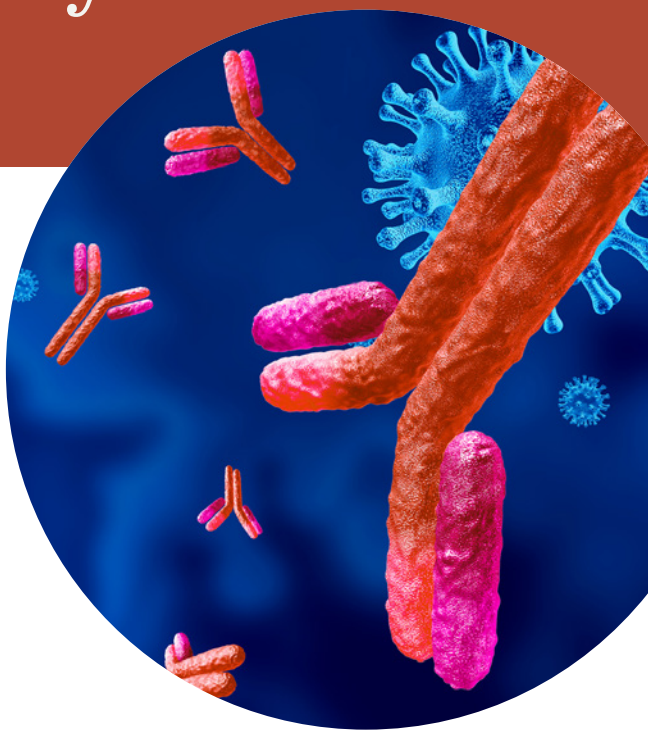
Optimizing Biologics Discovery

Overcoming Barriers to Biologics Innovation

Dotmatics

The Promise and Pressures of Biologics Discovery



Biologics have delivered breakthrough treatments for cancer and rare diseases and continue to gain ground in other wide-ranging areas, from neurological and metabolic disorders to respiratory and cardiovascular diseases.

They also offer favorable safety profiles, longer patents, and relatively low generic competition compared to small molecule drugs.

The statistics illustrate incredible momentum:

>20%

of new molecular entity approvals by the FDA are for biologics[1,2]

150+

monoclonal antibodies have been approved to date[3]

$100s

of millions in quarterly investment for biologics in R&D[4]

$700+

billion projected market value by 2030[5]

The potential of biologics is extraordinary. Unfortunately, so is the pressure to innovate despite notoriously high development costs, imminent patent cliffs, and growing pressure to lower drug costs to improve patient access to novel therapies.

Barriers to Innovation in Biologics

With pressures mounting, biologics innovators must work both smarter and faster, beginning in the earliest days of discovery. But, as discussed in the following pages, there are many barriers to innovation, including diversification, structural and process complexity, workflow intricacy, and disconnected systems.

1 Diversification

2 Structural and Process Complexity

3 Workflow Intricacy

4 Disconnected Systems

Diversification

Scientific advances have helped create a great level of diversity in biologics. While antibodies lead the market, numerous other modalities are gaining ground. Table 1 summarizes the current FDA classification of biologics and the regulatory body tasked with their evaluation.[6]

Therapeutic Biological Products: Types and Approval Body*

Center for Drug Evaluation & Research (CDER)

- Monoclonal antibodies
- Proteins
  - Cytokines (e.g., interferons)
  - Enzymes (e.g.,thrombolytics)
  - Novel plant, animal or microorganism, recombinant proteins**
- Immunomodulators***
  - Growth factors
  - Cytokines

*Combination and conjugate products assigned for review based on their primary mode of action.

**Excludes vaccines and blood products (which are regulated by the CBER).

***Non-vaccine and non-allergenic products intended to treat disease by inhibiting or modifying a pre-existing immune response.

