Global Healthcare Trends and Outlook

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Principal, Thought Leadership
Outline

• The global pharmaceutical market: description and trends
• The global generic market trends
• Trends in new launches: innovator products and generic medicines
• Will the future generic medicines launches be sufficient to cope with the high costs of new innovative medicines?
• Will future biosimilar launches balance the new high cost innovative medicines?
• Summary
We live in difficult times…

**Political instability**
- Ukraine, South Africa, Brazil

**Oil price exposure; depreciating currency**
- Russia, Nigeria, Venezuela, Algeria, Brazil
  - ME and USA IMPACT

**Runaway inflation, default risk**
- Venezuela, Argentina, Egypt

**IP breakdowns, Bribery Allegations**
- India, China, Nigeria, Turkey

**Refugee crisis**
- Syria, Turkey, Lebanon, Iraq
  - EUROPE IMPACT

**Terrorism**
- Nigeria, Pakistan, India, Egypt, Turkey
  - GLOBAL IMPACT
We live in difficult times….

Political instability
- Ukraine, South Africa, Brazil

Oil price exposure; depreciating currency
- Russia, Nigeria, Venezuela, Algeria, Brazil

Runaway inflation, default risk
- Venezuela, Argentina, Egypt

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- India, China, Nigeria, Turkey

One constant, the need for healthcare

Refugee crisis
- Syria, Turkey, Lebanon, Iraq

Terrorism
- Nigeria, Pakistan, India, Egypt, Turkey
Global pharma has grown 6.5% over the last 5 years to $936BN

Global sales (2011-16)

<table>
<thead>
<tr>
<th></th>
<th>Sales ($LCUS Bn)</th>
<th>% Share</th>
<th>% Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global Total</td>
<td>936</td>
<td></td>
<td>6.5%</td>
</tr>
<tr>
<td>USA</td>
<td>438</td>
<td>46.8%</td>
<td>5.9%</td>
</tr>
<tr>
<td>JAPAN</td>
<td>78</td>
<td>8.3%</td>
<td>-1.6%</td>
</tr>
<tr>
<td>CHINA</td>
<td>75</td>
<td>8.0%</td>
<td>7.9%</td>
</tr>
<tr>
<td>GERMANY</td>
<td>37</td>
<td>4.0%</td>
<td>4.2%</td>
</tr>
<tr>
<td>FRANCE</td>
<td>29</td>
<td>3.1%</td>
<td>3.4%</td>
</tr>
<tr>
<td>ITALY</td>
<td>26</td>
<td>2.8%</td>
<td>6.6%</td>
</tr>
<tr>
<td>BRAZIL</td>
<td>22</td>
<td>2.3%</td>
<td>11.1%</td>
</tr>
<tr>
<td>UK</td>
<td>20</td>
<td>2.2%</td>
<td>4.9%</td>
</tr>
<tr>
<td>SPAIN</td>
<td>20</td>
<td>2.1%</td>
<td>4.0%</td>
</tr>
<tr>
<td>CANADA</td>
<td>17</td>
<td>1.8%</td>
<td>4.1%</td>
</tr>
</tbody>
</table>

Source: QI MIDAS MAT Q4 2016
Growth projected at 3-6% CAGR to $1.4tn by 2021
USA to continue to dominate growth and sales. China and Japan slow down.

Notes: *Subject to PPRS rebate; Ex-manufacturer price levels, not including rebates and discounts. Contains Audited + Unaudited data; Growth considered on par if the there is overlap between country and region CAGR ranges
Source: QuintilesIMS Market Prognosis Q1 2017
Healthcare policies mean European growth stagnant at 2.5% CAGR

Notes: *UK subject to PPRS rebates; **Current PPRS has capped growth to average of less that 2% per year to end 2018, growth for 2014 and 2015 was capped at 0%; Growth in LCUS$ unless otherwise stated; At ex-manufacturer price levels, not including rebates and discounts. Contains Audited + Unaudited data
Source: QuintilesIMS Market Prognosis March 2017
Wide dispersion in growth but CAGR falls to single digits...China dominates but moderating

