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

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## **Topics Covered in this Short course**

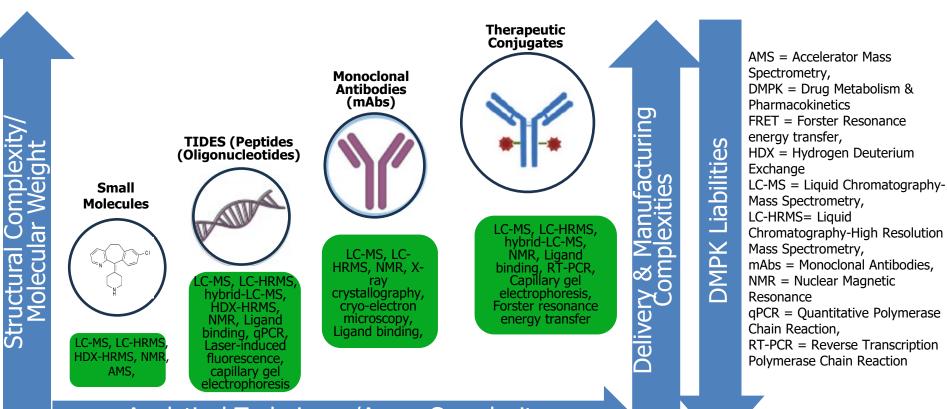
- Complex pathway of pharmaceutical R&D
- Bioanalysis of Peptides
- Bioanalysis of Oligonucleotides
- Bioanalysis of ADCs
- Bioanalysis of therapeutic proteins and biomarkers
- Integrating qualitative (Qual) and quantitative (Quant) Bioanalysis
- HRMS and QQQ applications to quantitative and qualitative workflows
- Various HRMS scan types available for Qual/Quant: TOF-MS, TOF-MS with IDA, SWATH (DIA) and MRM<sup>HR</sup>
- 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®<br>(systematic Name)      | Indication at Approval                          | Major R&D<br>Contributions |
|------|---------------------------------|--|---|----------------------------|
| 1982 | Recombinant Human Insulin       | Humulin®                                   | Diabetes  | Eli Lilly                  |
| 1986 | Monoclonal Antibodies (mAbs)    | Orthoclone®                                | Kidney transplant rejections                    | Ortho                      |
| 2000 | Antibody Drug Conjugates (ADCs) | Mylortarg®<br>(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)                    | Clostridum 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 Neparvovec-<br>Rzyl) | Vision Loss                                     | Spark                      |
| 2018 | Small Interfering RNA (siRNA)   | Onpattro® (Patisiran)                      | Peripheral Nerve Disease (Polyneuropathy)       | Alnylam                    |
| 2018 | Peptide-Drug-Conjugates (PDCs)  | Lutathera® (Lutetium Lu 177<br>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**



Analytical Techniques/Assay Complexity