Innovative Medicines Division\(^1\)

Pharmaceuticals and Oncology Business Units

Meet Novartis Management | May 24-25, 2016

\(^1\) The deck reflects the new structure effective July 1, 2016
Executive summary

Innovative Medicines Division

- The division is well positioned among companies focused on innovative medicines; underpinned by excellence in R&D, global scale and leading brands within their disease areas.

- Therapeutic depth is increasing across franchises and the go-to-market model is evolving.

- 2016 is a transition year absorbing Gx Gleevec® impact, investing to build two potential multi-blockbusters:
  - Cosentyx®: Launched in three indications in major markets worldwide and the only fully human anti-IL17A inhibitor with sustained response and superiority vs. current treatments\(^1\)
  - Entresto®: First launches around the world in HFrEF and already included in clinical guidelines\(^2\). FortiHFy clinical program includes further pivotal studies, incl. PARAGON-HF in HFrEF, and further studies in HFrEF.

- Continued investment in R&D:
  - Investment across all 7 franchises with up to 6 near-term catalysts (LEE011; RLX030; AMG 334; OMB157; OAP030/RTH258; QAW039)\(^3\) and continued investment in 1st and 2nd generation IO therapies.

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\(^1\) Superiority vs etanercept in psoriasis (PsO) and ustekinumab in PsO (source: European SmPC)

\(^2\) 2016 ESC guidelines (Europe) and 2016 ACC/AHA guidelines (US)

\(^3\) Novartis has licensed rights to AMG 334 and OAP030 outside the US – see relevant franchise sections and appendix for further information
Agenda

- Overview
- Pharmaceuticals Business Unit
- Oncology Business Unit
Novartis Innovative Medicines ranked #2

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Company</th>
<th>Rx Sales¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Roche</td>
<td>$36bn</td>
</tr>
<tr>
<td>2</td>
<td>Novartis</td>
<td>$33bn²</td>
</tr>
<tr>
<td>3</td>
<td>Pfizer</td>
<td>$32bn</td>
</tr>
<tr>
<td>4</td>
<td>GILEAD</td>
<td>$32bn</td>
</tr>
<tr>
<td>5</td>
<td>Johnson-Johnson</td>
<td>$28bn</td>
</tr>
<tr>
<td>6</td>
<td>MERCK</td>
<td>$27bn</td>
</tr>
<tr>
<td>7</td>
<td>SANOFI</td>
<td>$23bn</td>
</tr>
<tr>
<td>8</td>
<td>AstraZeneca</td>
<td>$22bn</td>
</tr>
<tr>
<td>9</td>
<td>abbvie</td>
<td>$22bn</td>
</tr>
<tr>
<td>10</td>
<td>AMGEN</td>
<td>$21bn</td>
</tr>
<tr>
<td>11</td>
<td>GSK</td>
<td>$20bn</td>
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<tr>
<td>12</td>
<td>Eli Lilly</td>
<td>$16bn</td>
</tr>
<tr>
<td>13</td>
<td>Allergan</td>
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<tr>
<td>14</td>
<td></td>
<td>$14bn</td>
</tr>
<tr>
<td>15</td>
<td></td>
<td>$12bn</td>
</tr>
<tr>
<td>16</td>
<td>Bristol-Myers Squibb</td>
<td>$13bn</td>
</tr>
<tr>
<td>17</td>
<td>Kethring Egis</td>
<td>$11bn</td>
</tr>
<tr>
<td>18</td>
<td>TEVA</td>
<td>$11bn</td>
</tr>
<tr>
<td>19</td>
<td>Astellas</td>
<td>$10bn</td>
</tr>
<tr>
<td>20</td>
<td>Teikoku</td>
<td>$10bn</td>
</tr>
</tbody>
</table>

Source: Evaluate Pharma April 2016

1. Rx sales excludes undisclosed partner sales, OTC, Gx, Vaccines & Other sales (eg Royalties, Alliance etc.). Major vaccines excluded for the top 10: Prevnar® Family (Pfizer), Pediarix® (GSK), Gardasil® (Merck), Zostavax® (Merck), Fluzone® (Sanofi) & Pentacel® (Sanofi)

2. Novartis Innovative Medicines Division sales revised to reflect the new divisional structure (i.e. Alcon Pharma moves to Pharma unit and Mature Products moves to Sandoz)
Innovative Medicines Division: Our strategy remains the same...