Top 20 Pharmerging Markets Forecast Growth Dynamics

Bubble Size proportional to 2016 LCUS$ Sales

- $100bn
- $20bn
- $7bn

Historic CAGR (2011-16)

Forecast CAGR (2016-21)

- Turkey
- India
- Russia
- Brazil
- China

Pharmerging Historic CAGR: 10.8%

Pharmerging Forecast CAGR: 7.4%

Notes: At ex-manufacturer price levels, not including rebates and discounts. Contains Audited and Unaudited data; Argentina excluded due to hyperinflation
Source: QuintilesIMS Market Prognosis March 2017
A third of global expenditure comes from five therapy areas

<table>
<thead>
<tr>
<th>Therapy area</th>
<th>US</th>
<th>EU5</th>
<th>Japan</th>
<th>Pharmerging</th>
<th>RoW</th>
<th>Global Share</th>
<th>Global Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncology</td>
<td>46%</td>
<td>21%</td>
<td>10%</td>
<td>9%</td>
<td></td>
<td>$96 bn</td>
<td>21%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>65%</td>
<td>9%</td>
<td>12%</td>
<td></td>
<td></td>
<td>$77 bn</td>
<td>16%</td>
</tr>
<tr>
<td>Autoimmune</td>
<td>65%</td>
<td>15%</td>
<td></td>
<td></td>
<td></td>
<td>$55 bn</td>
<td>15%</td>
</tr>
<tr>
<td>Pain</td>
<td>39%</td>
<td>14%</td>
<td>23%</td>
<td></td>
<td></td>
<td>$48 bn</td>
<td>3%</td>
</tr>
<tr>
<td>Respiratory</td>
<td>59%</td>
<td>14%</td>
<td>9%</td>
<td></td>
<td></td>
<td>$42 bn</td>
<td>5%</td>
</tr>
<tr>
<td>Antihypertens.</td>
<td>23%</td>
<td>14%</td>
<td>26%</td>
<td></td>
<td></td>
<td>$41 bn</td>
<td></td>
</tr>
<tr>
<td>Antibacterials</td>
<td>19%</td>
<td>11%</td>
<td>49%</td>
<td></td>
<td></td>
<td>$39 bn</td>
<td></td>
</tr>
<tr>
<td>Mental Health</td>
<td>52%</td>
<td>14%</td>
<td></td>
<td></td>
<td></td>
<td>$32 bn</td>
<td></td>
</tr>
<tr>
<td>Viral Hepatitis</td>
<td>48%</td>
<td>22%</td>
<td></td>
<td></td>
<td></td>
<td>$32 bn</td>
<td></td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>39%</td>
<td>19%</td>
<td>16%</td>
<td></td>
<td></td>
<td>$31 bn</td>
<td></td>
</tr>
</tbody>
</table>

Source: QuintilesIMS MIDAS MAT Q4 2016, Rx only
Over 60% of global growth comes from just five TAs

Absolute one year growth 2016 (LCUS$ Bn)

<table>
<thead>
<tr>
<th>Category</th>
<th>US</th>
<th>EU5</th>
<th>Japan</th>
<th>Pharmerging</th>
<th>All Others</th>
<th>Share of global growth 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncology</td>
<td>53%</td>
<td>21%</td>
<td>11.7</td>
<td>21%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>80%</td>
<td>9.3</td>
<td></td>
<td>16%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autoimmune</td>
<td>79%</td>
<td>10%</td>
<td>8.7</td>
<td>15%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>64%</td>
<td>3.9</td>
<td></td>
<td>7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td>86%</td>
<td>3.0</td>
<td></td>
<td>5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>76%</td>
<td>2.8</td>
<td></td>
<td>5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GI</td>
<td>59%</td>
<td>1.7</td>
<td></td>
<td>3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous System</td>
<td>73%</td>
<td>1.7</td>
<td></td>
<td>3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>-44%</td>
<td>145%</td>
<td>1.6</td>
<td>3%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MS</td>
<td>68%</td>
<td>1.4</td>
<td></td>
<td>3%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Concentration has reduced from the previous iteration (73% in top 5 TAs) because we have passed peak Hepatitis C