Center for Biologics Evaluation & Research (CBER)

- Cellular products
  - human, bacterial or animal cells (e.g., pancreatic islet cells for transplantation
  - cellular components (e.g., as whole cells, cell fragments, or other components)
- Gene therapy products (nucleic acids, viruses, or genetically engineered microorganisms.)
- Vaccines
- Allergenic extracts
- Antitoxins, antivenins, and venoms
- Blood, blood components, plasma derived products

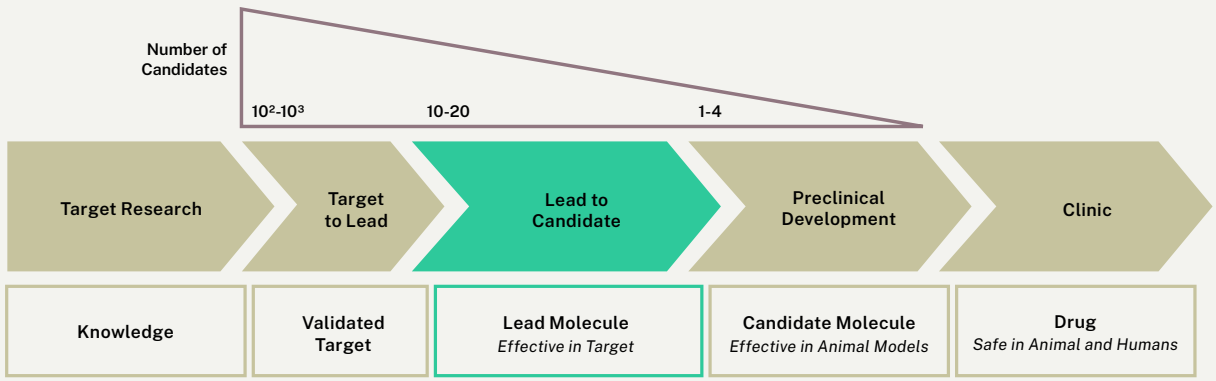
While this diversification has led to incredible discoveries and treatments, it's also made researchers' lives more complicated. Diversification in modalities also means diversification in processes, data types, and even regulatory pathways. The challenging pursuit of using living materials for therapeutic purposes is made even harder by the need to explore multiple modalities.

It is crucial to be able to accurately and efficiently characterize biologics to ensure no unwanted variations have been introduced. As R&D teams expand the reach of their biology-based therapeutics programs, they need to find an enterprise-grade software platform that can grow with them and keep up, in terms of both managing data and supporting automated processing and result generation to support the varying workflows used to pursue different modalities.

Structural and Process Complexity

Biologics are much more complex than small molecule drugs and regulations and processes are correspondingly more complex too. Biologics can contain unique combinations of smaller structures, may be conjugated with chemical drugs, and product quality is often greatly impacted by manufacturing process.[7]

Figure 1: Steps in Large Molecule Early Development



Characterizing biologics is inherently difficult. While researchers may use a variety of methods to get as much insight as possible, full characterization is often impossible.[7] Consider antibody-drug conjugates, for example. Researchers often rely on a variety of state-of-the-art protein analytical tools to analyze data coming from techniques like two-dimensional high-performance liquid chromatography, capillary electrophoresis, and high-resolution mass spectrometry.[8-10] The marrying of biology and chemistry results in a wealth of disparate, non-standardized data that must be analyzed in a flexible, scalable, and combinatorial way. Creating a unified technology platform to support this level of cross-domain research can be incredibly problematic.

Another challenge with biologics is they are often profoundly affected by the processes used to produce them. Biologics development and manufacturing are governed very strictly by regulatory bodies and there is considerable variation around the world. In the USA, this is the purview of CBER, and in the EU the EMA has oversight.[11] In the case of the EMA, they have had regulations for biosimilars since 2004.[12] This oversight aims to reduce the risk of process-related structural alterations, which could impact efficacy or safety while remaining undetectable via routine characterization techniques.[7] The processes involved in creating biologics vary according to molecule type and cellular or expression processes. Workflows frequently require cross-functional collaboration and generate vast amounts of complex, disparate data. This makes process standardization and control incredibly challenging. Teams will need a flexible R&D platform that can accommodate their unique workflows and datasets.

Workflow Intricacy

What's more important—speed or accuracy?

It is an impossible choice, yet one that biologics discovery teams are often forced to make as their workflows become increasingly complex, with many different processes and data types.