Aspire to:
- Record # of approvals
- Top tier in sales and profit growth
- Strong reputation

1. Disease area focused portfolio (from development to commercialization) with truly global footprint
2. Evolving our Business Model, incl. transforming Medical Education and strengthening capabilities in Digital Medicines and Real World Evidence
3. Great people and culture based on shared values

RIGHT drug ✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️
...and we are re-imagining the go-to-market model

Research and drug discovery

- CLINICAL DEVELOPMENT
- REGISTRATION
- REIMBURSEMENT
- COMMERCIALIZATION

Patients
("undifferentiated / not personalized")

- Healthcare providers
- Payors
- Payors
- Data analytics & insights
- Data generation

Person with a chronic condition

Specialists, GPs, nurses, dieticians, physical therapists, etc.

Private or public

Lifestyle & Vitals (e.g. wireless wearables)
Self-reported metrics (e.g. quality of life, adherence)

Data storage, integration and insights for patient, HCP and payor

HEALTH MANAGEMENT

OUTCOMES-BASED CONTRACTING
A strong track record of innovation: Leading number of total NCE / NME approvals across key geographies

New chemical/molecular entity (NCE / NME) approvals for selected companies
Q1 2011 – Q1 2016

<table>
<thead>
<tr>
<th>EU EMA</th>
<th>US FDA</th>
<th>Japan PMDA</th>
<th>China SFDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novartis</td>
<td>15</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>Merck/SGP</td>
<td>5</td>
<td>6</td>
<td>7</td>
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<tr>
<td>Pfizer/Wyeth</td>
<td>7</td>
<td>5</td>
<td>9</td>
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<tr>
<td>GSK</td>
<td>8</td>
<td>7</td>
<td>9</td>
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<tr>
<td>J&amp;J</td>
<td>12</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>BMS</td>
<td>9</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>7</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Roche/Genentech</td>
<td>7</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Sanofi</td>
<td>9</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>3</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Bayer</td>
<td>4</td>
<td>3</td>
<td>8</td>
</tr>
</tbody>
</table>

Current Novartis portfolio: 11 FDA Breakthrough Therapy Designations to date

1 Vaccines are excluded. (Source: FDA, EMA, PMDA, CFDA websites – snapshot as of April 1, 2016)
2 The number of 11 FDA Breakthrough Therapy designations (BTDs) includes compounds acquired from GSK (e.g. Tafinlar®) and the 3 recent Ilaris® BTDs. It excludes Bexsero®
The Innovative Medicines journey: Absorbing Gx, investing for growth and transforming the portfolio

Selected drivers of sales evolution
Illustrative timing

- Productivity improvements and effective resource allocation / prioritization
- Current Growth Products¹, incl. Oncology assets and launches of Entresto® / Cosentyx®
- Potential Future launches incl. LEE011, RLX030, AMG 334...
- Gx: Diovan®, Exforge®, Exelon® Patch, Glivec®
- Gx: Gilenya®, Afinitor®

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<tbody>
<tr>
<td>Margin expansion</td>
<td>Growth from Entresto®, Cosentyx®, Onco² fueling new launches, absorbing Gx</td>
<td>Transformed portfolio benefitting from launches</td>
<td></td>
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</tbody>
</table>

¹ Growth Products comprise products launched in a key market (EU, US, Japan) in 2011 or later, or products with exclusivity until at least 2020 in key markets
² Including and not limited to newly acquired Oncology assets from GSK transaction closed in March 2015
Two Business units and seven franchises to address unmet needs and compete through innovative solutions.
Immunology & Dermatology

- Atopic Dermatitis
- Psoriasis
- Psoriatic Arthritis
- Rheumatoid Arthritis
- Sjögren’s Syndrome
- Ankylosing Spondylitis
- Cholestatic Disorders
- Liver Disease
- Non-radiographic Axial Spondyloarthritis
- Transplant
Fully human IL17A inhibitor Cosentyx® on track for multi-blockbuster in rapidly growing segments

Potential to deliver USD ~4-5bn across Dermatology and Rheumatology

2 Potential Cosentyx® peak sales per indication, the years noted refer to achieved and expected years of approval in US and EU
Cosentyx® set new standards in skin clearance...