Source: QuintilesIMS MIDAS MAT Q4 2016, Rx only
Biologics have grown twice as fast as small molecules

Small molecules faced increased genericisation from 2014

Global biologic sales and trends (2011-16)
Billions of USD

Biologics – 2016 Share of sales

- 59%
- 11%
- 7%
- 6%
- 17%

Biologics – Share of 5 yr growth

- 68%
- 11%
- 8%
- 4%
- 9%

Source: QuintilesIMS MIDAS MAT Q4 2016; Q1 Market Prognosis March 2017; Share of growth in LC$. Brazil and Mexico non-retail included
## Impact of launches of Specialty products compared to earlier primary care products

<table>
<thead>
<tr>
<th>Drug</th>
<th>Category</th>
<th>Paper</th>
<th>Indication</th>
<th>2-year global sales post launch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celebrex</td>
<td>Primary care</td>
<td>LE1</td>
<td>Arthritis (OA/RA)</td>
<td>$3.9bn</td>
</tr>
<tr>
<td>Lipitor</td>
<td>Primary care</td>
<td>LE1</td>
<td>Lipid regulator</td>
<td>$3.0bn</td>
</tr>
<tr>
<td>Viagra</td>
<td>Primary care</td>
<td>LE1</td>
<td>Erectile dysfunction</td>
<td>$1.7bn</td>
</tr>
<tr>
<td>Avandia</td>
<td>Primary care</td>
<td>LE1</td>
<td>Diabetes</td>
<td>$1.1bn</td>
</tr>
<tr>
<td>Combivir</td>
<td>Specialty</td>
<td>LE1</td>
<td>HIV infection</td>
<td>$0.9bn</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Category</th>
<th>Paper</th>
<th>Indication</th>
<th>2-year global sales post launch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harvoni</td>
<td>Specialty</td>
<td>LEV</td>
<td>Hepatitis C</td>
<td>$33.0bn</td>
</tr>
<tr>
<td>Sovaldi</td>
<td>Specialty</td>
<td>LEV</td>
<td>Hepatitis C</td>
<td>$13.8bn</td>
</tr>
<tr>
<td>Tecfidera</td>
<td>Specialty</td>
<td>LEV</td>
<td>Multiple sclerosis</td>
<td>$5.1bn</td>
</tr>
<tr>
<td>Opdivo</td>
<td>Specialty</td>
<td>LEV</td>
<td>Cancer</td>
<td>$3.3bn</td>
</tr>
<tr>
<td>Sovriad</td>
<td>Specialty</td>
<td>LEV</td>
<td>Hepatitis C</td>
<td>$3.0bn</td>
</tr>
</tbody>
</table>

Source: QuintilesIMS Midas LC US $ Q3 2016; QuintilesIMS Thought Leadership Launch Excellence model
Notes: Sales are normalised to take into account launch quarter and do not represent calendar sales.
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• The global pharmaceutical market: description and trends
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  • Trends in new launches: innovator products and generic medicines
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• Summary
Generics are taking an increased share of the market

**GENERICS MARKET SHARE (US$, Units) 2006 VS. 2016**

- **North America**: 52% → 70%
- **North America**: 16% → 23%
- **LATAM**: 65% → 80%
- **LATAM**: 45% → 65%
- **Europe**: 47% → 62%
- **Europe**: 26% → 29%
- **Japan**: 31% → 40%
- **Japan**: 16% → 18%
- **Asia/Australasia**: 74% → 71%
- **Asia/Australasia**: 31% → 43%
- **Africa/Middle East**: 65% → 69%
- **Africa/Middle East**: 46% → 49%