For example, antibody researchers are:

- Using machine learning and combined in vitro and in vivo data for antibody design programs.[13, 14]
- Merging and analyzing data from multiple display techniques to develop libraries.[15]
- Applying data from scientific and patent literature to improve rational antibody design.[16]
- Creating complex methods to prove the similarity of biosimilar candidates to their references.[17]

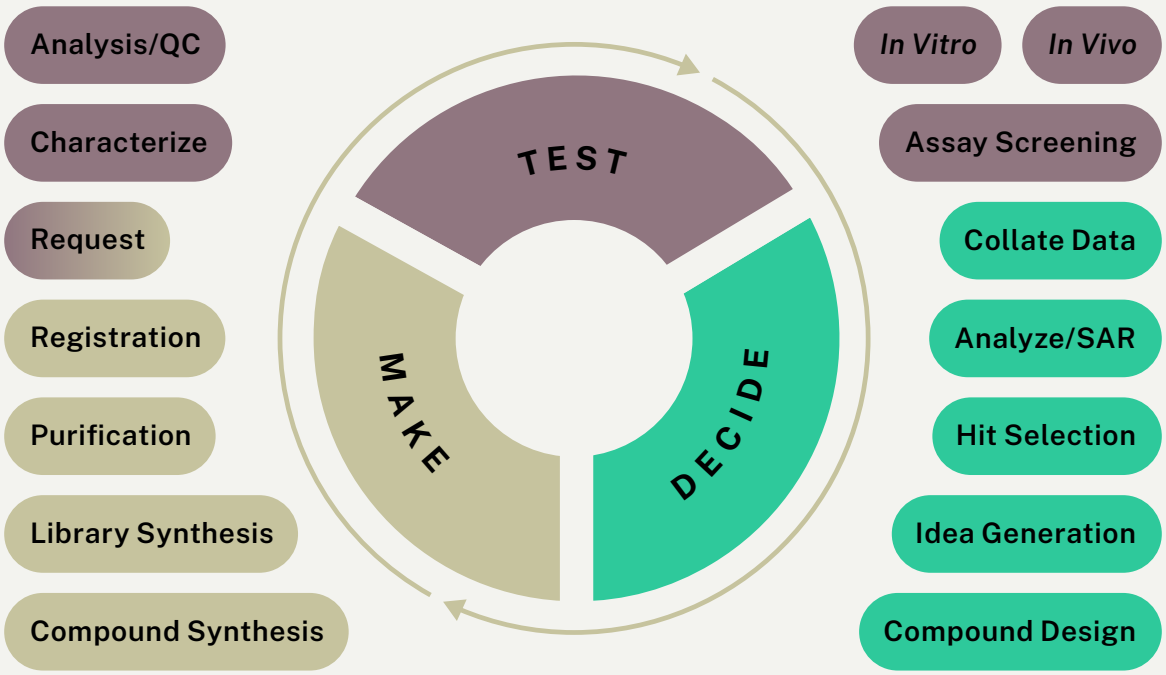
Collaborating across domains to develop higher complexity therapeutics like antibody-drug conjugates, multispecific antibodies, fusion proteins, etc.

While these approaches can help bring about the next great breakthrough, they often result in disjointed workflows. Such workflows typically rely on manual handling of data as they are passed from one step to the next, which wastes time and risks introducing errors. The situation is often further complicated because the software used in different parts of the workflow steps typically lacks the capacity to analyze all research data, making it nearly impossible for researchers to truly understand the depth of their data and use it to inform decisions.

Unfortunately, teams looking to streamline their complex workflows often remain disappointed even after investing time and money into point products promising to deliver speed and accuracy. Why? Because point products are most often quick fixes, not long-term enterprise solutions. They may help a few users or groups with specific tasks, but they generally don't help at a larger scale when researchers need to work together and share data to move projects forward. And while cobbling together point products can create the illusion of a customized solution, the truth will quickly be revealed as valuable time is lost manually moving data between point solutions, or worse, scientific meaning is corrupted when a data transfer does not map data between systems correctly.

To innovate in today's high-pressure market, biologics discovery teams need an enterprise-wide solution that supports all steps of the make-test-decide innovation cycle, as illustrated in Figure 1. With an enterprise solution, all of the data generated is fed into a central repository and followed through various iterations of analyses by cross-disciplinary team members, with subtle differences in the dataset highlighted along the way.

