

# Translational Science in 2017

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**A**cross the globe, this year's discussions in translational science and medicine focused mainly on oligonucleotides-based therapeutics (including the implications of CRISPR), personalized medicine, and clinical trials.

## **Oligonucleotides-Based Therapeutics**

Oligo-based therapies (such as small interfering RNAs (siRNAs), antisense oligonucleotides (ASOs), microRNAs, aptamers, CRISPR, and others) offer a broad spectrum of treatments for a wide range of disease states. The range of synthetic nucleic acid drugs in development and the number of companies manufacturing them has increased steadily over the past two years. In the US, for example, nucleic acid therapeutic programs have risen from 119 in 2015 to 164 in 2017, and a **total of six** oligo-based therapeutics were ready to file for FDA approval by the end of 2017.

As these therapeutics approach clinical productivity, experts are discussing best practices and CMC challenges alongside **potential applications in rare diseases, immuno-oncology, and personalized medicine**. In particular, these therapies are beginning to make their way into targeted oncology therapies that currently make up more than a third of the oncology drugs used in the US and nearly a quarter of drugs used in Europe and Japan.

Widely-discussed **scientific and regulatory topics** related to oligo-based therapeutics in 2017 included the following:

- Use of biomarkers to interpret pharmacokinetic and pharmacodynamic parameters and dose-response relationships.
- Safety or efficacy of current oligonucleotide therapies that modulate innate immunity to treat cancers.
- Best practices to address CMC challenges in preclinical and clinical development of increasingly complex therapies.
- The approach of regulatory bodies to differentiate and approve therapies that serve a wide range of functions, such as mRNA-based therapies.
- Defining and evaluating clinically meaningful endpoints in trials.
- Potential application of **CRISPR-Cas9 technology** to treat genetic and other diseases.

For an overview of translational science and medicine articles published by DIA, listen to these podcasts featuring **Dr. Gary Kelloff** and **Dr. David Parkinson**.

## **Personalized Medicine**

Techniques like **oligo-based therapies** have brought us closer to personalized medicine initiatives as they facilitate rapid *in silico*, patient-specific drug design. Furthermore, the US made significant advancements earlier this year, when the US FDA **approved Keytruda**, an immunotherapy drug for treating tumors, and CART-T, the **first gene therapy** for cancer, made by Novartis.



## Clinical Trials

Much of the discussion on clinical trials in 2017 focused on transparency of clinical research outcomes as well as operational and safety issues and the use of artificial intelligence (AI).

### **Clinical Trial Disclosure (CTD)**

- **Clinical trial information transparency** took an important turn in 2017 and confronted clinical trial researchers and sponsors with a series of new registration requirements. The US, Canada, and Europe issued four Clinical Trial Registration and Transparency guidelines that can be viewed in this [infographic](#).
- DIA has provided a [resource packet](#) to help healthcare professionals prepare for the new guidelines.

### **Improving Clinical Trial Operations and Research**

- The FDA, National Institutes of Health (NIH), and TransCelerate BioPharma collaborated on a [Common Protocol Template \(CPT\)](#) to harmonize clinical trial protocols, expedite reviews, and accelerate the delivery of medicines to patients. [The recently launched template](#) aligns research objectives and trial endpoints with accepted data standards. An enhanced, technology-enabled CPT is available [here](#).
- **Organs-on-chips, or “tissue-chips”** have reduced the cost and duration of traditional drug discovery approaches and are being used to model disease and test drug efficacy and safety prior to clinical trials.
- The NIH NCATS Tissue Chip for Drug Screening program has recently announced [13 awards](#) totaling \$15 million to develop 3-D tissue chip research platforms.
- The use of [technology in clinical trials](#), from [wearables to artificial intelligence](#), has been pivotal in addressing the increased push for precision medicine while simultaneously cutting costs and valuable research time.

### **Improving Clinical Trial Safety**

- The EMA [revised its First-In-Human \(FIH\) policy guidelines](#) on the heels of a fatal accident that occurred during a French phase I trial in January 2016. The revised guideline specifically provides criteria for calculating starting doses, dose escalations, maximum dose, and when to terminate a study. The new guideline goes into effect January 2, 2018.
- DIA started a FIH working group at the 2017 *DIA EuroMeeting* to discuss the clinical and nonclinical aspects on first-in-human studies and the current challenges for conducting these studies.



## WHAT LIES AHEAD?

“With the advancement of new technologies like gene therapy, there will be a growing emphasis on moving potential gene therapy treatments from the research bench to patients more quickly.”

**Jeffrey Sherman, MD**

*Chief Medical Officer & EVP  
Horizon Pharma, Inc.*

[BACK TO ISSUE](#)