Promise of personalized therapeutics

**TODAY: One-size-fits-all**

- Full benefit
- Partial benefit
- No benefit

**TOMORROW: Genomics-based**

- DNA analysis
- Customized therapy
CRA: Policy implications of personalized medicine

- Objectives:
  - Characterize the benefits of personalized medicine
  - Identify barriers and enablers for development and use of personalized medicine
  - Propose policy recommendations

- Study was completed in July 2018 in collaboration with EBE (European Biopharmaceutical Enterprises) and EFPIA (European Federation of Pharmaceutical Industries and Associations)

Genomics are driving clinical trials

Phase I-IV clinical trials utilizing biomarkers by trial start year, 2003 - 2016

Source: Pharma Intelligence; The Benefits of Personalised Medicine to patients, society, and healthcare systems, CRA – July 2018.
Today’s focus

Current pharma business model does not apply for genomics-based personalized therapeutics

Value-based models with industry partnerships are needed to support commercialization of personalized therapeutics
Traditional pharma business model: Recoup R&D costs with ‘blockbuster’ medicines

**Traditional ‘blockbuster’ pharma business model**

- **Investment**
  - **Discovery, Phl-III**
  - **PhlIV**

- **Revenue**
  - **Launch, maturity, decline**

- **Time**

**Graphical Representation**
- Large number of candidates with significant upfront R&D cost
- Small number of drugs with global sales (> $1bn)
Personalized medicine is evolving → Need for commercial innovation in the pharmaceutical industry

Blockbuster medicine

Targeted medicine for subset

Precision medicine

Genomics-based personalized therapeutics

Enables development of targeted therapies, which can be for patient subsets OR individual patients
With genomics-based personalized therapeutics, the traditional model does not apply

**Blockbuster medicines**
- Focus on **mass phenotype**
- Typically, **well-defined clinical trial process**
- **Large investment in clinical trials**
  - Average time from PhI-III of **10 years**
  - Average cost for clinical development and post-approval: **$2.87 bn** per drug* 
  - Mean of **800 subjects** per PhIII trial
  - Average success rate of **10%**

*2013 dollars

**Genomics-based**
- **Targeted approach** to drug discovery leveraging genomics databases
- Similar requirement for clinical trials, but possibility of approval on PhII data
  - Possibly **smaller trial sizes** with biomarker-positive participants
- **Continued investment** in data
- Co-development of **companion diagnostic based on biomarkers**
- **Success rate:** **25%?**

With genomics-based personalized therapeutics, the traditional model does not apply

Blockbuster medicines
- Regulatory approval based on proof of efficacy and safety
- Price and access reflective of one-size-fits-all approach to prescribing
  - Most drugs prescribed today are effective in less than 60% of treated patients
  - Drugs with less specificity but potentially large volume impact typically face challenges in obtaining access as payers are looking for value-for-money

Genomics-based
- Value-based pricing and access
  - Companion diagnostic to predict responders included within price / access
- Continued data collection and management with statistical analysis to evaluate response to drug in genetic group
- Investment in additional infrastructure to support diagnostic testing / product delivery

With genomics-based personalized therapeutics, the traditional model does not apply

**Blockbuster medicines**
- **Meet demand**, but critical to success?
- **Global sourcing** to reduce costs
- Leverage **standardized distribution channels**
- **New era of biologics** → increasing value of manufacturing
  - Supply security
  - Yield rates and cost efficiency

**Genomics-based**
- **Integral part of care delivery**
- **Supply chain innovation** likely to become critical for success
  - Specialized labour and distribution
- **Supply chain security and coordination**
  - Personal information
- Supply costs become **significant component of therapy cost**

*Source: Perspectives and Learnings in Life Sciences Innovation: Opportunities for Growth. Takizawa, B. March 2018.*
With genomics-based personalized therapeutics, the traditional model does not apply

Blockbuster medicines

- **Large, dispersed salesforce**
  - 100,000 reps in 2005 down to 71,000 reps in 2016 in the U.S. market
  - Typically **primary care** outpatient physician targets (e.g., 100,000+ physicians within statin market)
- Sales reps play role in **drug-specific education and brand choice**

Genomics-based

- **Patient finding** is a critical success factor
- Niche salesforce requiring **tailored marketing and different capabilities**
- Sales rep becomes an **account manager**, with multi-faceted role:
  - Greater focus on disease education and therapy awareness (MSL)
  - Screening and patient ID support
  - Explaining reimbursement and providing link to service delivery and CoE

*Source: 5 Trends Shaping the Pharma Sales Force, LaMotta, L. Sept 2017.*
Today’s focus

The challenge

Current pharma business model does not apply for genomics-based personalized therapeutics

The opportunity

Value-based models with industry partnerships are needed to support commercialization of personalized therapeutics
Genomics-based business model requires infrastructure and continued investment to support commercialization.