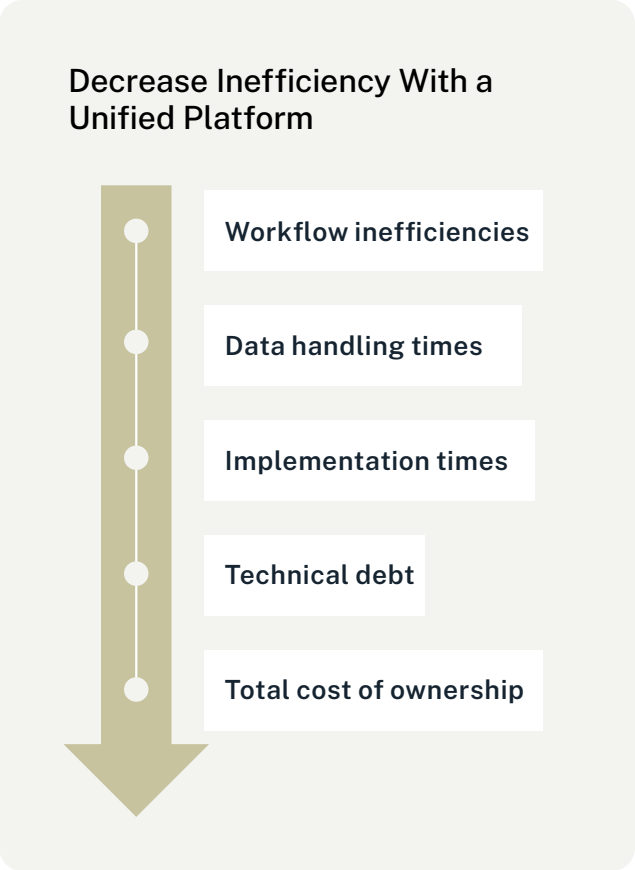
Figure 1: Intricate Workflows Require an United Enterprise-Wide Solution



Disconnected Systems

For far too long building an R&D infrastructure has meant cobbling together rigid, single-purpose lab systems, legacy software, and users' preferred research tools. Everyone suffers with this approach, from IT staff implementing and supporting the solutions, to the scientists using them, to the budget managers paying for them.

Disconnected systems put IT managers under constant pressure to keep pace. They face one lengthy and costly integration project after another, and they are often left with results that are cumbersome and inflexible. Perhaps more importantly, an absence of genuine connectivity between lab solutions and a lack of truly unimpeded data flow across the research workflow impacts not just efficiency, but also insight—something that can make or break collaborative, data-driven research labs.



Teams can break the status quo by investing in a united solution that will reduce workflow inefficiencies, implementation costs, technical debt, and total cost of ownership. By uniting all data and tools on one platform, everyone benefits.

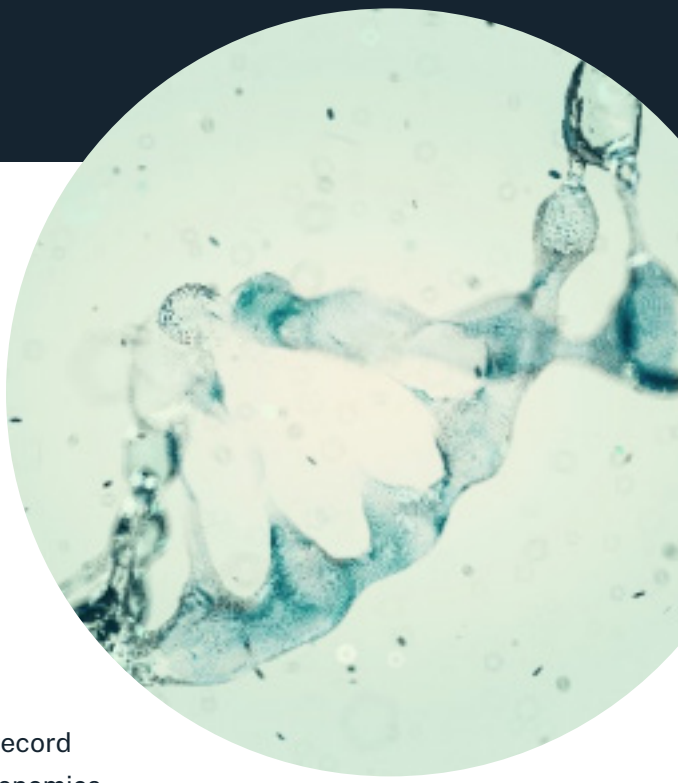
For example:

- Researchers can quickly capture, find, share, and use data without the need to switch between applications and transfer data because everything is tied back to one platform.
- IT managers can reduce the time and cost of implementing and supporting disconnected solutions and reduce technical debt by working with a single vendor whose solution spans the entire research workflow.

