Agenda

• A new digital world
• Why now for Pharma
• Healthcare is changing
• Clinical Development is Changing
• Regulatory Viewpoints
• A thought on a New Drug Development Paradigm
• Advanced Analytics
Healthcare is in the Midst of a Digital Revolution

Industries disrupted by Digital:
- Camera (Kodak)
- Movie/Videos (Blockbuster)
- Communications (US Mail)
- Music (Virgin Records)
- Books
- Retail
- Banking
- Investment
- Advertising
- Libraries
- Taxi
- Automotive
- Television
- Hotel

"If you went to bed last night as an industrial company, you’re going to wake up this morning as a software and analytics company."

Jeff Immelt
Chairman and CEO, GE

How has digital changed your daily life?
Why Now .... Population Dynamics

According to the United Nations, the world's population is expected to increase by one billion people by 2025. Of that billion, 300 million will be people aged 65 or older, as life expectancy around the globe continues to rise. Additional healthcare resources and service innovation is needed globally to deliver the long-term care and chronic disease management services required by a rapidly increasing senior population.

Approximately 80% of older adults have at least one chronic disease, and 77% have at least two. Four chronic diseases—heart disease, cancer, stroke, and diabetes—cause almost two-thirds of all deaths each year.

U.S. faces 90,000 doctor shortage by 2025, medical school association warns
Why Now .... Healthcare costs
Why Now .... AI

Pharmaceutical companies hope computers can help them find new medications that are faster, cheaper—and more likely to be effective.

Bringing a new pharmaceutical drug to market takes about 12 years and can reach upwards of $1 billion in R&D expenditures, industry leaders are now seeking more efficient methods of approaching this process and machine learning is emerging as a potential solution.

**How AI Is Transforming Drug Creation**
Pharmaceutical companies hope computers can help them find new medications that are faster, cheaper—and more likely to be effective.

**Novartis collaboration with IBM Watson for the purpose of improving health outcomes and for breast cancer patients**

**Johnson & Johnson a collaborative effort with IBM’s**

**Genentech a member of the Roche group collaboration with GNS Healthcare (a precision medicine company)**
Why now .... Data

IBM Explorlys Platform

The future of health begins with All of Us

Project Baseline

ClinicalStudy DataRequest.com

23andMe

TransCelerate BIOPHARMA INC.

the HUMAN project

CPRD

TRUVENT HEALTH ANALYTICS

IBM Watson Health™

Project Data Sphere®

biobank uk

Improving the health of future generations
Healthcare is changing....

Yale researchers tapping into emerging secure cloud platform for sharing patient data - HUGO
New Entrants in the Drug Development Field
New Healthcare Paradigms

- Growing trend for strong evidence on Pharmaceuticals from outside of Pharma
- Clinical Decision Support Tools start to gain traction
- Patient becoming more involved...
- Questions on Data Ownership

Where will Drug Development now fit within this digitally driven evolving ecosystem?
Clinical Development / Trial Support

- Biomarker Identification
- Protocol Optimization
- Physician Targeting / Patient Recruitment
- External Control Arms

Smart Study Design and Efficient Execution

Roche’s External Control Arms Show What Real-World Evidence Can Look Like In Practice


Pre-study feasibility and identifying sensitivity analyses for protocol pre-specification in comparative effectiveness research.
Medical Affairs / Launch Support

- Pragmatic Clinical Trials (PCTs)
- HEOR Support
- Value Demonstration
- Formulary Placement

**Demonstrating Effectiveness Outside of RCTs**

Creating and using real-world evidence to answer questions about clinical effectiveness.


Epoetin Biosimilars in the Treatment of Renal Anemia: What Have We Learned from a Decade of European Experience?

EHRs have the potential to resolve bottlenecks in clinical research

- EHRs routinely used in clinical care

- In many European countries almost 90% of health records are digital with longitudinal axis of over 10 years

- Need of trustworthy partnerships with hospital networks and Pharma

- Focus on data privacy and legal/ethical concerns

- Data standardization and harmonization work needed
Leveraging Healthcare Data to Optimize Drug Development

Data Types

- Real-World Data
  - Claims
  - EMR
  - Mobile
  - Questionnaires

- Clinical Trials
  - Clinical Data
  - 'Omics

- Pre-Clinical Development
  - 'Omics
  - Phenotypes

Insights:

- Efficacy to effectiveness
- Event prediction
- Disease progression
- Medication initiation and switching
- Personal care pathways
- Value-based therapies
- Biomarker discoveries
- Patient stratification/subpopulations
- Adverse events
- Drug repurposing
- Novel targets
- Drug combinations
- Diagnostics
January 31, 2019 - Real-world data gathered directly from EHRs and other data sources, paired with advances in machine learning, will be crucial for architecting the next generation of successful clinical trials, says FDA Commissioner Dr. Scott Gottlieb.
Regulators opening up to RWE and creating new legislation

- **FDA**
  - 21\textsuperscript{st} Century Cures Act
  - Promoting the Use of Complex Innovative Designs in Clinical Trials
  - Guidance on Use of Electronic Health Record Data in Clinical Investigations

- **EU**
  - IMI initiatives like EHR4CR
  - Topic at the European Commission/EMA–FDA bilateral meeting  18-19 June 2018
Extract from FDA Commissioner Scott Gottlieb statement in January 2019

• Digital technologies create new opportunities to transform health care and empower patients to make better informed decisions about their health. Digital tools are rapidly evolving, and to keep pace with this promising innovation, the FDA must modernize its approach to regulation.

• I announced in the Digital Health Innovation Action Plan that the FDA would pilot a Digital Health Precertification (Pre-Cert) Program to make sure that patients continue to have access to new treatments that meet our gold standard for safety and effectiveness. Since that announcement, we’ve been advancing policies that reimagine our oversight of digital health tools to be more efficient and promote patient safety throughout the product lifecycle.

• We’ve seen the promise of innovation in products like artificial intelligence software that can help alert physicians to a potential stroke and smart watches that can help identify atrial fibrillation.

• Today, we’re announcing that, based on the Pre-Cert pilot, we’ve drafted a regulatory framework to test new approaches for the review of digital health device applications.
Real-World Outcomes of Patients with Metastatic Non-Small Cell Lung Cancer Treated with Programmed Cell Death Protein 1 Inhibitors in the Year Following U.S. Regulatory Approval

SEAN KHOZIN, a KENNETH R. CARSON, b,c JIZU ZHI, a MELISA TUCKER, b SHANNON E. LEE, b DAVID E. LIGHT, b MELISSA D. CURTIS, b MARTA BRALIC, b IRENE KAGANMAN, b ANALA GOSSEI, b PHILIP HOFMEISTER, b ARACELIS Z. TORRES, b REBECCA A. MIKSAD, b GIDEON MICHAEL BLUMENTHAL, a RICHARD PAZDUR, a AMY P. ABERNETHY b

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Non-small cell lung cancer • Real-world evidence • Electronic health records • Overall survival • Nivolumab • Pembrolizumab
Current regulatory experience with FDA for ML

- ML algorithms initially will be evaluated on a case-by-case basis, both within CDER and CDRH.
- FDA has not moved toward creating a universal policy on ML.
- OCE is leading the way in terms of building its capacity around ML algorithms.
- If the Oncology group’s efforts are successful, they could provide a model for other Review Divisions to follow in ML.
- The emergence of public-private partnerships (PPPs) focused on ML is a promising development. These types of consortia could be a key part of the solution to the data sharing/data availability problem.
- CDRH has an internal group looking at machine learning; it is also participating (via a PPP) in a recently launched Artificial intelligence (AI) Initiative aimed at developing AI approaches in the areas of quality, regulatory affairs and supply chain operations.
- One of the challenges for CDRH is how to approach ML software that is updated frequently.
New Drug Development Paradigm
Developing a New Paradigm for Drug Development – Meeting October 7th 2016

• A group of Life sciences professionals held a 1-day meeting with MIT Media Lab to discuss the potential to develop a new paradigm for drug development. This was prompted by a changing healthcare environment resulting from the adoption of new technologies and the evolution of systems biology.

• A model proposed taking a molecule into patients via examining extensively the action of the molecule on a small cohort using a systems biology approach.

• For this to be successful the group felt that:
  – Pharmaceutical Industry, Providers and Payers would have to develop a robust, consistent and dynamic data sharing environment
  – Clarity would be needed on who owns data and how broad access is achieved to accelerate research
  – New incentive models would need to be developed across multiple stakeholders in the clinical trial ecosystem to ensure strong participation and data sharing
  – A new paradigm on potential liability will need to be introduced requiring new models of indemnification (e.g. joint liabilities)
  – Regulators would have to be open to the new model and build the associated needed capabilities and resources
The Challenge

Traditional approach to drug development requires sequential drug testing through phase

Phase 1 ➔ Phase 2a ➔ Phase 2b ➔ Phase 3 ➔ Registration ➔ Phase 3b ➔ Phase 4

In some indications this has been successfully adapted e.g. with breakthrough designation but for many indications (Asthma, MS, Lupus, wet AMD, Neuroscience), the model is essentially unchanged

What if..

