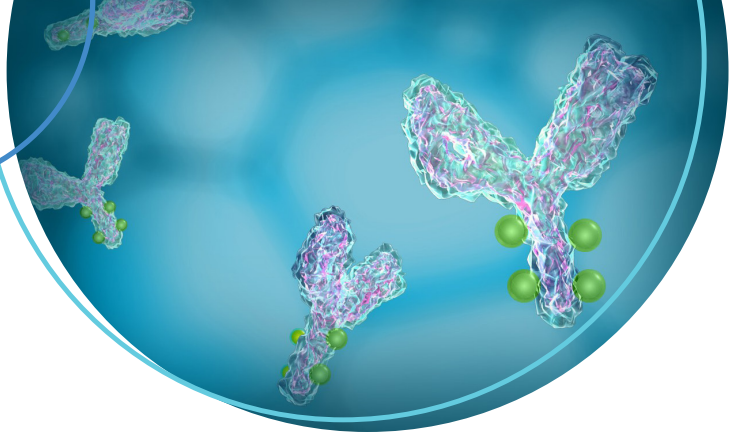
LABCORP BIOPHARMA LABORATORY SERVICES

Antibody-drug conjugate (ADC) capabilities

labcorp



Delivering global ADC development solutions

Antibody-drug conjugates (ADCs) continue to be a widely used and key modality of interest for the pharmaceutical industry due to their ability to deliver targeted cytotoxic payloads to solid tumors and blood-based malignancies that induce cell apoptosis for oncology patients.

While payload types continue to evolve beyond tubulin inhibitors and DNA-damaging agents, ADCs remain challenging given their highly complex and nuanced chemistry. For an ADC to be successful, the right combination of target-antigen, active linker payload, appropriate drug-to-antibody ratio (DAR), proper tumor indication, and payload conjugation site need to be considered.

Given this complexity, ADC drug developers face specific challenges in bringing their treatment candidates through the drug development continuum, including:

Toxicity

Elevated risk with high DARs and differing payload conjugation configurations

Immunogenicity

ADC mAb, linker, and payloads can have different impacts on the immune system response

PK/PD

More complex and frequent assessments given mAb, linker, and payload MOAs

Payload potency and efficacy

Tumor cell apoptosis and continued efficacy over time

Off-target effects

Unintended negative impacts beyond the tumor

ADC characterization and stability

Demonstrating DAR assessments and manufacturing process stability

Biomarker and companion diagnostic (CDx) development

Patient stratification and treatment for clinical trials as well as Day-1 post-approval readiness

How Labcorp Biopharma Laboratory Services can help

Labcorp Biopharma Laboratory Services is a highly experienced, comprehensive, and global ADC development partner with laboratory capabilities spanning early development through commercialization as well as expertise in oncology biomarkers and CDx co-development capabilities.

Supported 13 of the 15 **(87%) approved ADCs** currently on the market

Is supporting 16 of the 21 **(76%) mid to late clinical trial ADCs** currently in development

Has experience **with multiple generations of payloads**, including DNA-damaging agents, tubulin binders, and topoisomerase 1 inhibitors, as well as newer payload MOAs

Our specific ADC drug development and biomarker/CDx capabilities

Discovery

- Exploratory/nonregulated ADC DMPK, safety, *in vitro* assessments
- *In vivo* pharmacology, imaging, and focal radiation capabilities
- Human and syngeneic tumor models available

Antibody Reagents and Vaccines

- ADA positive control antibodies for ADCs for ADA/PK assays
- Antibody reagents for ADCs

Bioanalytical Services

- GLP/GCP nonclinical and clinical ADC PK/PD via LBA/LC-MS
- Quantity of free toxin, total antibody (+DAR 0), and drug-conjugated antibody (DAR > 0)
- Immunogenicity via ADA/nAb assessments

Companion Diagnostics (CDx) Development

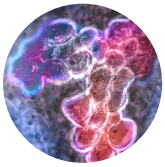
- CDx strategy consultation development, including design control, assay development, analytical and clinical validation, and commercialization services*

Toxicology/Immunotoxicology/Immunogenicity

- Nonclinical biodistribution and toxicokinetic ADC impact on relevant animal models (primate homologue, rodents for novel linkers and toxins) and human tissues
- Tumor samples to assess drug candidate targeting impact effectiveness
- Nonregulated bioanalytical ADC assessment of mAbs, linker, and payloads

Central Laboratory Services

- Safety testing
- Tumor assessment (immunohistochemistry)
- ADC receptor occupancy (flow cytometry)
- Novel methods to monitor internalization/ payload release
- Biomarker strategies and CDx support within clinical trial environment
- Immunotherapy (IO) and gene expressions/ mutations



Chemistry, Manufacturing and Controls

- ADC characterization
- Integrity of mAb and payload conjugation/ location
- Bespoke methods for ADCs
- ADC QC release**

*IVD being used for patient management, invasive sampling beyond standard of care, and/or high risk to patients
**QC release services available for U.S. and U.K. locations only; neat toxin reference standard lab safety limitations – requires discussion

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Need assistance advancing your ADC drug development program?

Labcorp Biopharma Laboratory Services can help. Please visit our website to submit a contact request or contact your local sales associate for further information.

Visit us at
oncology.labcorp.com/biopharma-partners#tech

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