Source: QuintilesIMS MIDAS MAT Q4 2016; Rx bound; Europe includes Turkey; Generics include Non-original branded products and unbranded products
The global generic market is forecast to grow at 5.8% CAGR
Pharmerging is dependent on generic products

Preference for branded generics is coupled with increase OOP spend

**Pharmerging Value (2016) bn USD**

- **China**: 64 bn USD (20% Other products, 46% Unbranded generics, 23% Non-Original Branded products, 4% Innovative branded products)
- **Brazil**: 21 bn USD (30% Other products, 30% Unbranded generics, 34% Non-Original Branded products, 4% Innovative branded products)
- **Russia**: 7 bn USD (12% Other products, 41% Unbranded generics, 40% Non-Original Branded products, 10% Innovative branded products)
- **India**: 14 bn USD (3% Other products, 80% Unbranded generics, 10% Non-Original Branded products, 1% Innovative branded products)
- **Other**: 49 bn USD (6% Other products, 51% Unbranded generics, 37% Non-Original Branded products, 6% Innovative branded products)
- **US**: 438 bn USD (8% Other products, 74% Unbranded generics, 8% Non-Original Branded products, 14% Innovative branded products)

**Pharmerging Volume (2016) bn SU**

- **China**: 161 bn SU (39% Other products, 37% Unbranded generics, 35% Non-Original Branded products, 5% Innovative branded products)
- **Brazil**: 100 bn SU (35% Other products, 50% Unbranded generics, 39% Non-Original Branded products, 6% Innovative branded products)
- **Russia**: 54 bn SU (5% Other products, 76% Unbranded generics, 39% Non-Original Branded products, 11% Innovative branded products)
- **India**: 325 bn SU (5% Other products, 62% Unbranded generics, 19% Non-Original Branded products, 13% Innovative branded products)
- **Other**: 415 bn SU (11% Other products, 62% Unbranded generics, 19% Non-Original Branded products, 13% Innovative branded products)
- **US**: 240 bn SU (5% Other products, 78% Unbranded generics, 5% Non-Original Branded products, 13% Innovative branded products)

<table>
<thead>
<tr>
<th></th>
<th>Value CAGR 2011-2016</th>
<th>Volume CAGR 2011-16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unbranded generics</td>
<td>9.2%</td>
<td>7.0%</td>
</tr>
<tr>
<td>Non-Original Branded</td>
<td>5.0%</td>
<td>6.1%</td>
</tr>
<tr>
<td>Innovative products</td>
<td>0.1%</td>
<td>4.9%</td>
</tr>
<tr>
<td>Pharmerging market</td>
<td>4.1%</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

Source: QuintilesIMS MIDAS MAT Q4 2016; Innovation (2016); OTC excluded; Excludes traditional Chinese medicines
What is driving the generic market?

• Affordability
• Headroom in budgets for newer treatments
• Treatment guidelines
• Incentives/ budgets for prescribers
• Patient co-payments
• Earnings for pharmacist
• Products coming off patent
To have an effective generics market there needs to be a coherent generics policy

Addressing supply and demand aspects

**Supply**
- Market access
- Reimbursement
- Competition

**Demand**
- Knowledge & perception
- Guidelines
- Targets
- Reference pricing
- Substitution
Outline

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• **Trends in new launches: innovator products and generic medicines**
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• Summary
Sovaldi only the first of several potential tsunamis

Are these innovations sustainable?