New "personalized" therapeutic business model:

- **Targeted investment in R&D with fewer candidates in pipeline**
- **Larger portfolio of drugs for smaller populations**

Diagram:
- **Discovery, Phl-III**
- **PhIV**
- **Continued data management & Dx support**
- **Launch, maturity, decline**

**CRA Charles River Associates**
Within drug development, pharma will need partnerships with data companies and infrastructure in regulatory bodies.

To successfully commercialize a genomics-based personalized Tx, pharma needs...

**Drug discovery & development**

- Access to genomic data
- Revised clinical trial design requirements

...this requires partnership with...

**Launch & patient access**

- Personal genomics companies
- Country / regional-level population genomics projects
- Regulatory / marketing authorization bodies
- Contract research organizations for running specialized trials
Strides are being made to develop population-based genomics databases to facilitate drug discovery

<table>
<thead>
<tr>
<th>2018 partnership (not exhaustive)</th>
<th>Details</th>
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<tbody>
<tr>
<td>gsk 23andMe</td>
<td>• $300 million; DNA chip data, sequenced patients with common diseases</td>
</tr>
<tr>
<td>Roche flatiron</td>
<td>• $1.9 billion; focused on oncology outcomes based on medical data only in the US</td>
</tr>
<tr>
<td>REGENERON AstraZeneca abbvie Biogen Pfizer Alnylam</td>
<td>• $2.4 billion; &gt;100,000 tumors with panel sequencing of 400 known tumor genes in the US</td>
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<tr>
<td>biobankuk</td>
<td>• 500,000 exomes tied to ICD codes for diseases and diagnostic tests in the UK, targeted for end 2019</td>
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To ensure value is realized, countries will need to invest in data infrastructure alongside payer and policy changes.

To successfully commercialize a genomics-based personalized Tx, pharma needs...

- Value realization through pricing, access, and policy
- Investment in genomics databases linked to health records to capture outcomes

...this requires partnership with...

- CADTH
- Payers / HTA organizations responsible for value assessment, pricing & access
- National and international patient registries and genomics databases
Once on the market, pharma companies will require partnerships with providers and diagnostics companies to reach their patients.

To successfully commercialize a genomics-based personalized Tx, pharma needs:

- Patient finding support (screening tools, access to individual patients)
- Companion diagnostics for patient treatment selection and testing infrastructure
- Genomic data
- Healthcare providers / CoEs
- IVD / molecular diagnostics companies
- Laboratories
Implementation of companion diagnostic testing can be a challenge without investment in infrastructure

### Current situation regarding implementation of CDx testing

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
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<tr>
<td>Medicine approval</td>
<td>Targeted therapy clinical trials are successful &amp; medicines get approved</td>
</tr>
<tr>
<td>Medicine reimbursement</td>
<td>Medicine reimbursement approved (country by country basis)</td>
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<tr>
<td>Lab adoption</td>
<td>Demand for CDx testing reaches the labs, doctors wish to start ordering testing to prescribe new medicines</td>
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<tr>
<td>Selection of technology</td>
<td>Labs evaluate various technology and decide which test they wish to adopt</td>
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<tr>
<td>Capacity building</td>
<td>Labs/healthcare systems invest in infrastructure and expertise</td>
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<tr>
<td>Quality control</td>
<td>Labs embed the test in established local quality systems;</td>
</tr>
<tr>
<td>Clinical Dx service offered</td>
<td>CDx testing offered to patients as clinical service</td>
</tr>
<tr>
<td>Maintenance of quality</td>
<td>Labs may seek to join External Quality Control programmes and/or obtain ISO accreditation</td>
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Industry needs to continue to shape the evolving genomics and personalized medicine environment across markets

Recommendations for industry

- R&D partnership
- Policy engagement
- Payer engagement
- Commercialization partnership

Relative value and order of company-driven strategies will be specific to individual product and market situation
Dr. Gregory K. Bell
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