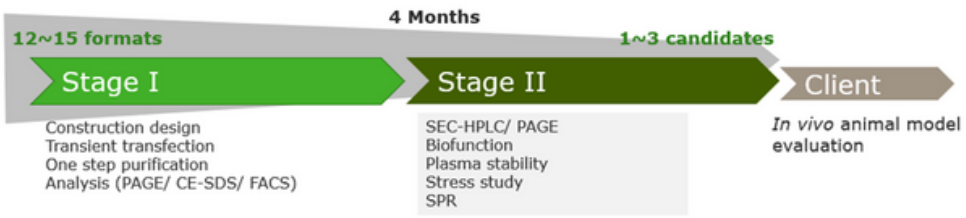


Figure 1. Early-stage format development is typically divided into two phases, with Stage I focusing on the integrity screening of formats and Stage II involving a comprehensive condition evaluation.

During Stage I, depending on the MoA requirements, multiple formats are initially designed for screening. Through a one-step purification process, results for yield, integrity analysis, and functional testing are obtained, allowing for the preliminary exclusion of formats unsuitable for further development. In Stage II, to obtain more precise comparative results, the correct format monomer is purified. Functional analysis and stability assessments are then conducted based on different MoA requirements.

Case study

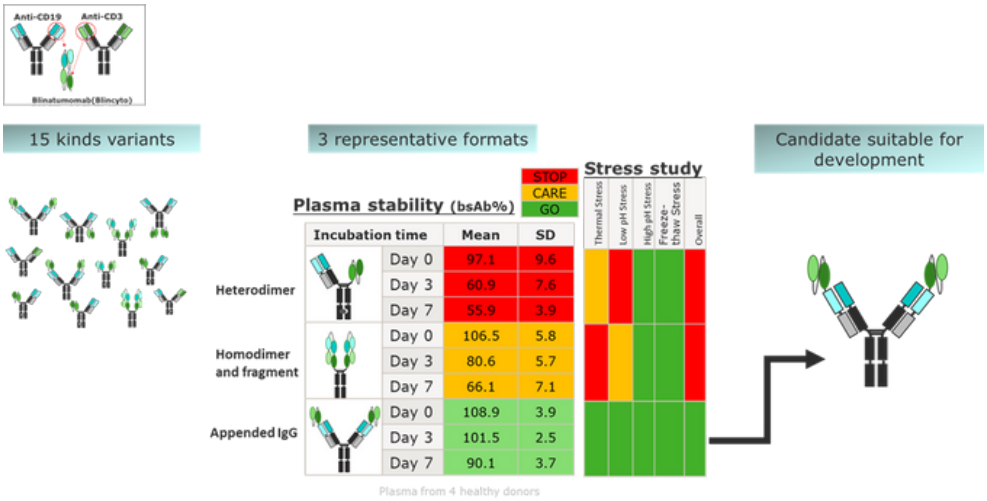


Figure 2. In the comprehensive evaluation of Stage II, BsAb formats with druggability potential can be screened and identified.

The Importance of Comprehensive Assessments

Conducting comprehensive assessments allows the exclusion of unsuitable formats during the initial stages of process development, while retaining those deemed suitable for in vivo safety and efficacy testing in animal models. This strategic screening identifies BsAb formats exhibiting promising druggability characteristics, paving the way for their further development. This early and thorough testing of diverse formats serves to significantly mitigate risks and reduce production costs in later stages. Neglecting this critical screening process may result in stability challenges during scale-up processes and potential clinical risks. Formats unsuitable for development may show limited progress in process improvement, and their safety concerns could pose a risk of clinical failure in the future. Therefore, the strategic and comprehensive assessment of different formats at the outset is imperative for successful applications in clinical and commercial stages.

About Mycenax

Mycenax is a dedicated CDMO specializing in process development and cGMP manufacturing of biologics and biosimilars. We provide integrated DNA-to-Drug Product services for mAbs, ADCs, plasmid DNA, cell therapies, vaccines, and more through advanced platforms and PIC/S GMP-compliant facilities. Our GMP site is approved by EMA, MHRA, PMDA, Health Canada and MFDS, and has successfully passed over 70 global client audits, ensuring the highest standards of quality and compliance.