**Hepatitis-C market**
2012-2015

- Historic sales (Bn US$)

<table>
<thead>
<tr>
<th>Year</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>$10</td>
<td>$12</td>
<td>$15</td>
<td>$32</td>
</tr>
</tbody>
</table>

$32 Bn

- Analyst forecast (Bn US$)

<table>
<thead>
<tr>
<th>Year</th>
<th>2014</th>
<th>2016</th>
<th>2018</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>$18</td>
<td>$20</td>
<td>$22</td>
<td>$25</td>
</tr>
</tbody>
</table>

$18-22 Bn

**Immuno-Oncology**

- Historic sales (Bn US$)

<table>
<thead>
<tr>
<th>Year</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>$5</td>
<td>$6</td>
<td>$8</td>
<td>$10</td>
</tr>
</tbody>
</table>

$6-8 Bn

- Analyst forecast (Bn US$)

<table>
<thead>
<tr>
<th>Year</th>
<th>2014</th>
<th>2016</th>
<th>2018</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>$1</td>
<td>$2</td>
<td>$4</td>
<td>$8</td>
</tr>
</tbody>
</table>

$6-8 Bn

**Respiratory biologics**

- Analyst forecast (Bn US$)

<table>
<thead>
<tr>
<th>Year</th>
<th>2014</th>
<th>2016</th>
<th>2018</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>$5</td>
<td>$7</td>
<td>$10</td>
<td>$15</td>
</tr>
</tbody>
</table>

$5-7 Bn

**PCSK9 inhibitors?**
2016-2020 will set a record for launches when the current innovation rich pipeline approved

22% increase from the previous 5 years

Number of New Active Substances (NAS) launches 1996-2020

- 1996-2000: 223
- 2001-2005: 165
- 2006-2010: 146
- 2011-2015: 184
- 2016-2020: 225

Source: IMS Health, IMS Institute for Healthcare Informatics, October 2015
The cancer treatment landscape has been transformed since 2011 by new medicines targeting 22 different cancer types.

**New Active Substance Launches 2011–2016 by Indication**

- **Pancreatic**
  - irinotecan liposome

- **Neuroblastoma**
  - vandetanib
  - cabozantinib
  - lenvatinib

- **Thyroid**
  - bosutinib (CML)
  - ormeloxifene
  - mepesuccinate (CML)
  - radotinib (CML)
  - obinutuzumab (CLL, FL)
  - ponatinib (CML, ALL)
  - blinatumomab (ALL)
  - ibritinib (CLL)
  - ofatumumab (CLL)
  - venetoclax (CLL)

- **GIST**
  - prazosin

- **Leukemia**
  - pembrolizumab
  - nivolumab
  - atezolizumab

- **Bladder**
  - dinutuximab

- **Head & Neck**
  - pembrolizumab
  - nivolumab
  - axitinib

- **Renal**
  - pemipomab
  - emtansine

- **Breast**
  - pertuzumab
  - ado-trastuzumab emtansine
  - palbociclib

- **Lung**
  - palbociclib
  - ipilimumab
  - vemurafenib
  - trametinib
  - dabrafenib

- **Sarcoma**
  - pembrolizumab
  - nivolumab
  - cobimetinib
  - T-VEC

- **Prostate**
  - regorafenib
  - ziv-aflibercept
  - tipiracil/trifluridine

- **Melanoma**
  - romidepsin (PTCL, CTCL)
  - brentuximab vedotin (Hodgkin's, ALCL)
  - paximcon (NHL)
  - rituximab (NHL)
  - idelalisib (CLL, FL, SLL)
  - mogamulizumab (ATCL)
  - belinostot (PTCL)
  - ibritinib (MCL, WM)
  - bortezomib (MCL)
  - chidarnide (PTCL)
  - venetoclax (CLL)
  - nivolumab (Hodgkin's)

- **Colorectal cancer**
  - olaparib
  - bevacizumab
  - rucaparib

- **Lymphoma**
  - polatuzumab

- **Ovarian**
  - cibraratumab

- **Cervical**
  - vismodegib
  - sonidegib

- **Multiple myeloma**
  - carfilzomib
  - pomalidomide
  - daratumumab
  - ixazomib
  - panobinostat
  - elotuzumab

