THE IND ADVANTAGE:

why early derisking is a strategic imperative for complex biologics

As pipelines grow more ambitious, early identification and the mitigation of manufacturability, stability and immunogenicity risks have become the critical factors separating programmes that reach IND on time from those that don't

Biotherapeutic drug production is expensive, convoluted and resource-intensive. This challenge is becoming even more pronounced as biologics grow increasingly complex, with advanced formats adding additional layers of developability and manufacturing risk. The pressures are particularly acute during early development when timelines are tightly coupled to funding milestones, partnerships and valuation. Investor confidence is critical at this stage and programmes that demonstrate a clear path to Investigational New Drug (IND) submission stand out.

Early planning must anticipate later-stage hurdles that can derail progress. Issues affecting manufacturing feasibility, product stability, immunogenicity and immunosafety are common pitfalls. If addressed late, they can require cell line rework, process redevelopment or product reformulation, thereby introducing delays, regulatory complications (including clinical holds) and lost momentum. In many cases, these risks are not solely a function of the molecule itself, but of how early they are identified and addressed.

Thus, early derisking is no longer optional. This strategic imperative is driving a shift towards proactive risk mitigation, particularly among biotechs partnering with CDMOs. These collaborations rely on integrated approaches that bring together developability assessment, optimisation and manufacturing expertise within a single strategy.

Identifying the big risks early

For biologics, numerous make-or-break factors must be addressed upfront to define a molecule's developability. One of the most critical is manufacturability, which can be compromised by poor expression yields, assembly challenges and purification or scalability constraints.

Early derisking should also encompass stability and product quality. Formulation and stress testing can prevent aggregation, degradation and loss of potency, which can significantly impact timelines to IND and beyond. These considerations are especially important for advanced formats such as bispecifics, antibody-drug conjugates (ADCs) and fusion proteins, for which increased structural and functional complexity introduces additional risks. Immunogenicity is another key early-stage risk. Given its potential impacts on safety, efficacy and patient outcomes, it can be far more difficult to address once clinical material is established.

Key early derisking techniques

Enabling the rapid identification of sequence liabilities and predicting immunogenicity and post-translational risks, in silico assessments are important tools in early development. They can also support smarter construct design and early optimisation, including sequence or format adjustments to inform lead candidate selection before advancing to development.

Promoting well-characterised and scalable platforms, selecting the right expression system is also foundational. This supports alignment with critical quality attributes (CQAs) from the outset and reduces risk down the line. Combined with flexible construct design and ongoing optimisation, these strategies support an integrated phase-appropriate approach. An optimised construct links in silico insights, analytics, cell line development, formulation and process design, reinforcing end-to-end thinking rather than siloed decision-making.

Shifting from reactive to proactive strategic thinking

Addressing manufacturing challenges at later stages both hinders commercialisation and also delays the delivery of critical therapies to patients. Conversely, programmes that address these risks early are better positioned to move faster without compromising quality or reliability. By proactively engineering success through early derisking, developers can strengthen their credibility, create long-term value for investors and reduce costly disruptions. For today's increasingly complex biologics, early derisking represents one of the clearest paths to speed, confidence and sustainable success.

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