

**Short Course: Antibody-Drug Conjugates, Oligonucleotides,
Peptides, and Other Complex Drug Modalities Characterization
and Quantification by Mass Spectrometry**

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**73rd ASMS Conference on Mass Spectrometry and
Allied Topics, Baltimore, MD**

Topics Covered in this Short course

- Complex pathway of pharmaceutical R&D
- Bioanalysis of Peptides
- Bioanalysis of Oligonucleotides
- Bioanalysis of ADCs
- Bioanalysis of therapeutic proteins and biomarkers
- Integrating qualitative (Qual) and quantitative (Quant) Bioanalysis
- HRMS and QQQ applications to quantitative and qualitative workflows
- Various HRMS scan types available for Qual/Quant: TOF-MS, TOF-MS with IDA, SWATH (DIA) and MRM^{HR}
- Application of Qual/Quant for ADC bioanalysis
- DMPK studies for small molecules vs complex drug modalities
- Relevant regulatory guidance for complex drug modalities
- Metabolites in safety testing (MIST)
- Radiolabeled studies
- New technologies to improve sensitivity, speed and coverage for complex drug modalities

Key Developments in the Complex Drug Modalities

Year	Biopharmaceutical Category	Drug Trade Name® (systematic Name)	Indication at Approval	Major R&D Contributions
1982	Recombinant Human Insulin	Humulin®	Diabetes	Eli Lilly
1986	Monoclonal Antibodies (mAbs)	Orthoclone®	Kidney transplant rejections	Ortho
2000	Antibody Drug Conjugates (ADCs)	Mylortarg® (Gemtuzumab Ozogamicin)	Acute Myeloid Leukemia (AML)	Pfizer/Wyeth
2011	Immune Checkpoint Inhibitors	Yervoy® (Ipilimumab)	Melanoma	Bristol-Myers Squibb
2014	mAbs	Keytruda® (Pembrolizumab)	Non-small cell lung cancer (NSCLC)	Merck
2016	Antibacterial mAbs	Anthim® (Oblitoxaximab)	Bacillus Anthracis (anthrax)	Elusys Therapeutics
2016	Antibacterial mAbs	Zinplava® (Bezotoxumab)	Clostridium difficile (life-threatening diarrhea)	Merck
2017	CAR-T Cell Therapies	Kymirah® (Tisagenlecleucel)	Acute Lymphoblastic leukemia (ALL)	Novartis
2017	The first in vivo Gene Therapy	Luxturna® (Voretigene Neparovec-Rzyl)	Vision Loss	Spark
2018	Small Interfering RNA (siRNA)	Onpatro® (Patisiran)	Peripheral Nerve Disease (Polyneuropathy)	Alnylam
2018	Peptide-Drug-Conjugates (PDCs)	Lutathera® (Lutetium Lu 177 Dotatate)	Pancreas or Gastrointestinal Cancer	Novartis
2021	mRNA Vaccines	Comirnaty®	Prevention of COVID-19	Pfizer/BioNTech
2023	CRISPR-Based Therapies	Casgevy®	Sickle Cell Disease	Vertex
2023	CRISPR-Based Therapies	*Lyfgenia®	Sickle Cell Disease	Bluebird Bio

CAR-T = chimeric antigen receptors or chimeric T cell receptors; CRISPR=clustered regularly interspaced short palindromic repeats, a family of DNA sequences found in the genomes of prokaryotic organisms such as bacteria and archaea. *: Black box warning for possibly developing blood cancer

Complex Modalities Result in Complex Drug Discovery and Development