- **Gastric**
  - ramucirumab

- **Basal cell carcinoma**
  - ramucirumab

- **Prostate**
  - abiraterone acetate
  - enzalutamide
  - ra 223 dichloride

- **Gastric**
  - carfilzomib

- **Multiple myeloma**
  - pembrolizumab

- **Lymphoma**
  - ruxolitinib

- **Rhabdomyosarcoma**
  - vincristin

Source: QuintilesIMS, ARK R&D Intelligence, Feb 2017; QuintilesIMS Institute, Mar 2017
Over the last 20 years, therapy options for multiple tumor types have increased significantly

Number of Treatment Options over Time for Selected Tumors (1996–2016)

<table>
<thead>
<tr>
<th></th>
<th>1996</th>
<th>2006</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer</td>
<td>2</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>3</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Lung Cancer</td>
<td>4</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Melanoma</td>
<td>11</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>CLL</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>HER2</td>
<td>Hormonals</td>
<td>Chemotherapy</td>
<td>CDK</td>
</tr>
<tr>
<td>Others</td>
<td>Immunotherapy</td>
<td>EGFR</td>
<td>ALK</td>
</tr>
<tr>
<td>BRAF</td>
<td>Anti-CD</td>
<td>Other small molecules</td>
<td></td>
</tr>
</tbody>
</table>

Source: Drugs@FDA, Feb 2017; QuintilesIMS, ARK R&D Intelligence, Feb 2017; QuintilesIMS Institute, Mar 2017
The number of treated melanoma patients has nearly tripled with the launch of novel agents

Increase in Number of Treated Patients for Melanoma

Source: QuintilesIMS, Real World Insights Oncology US EMR Data, Dec 2016; QuintilesIMS Institute, Mar 2017
Availability of novel agents for NSCLC has also increased the number of treated patients.

Source: QuintilesIMS, Real World Insights Oncology US EMR Data, Dec 2016; QuintilesIMS Institute, Mar 2017
The global R&D pipeline for oncology remains robust with 631 unique molecules in late-phase development.

Global Late Phase Oncology Pipeline in 2016

Source: QuintilesIMS ARK R&D Intelligence, QuintilesIMS Institute, Dec 2016
Oncology growth is expected to be 6–9% per year through 2021, when global costs are expected to exceed $147Bn

Global Oncology Costs and Growth, US$Bn, 2011–2021

CAGR 2011–2016: 7.9%
Projected CAGR 2016–2021: 6–9%

Source: QuintilesIMS, MIDAS, Q4 2016, QuintilesIMS Institute, Mar 2017
Transformation in Disease Treatments

Innovation drives transformation of disease treatments in 2020

- Use of medicines in 2020 will include **943 New Active Substances** introduced in the prior 25 years, new medicines in recent years will be **weighted to specialty and biologics**
- Patients will have greater access to breakthrough therapies, clusters of innovation around hepatitis C, autoimmune diseases, heart disease, orphan diseases and others
- **Cancer treatments** represent the largest category of the **225 new medicines** expected to be introduced within the next five years
- Technology will enable changes to treatment protocols, shift patient engagement, accountability and patient-provider interaction accelerate the adoption of behavior changes proven to improve patient adherence to treatments
- By 2020, over **470 drugs** will be available to treat orphan diseases for the 7,000 rare diseases with no or limited treatments available
- While global medicine spending on orphan is expected to be 1-2%, it will be as much as 10% in developed markets such as the U.S.