Solution

Dotmatics Biologics Discovery Solution

Overcome barriers to innovation with the Dotmatics Biologics Discovery Solution.



What Makes Leading Biologics Innovators Choose Dotmatics?

End-to-End Workflow Support

A single R&D platform to support both the biology and chemistry efforts needed to pursue the development of different modalities, including antibodies, CAR-T, and RNA therapies.

Accelerated Research

Specialized bioinformatics, proteomics, and molecular biology applications paired with guided templates that help researchers record novel exploration and standardize experiments in areas such as genomics, peptide and protein chemistry, and tissue and animal phenotyping.

Easier Collaboration

A united platform for internal teams and external CROs to securely share data, make requests, and manage workload in areas such as vector design, animal immunization, sequencing and cloning, protein expression, characterization and purification, microscopy, and flow cytometry. Dashboards to monitor mass spectrometry data across the globe.

Real-Time Decision Support

Automated data capture and unrivaled data storage, analysis, relationship tracking (e.g., parent-child, concept-batch) and reporting capabilities to help teams quickly access and use their diverse data, including samples, assay data (biophysical, DMPK, kinetic, single-point), SAR results, variants and mutation results, flow cytometry data, SPR, animal measurements, clinical measurements, etc.

Lower Technical Debt

Scalable platform featuring best-of-breed software connectivity, instrument-integration capabilities, and flexible configuration options that let companies replace obsolete software, fill capability gaps, reduce total cost of ownership, and avoid the expense of working with multiple vendors whose products don't easily integrate or scale.

Dotmatics supports multi-modal biologics discovery by providing capabilities that help teams progress research, capture data across disciplines, and inform critical decisions, including:

Electronic Laboratory Notebook

Capture, store and search experiments.

Scientific Search

Search and report across research databases.

Visualization & Analytics

Analyze, graph and present your scientific work.

Assay Development

Develop new assays for screening experiments with GraphPad Prism.

Assay Data Management

Capture and analyze all types of screening experiments.

Experiment Planning

Simulate modern molecular biology experiments and procedures with SnapGene.

Entity Registration

Register sequence-based, chemically-modified and structureless biological entities.

Bioinformatics

Comprehensive nucleic acid and protein sequence design and analysis with Geneious Prime.

Antibody Sequence Analysis

Advanced analytics and intuitive visualizations for a wide range of antibody-like molecules with Geneious Biologics.

Biomolecule Analysis

Identify and report sequences and variations using data from liquid mass spectrometry, liquid chromatography, and capillary electrophoresis.

Sample Management

Search sample and materials inventory that tracks relevant data across locations throughout the R&D process.

Requesting & Tracking

Manage the requesting and assignment of laboratory tasks and track progression of samples.

Dotmatics Biological Solutions at Work

CANCER RESEARCH INSTITUTE.

Uniting Data and Teams at the Cancer Research Institute

The Cancer Research UK - Cancer Therapeutics Unit is the largest academic cancer drug discovery and development group worldwide. Its research teams cover every aspect of new drug discovery and development, from cell and molecular biology through to chemical synthesis of new agents and their evaluation in clinical trials.

> “Having the Dotmatics Platform not only enables us to work closely with collaborators, it means that there is one single repository for all data, regardless of where it’s generated. You really can’t underestimate the impact of being able to freely access data, analyze it, see the correlations, and then being able to use it.”

JULIAN BRAGG

Director Chemistry,
Cancer Research Institute

Dotmatics Biological Solutions at Work

Enhancing Science and Discovery at M6P Therapeutics

M6P Therapeutics develops recombinant enzyme and gene therapies for lysosomal storage disorders by regulating mannose 6-phosphate levels.

> "The Dotmatics group invested in our patient-first company vision immediately and we understood that our collaboration would immediately yield better science and discovery."

MICHAEL DIGRUCCIO

Scientist,
M6P Therapeutics

Make Your Biologics Work Flow

Request a demonstration today to explore how Dotmatics can help your biologics discovery teams find better candidates, faster.

Request a Demo

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