A radical new approach to drug development could be adopted which deploys new technology such as systems biology, machine learning, cloud technology with increased predictability of the outcome?

What would this be?
New Process – Parallel in-silico development

- Repurposed drugs
  - Failed drugs
  - Difficult to develop drugs
  - High risk programs

Start development
- Data Map
- Data structure
- Agreed with stakeholders

100 pts. or 50 pts.
- Data sharing
- Algorithmic approach

Adaptive licensing
Breakthrough
PRIME
Accelerated Approval

Continual data feed into decision support tools

EHR driven trials and follow up
- Increased predictability
  - Machine learning

- Use network analysis to determine stratification, response factors and responder/non-responder groups

- Deep personal data cloud on each person
  - System biology approach*

Monday, March 11, 2019
Dynamic Digital Tool vs. the Label

Current Label

Personalized Digital Label

Table 1

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NGS Results

- Age
- Race
- Gender
- Biome Profile
- Dietary Profile
- Activity/Sleep Profile
- Behavioral Biomarker
- Biomarker Results
- Drug Dosing Regimen
Potential Opportunities for Artificial Intelligence and Machine Learning in Clinical Development

Clinical Trial Development Process opportunities to use with how AI/ML

- Research Hypothesis
- Protocol Development
- Site Set Up
- Subject Recruitment
- Data Collection
- Patient Engagement & Education
- Chatbot Help Line
- Trial Analysis & Reporting
- Submission
- Safety Evaluation

Opportunities

- Clinical Trial Matching
- Chatbots
- Deep Neural Networks
- Open Data
- Open Science
- Data Analytics

Artificial Intelligence applications beyond Clinical Trials

- Sensors
- Systems Biology
- Voice Recognition
- EHRs
- Precision Medicine
PRECISION MEDICINE: Integrating multi-omics, clinical and real world data

Creation of topological maps of health/disease
Causal Machine Learning for Healthcare Data

- Discerns complex causal mechanisms & predictors across populations & on an individual level
- Enables simulations of ‘what-if’ scenarios to identify effects on outcomes
- Incorporates all raw data
- Unlimited data types at once
- Millions of variables, billions of data points, and their interactions

- Rapidly searches massive hypothesis space
- Captures inherent variation in the data

- Incorporates all raw data
- Unlimited data types at once
- Millions of variables, billions of data points, and their interactions
Improving Outcomes and Reducing Costs Means Being Patient-Centric: There is a “Right Treatment” for the Right Patient at the Right Time.
A confluence of macro-level factors is leading to a burning platform - to harness data and adopt analytics that disrupt pharma business as usual

- **Explosion of data** (e.g., by 2020 healthcare data doubles every 3 months versus 3 years)
- **Nature of data is changing** (e.g. traditional R&D data now linked to EHR, etc.) such that the static is becoming dynamic
- **Expansion of data availability** (e.g. patient group data in social media, mobile apps, multi-omics, sensors, imaging, etc.)

**The Explosion of Healthcare Information...**

**...and New Capabilities in Advanced Analytics...**

- **Cognitive computing and machine learning** (e.g. information clustering and deep learning driving decisions making previously intractable problems solvable)
- **Integrated-Interactive dashboards** (e.g. Integrated cross functional real time data views constructed on agile data lakes)
- **New technology-focused entrants** (e.g., IBM Watson, Google/Alphabet, AWS, SFDC, Moderna, Illumina) are challenging the traditional models within healthcare and bio pharma

**...Are Redefining the Nature of Work in Healthcare**

- Integration of clinical trial, omic/imaging data, real world evidence and social media is creating **new sources of safety and value signals for Pharma and Regulators**
- Focus on **developing personalized treatment pathways** for patients
- **New methods to engage patients and providers** and including them more in the process of diagnosis, treatment and monitoring
- Increasing reliance on building **ecosystems** to address the needs for evolving information capabilities

**The Burning Platform:** As technology, data, expertise, and investment in this area continues to unfold, future financial sustainability in pharma is dependent on the ability to utilize data as a critical asset to deliver augmented intelligence in decision-making across the value chain and to leverage advanced analytics/cognitive approaches to do so.
Final Thoughts

• A major step to move forward is to address data aggregation and availability
• Next generation is not just for evidence generation but also can improve efficiencies
• Confidentiality concerns will be and have to be addressed e.g. Blockchain
• Digital Health and RWD are all about Advanced Analytics and programming
• Academia and Pharma need to co operate more to realize the value of the new Data Science era
• Pharma Data Science in Clinical Development is a lot broader than the Clinical Trial