Outline

• The global pharmaceutical market: description and trends
• The global generic market trends
• Trends in new launches: innovator products and generic medicines
• Will the future generic medicines launches be sufficient to cope with the high costs of new innovative medicines?
• Will future biosimilar launches balance the new high cost innovative medicines?
• Summary
Developed Markets Patent Expiry Exposure and Impact Constant US$Bn

<table>
<thead>
<tr>
<th>Year</th>
<th>Pre-expiry Spending - Small Molecule</th>
<th>Lower Brand Spending - Small Molecule</th>
<th>Pre-expiry Spending - Biologic</th>
<th>Lower Brand Spending - Biologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>$141</td>
<td>$16</td>
<td>$131</td>
<td>$59</td>
</tr>
<tr>
<td>2012</td>
<td>22</td>
<td>-16</td>
<td>17</td>
<td>-9</td>
</tr>
<tr>
<td>2013</td>
<td>44</td>
<td>-35</td>
<td>31</td>
<td>-8</td>
</tr>
<tr>
<td>2014</td>
<td>29</td>
<td>-20</td>
<td>34</td>
<td>-8</td>
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<tr>
<td>2015</td>
<td>18</td>
<td>-14</td>
<td>29</td>
<td>-6</td>
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<tr>
<td>2016</td>
<td>7</td>
<td>-24</td>
<td>16</td>
<td>-9</td>
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<tr>
<td>2017</td>
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<td>-6</td>
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<tr>
<td>2018</td>
<td>15</td>
<td>-29</td>
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</tr>
<tr>
<td>2019</td>
<td>17</td>
<td>-28</td>
<td>21</td>
<td>-21</td>
</tr>
<tr>
<td>2020</td>
<td>16</td>
<td>-34</td>
<td>21</td>
<td>-21</td>
</tr>
</tbody>
</table>

Source: IMS Institute for Healthcare Informatics, October 2015

Note: Pre-expiry spending is the actual and estimated spending in the 12 months prior to loss of exclusivity (LOE) and is shown for developed markets only. Lower Brand Spending is the actual and estimated decline in spending on brands facing LOE. Estimates are based on patent expiry dates or expected generic/biosimilar availability, and historic analogues where available. Biologics and small molecules are modeled separately. Biologic brand losses are based on any non-original biologic competitor, regardless of approval type.
Small molecules are becoming increasingly important in the specialty field

**Global Specialty Sales (2011-16)**
bn LCUS$

- Specialty Biologic
- Specialty Small Molecule

CAGR % (2011-16)

2011: 166
  - 59% Specialty Biologic
  - 41% Specialty Small Molecule
2016: 307
  - 53% Specialty Biologic
  - 47% Specialty Small Molecule

Top 10 companies share of specialty 2016
- 11% Specialty Biologic
- 16% Specialty Small Molecule

**Global Pipeline (Jan 2017)**

- Preclinical
  - Biologic: 817, Small Molecule: 950
- Phase I
  - Biologic: 484, Small Molecule: 614
- Phase II
  - Biologic: 582, Small Molecule: 809
- Phase III
  - Biologic: 204, Small Molecule: 341
- Pre-reg/Reg
  - Biologic: 92, Small Molecule: 164

Total pipeline is 43% biologics

Source: QuintilesIMS Market Prognosis Q4 2016; QuintilesIMS Institute Feb 2017
Outline

• The global pharmaceutical market: description and trends
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• Summary
Historically biosimilar competition restricted but the future is very different

Top Biologic Therapy Areas, Europe sales (2016)

- Autoimmune 20%
  - Etanercept
  - Infliximab
- Oncologics 20%
  - Rituximab
  - Trastuzumab
- Antidiabetics 9%
  - Insulin glargine
- Hematopoietic Growth Factors 2%
- Erythropoietins 4%
- Growth Hormones 2%

Source: QuintilesIMS MIDAS MAT Q3 2016; Europe excludes Russia and Turkey
Multiple Biosimilars are now approved in all three major regions

US, Japan, Europe Biosimilar molecule approvals to date

60% of biologic sales
3% of biosimilar sales

6% of biologic sales
8% of biosimilar sales

23% of biologic sales
87% of biosimilar sales

2006
somatropin
epoetin alfa
epoetin zeta
filgrastim

2008
2010
2012
2014
2016

insulin glargine
somatropin
etanercept
filgrastim
epoetin alfa
infliximab
insulin glargine injection*
darbepeotin alfa
follitropin alfa
etanercept
infliximab
etanercept

Source: IMS Health MIDAS Q3 2016 (Europe excludes Russia and Turkey); EMA website Jan 2017; FDA website June 2016; Japan approval dates from Gabionline April 2016; *Basaglar is not a biosimilar in the USA, it is a follow-on biologic; excludes Non-original biologics
Europe makes up 22% of global biologic sales and 87% of biosimilar sales

All values are at list price before rebates

Global Biologic market dynamics, $247Bn

Global Biosimilar market dynamics, $1.8Bn

Source: IMS Health MIDAS MAT Q4 2016; Europe does not include Russia and Turkey
The next wave of biosimilars include trastuzumab, rituximab, adalimumab and bevacizumab in Europe

Europe: Recent biosimilar filings

<table>
<thead>
<tr>
<th>Originator Name (molecule name)</th>
<th>Therapeutic area</th>
<th>Total pending EMA applications</th>
<th>Originator protection expiry</th>
<th>European revenue 2016 (Bn €)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enbrel (etanercept)</td>
<td>Autoimmune</td>
<td>+ 1</td>
<td>Aug-15</td>
<td>€2.0 Bn</td>
</tr>
<tr>
<td>Lantus (insulin glargine)</td>
<td>Diabetes</td>
<td>+ 1</td>
<td>May-15</td>
<td>€1.1 Bn</td>
</tr>
<tr>
<td>Herceptin (trastuzumab)</td>
<td>Oncology</td>
<td>3</td>
<td>Jul-14</td>
<td>€1.8 Bn</td>
</tr>
<tr>
<td>Mabthera (rituximab)</td>
<td>Oncology</td>
<td>+ 2</td>
<td>Feb-13</td>
<td>€1.7 Bn</td>
</tr>
<tr>
<td>Avastin (Bevacizumab)</td>
<td>Oncology</td>
<td>2</td>
<td>Jan-22</td>
<td>€1.8 Bn</td>
</tr>
<tr>
<td>Humira (adalimumab)</td>
<td>Autoimmune</td>
<td>4</td>
<td>Apr-18</td>
<td>€3.4 Bn</td>
</tr>
<tr>
<td>Neulasta (pegfilgrastim)</td>
<td>Oncology</td>
<td>3</td>
<td>Aug-17</td>
<td>€0.5 Bn</td>
</tr>
</tbody>
</table>

US: Recent biosimilar filings and approvals

<table>
<thead>
<tr>
<th>INN name/ Common Name</th>
<th>Therapeutic area</th>
<th>Total pending FDA applications</th>
<th>Originator protection expiry</th>
<th>US revenue 2016 (Bn $)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neupogen (filgrastim)</td>
<td>Oncology</td>
<td>1</td>
<td>Dec-2013</td>
<td>$0.6 Bn</td>
</tr>
<tr>
<td>Enbrel (etanercept)</td>
<td>Autoimmune</td>
<td>1</td>
<td>2022</td>
<td>$7.1 Bn</td>
</tr>
<tr>
<td>Humira (adalimumab)</td>
<td>Autoimmune</td>
<td>1</td>
<td>Dec-16</td>
<td>$13.2 Bn</td>
</tr>
</tbody>
</table>

Source: EMA website January 2017; Quintiles website January 2017; Launch biosimilars have not been included; “+” indicates that biosimilars are already on the market for that molecule
Summary

• Ageing populations and social costs outpacing health care provision and in the absence of curative therapies will diminish share of budgets for medicines

• Specialty care innovation continues to grow but true innovation is happening in several therapeutic areas, not just specialty

• Payers will seek more intensive cost containment measures to drive down prices

• The need for affordable quality medicines remains key for sustainability of healthcare systems

*Cutting medicine prices is not the solution to reduce costs; improving outcomes should be the objective*

Efficient healthcare is the mantra
Thank you

alan.sheppard@quintilesims.com