Cosentyx® sustains superiority vs Stelara®

% PASI 90 respondents

<table>
<thead>
<tr>
<th>Week</th>
<th>Responders %</th>
<th>PASI 75</th>
<th>PASI 90</th>
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<tbody>
<tr>
<td>0</td>
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<tr>
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<td>48</td>
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<tr>
<td>52</td>
<td>100</td>
<td>76.2%</td>
<td>60.6%</td>
</tr>
</tbody>
</table>

p<0.0001

83.0% 88.9%

63.8% 68.5%

Psoriasis

Cosentyx® sustains efficacy up to three years

% PASI 75/90 respondents

<table>
<thead>
<tr>
<th>Week</th>
<th>Responders %</th>
</tr>
</thead>
<tbody>
<tr>
<td>52</td>
<td>0</td>
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<tr>
<td>60</td>
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<td>68</td>
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<td>140</td>
<td>0</td>
</tr>
<tr>
<td>148</td>
<td>100</td>
</tr>
</tbody>
</table>

88.9% 83.0%

68.5% 63.8%

8 in 10 psoriasis patients achieve clear or almost clear skin

1 Blauvelt A et al. 52-week results from the CLEAR study. Late breaking abstract at AAD 2016. March 5, 2016; Stelara® is a registered trademark of Johnson & Johnson
2 Bissonnette R et al. Presented at: EADV Oct 2015, Denmark
3 Cosentyx Summary of Product Characteristics, January 2015

| Meet Novartis Management | May 24-25, 2016 | Investor Presentation |
...delivers fast, sustained response in joints and skin in PsA

~80% of biologic-naïve patients achieve clinical efficacy (ACR20) through 1 year\textsuperscript{1,2}

\begin{center}
\begin{tikzpicture}
\begin{axis}[
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    height=0.3\textwidth,
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    ylabel={Responders %},
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    ymin=0, ymax=90,
    ytick={0,10,20,30,40,50,60,70,80,90},
    xtick={0,4,8,12,16,20,24,28,32,36,40,44,48,52},
    legend pos=north east,
]

\addplot[orange,mark=square] coordinates {
    (0,15.9)
    (4,63.5)
    (8,79.4)
    (12,68.7)
    (16,63.5)
    (20,58.2)
    (24,63.5)
    (28,68.7)
    (32,79.4)
    (36,68.7)
    (40,63.5)
    (44,58.2)
    (48,63.5)
    (52,68.7)
};
\addlegendentry{Cosentyx 150 mg (n = 67)}

\addplot[brown,mark=triangle] coordinates {
    (0,15.9)
    (4,63.5)
    (8,79.4)
    (12,68.7)
    (16,63.5)
    (20,58.2)
    (24,63.5)
    (28,68.7)
    (32,79.4)
    (36,68.7)
    (40,63.5)
    (44,58.2)
    (48,63.5)
    (52,68.7)
};
\addlegendentry{Cosentyx 300 mg (n = 63)}

\addplot[gray,mark=diamond] coordinates {
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    (4,63.5)
    (8,79.4)
    (12,68.7)
    (16,63.5)
    (20,58.2)
    (24,63.5)
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    (32,79.4)
    (36,68.7)
    (40,63.5)
    (44,58.2)
    (48,63.5)
    (52,68.7)
};
\addlegendentry{placebo (n = 63)}

\end{axis}
\end{tikzpicture}
\end{center}

~80% of patients also achieve no progression of structural damage through 2 years\textsuperscript{3}

In PsA, Cosentyx\textsuperscript{®} delivers rapid and clinically meaningful benefits\textsuperscript{1,2}

- Joint symptoms
- Skin symptoms
- Dactylitis & enthesitis

\textsuperscript{1} McInnes IB, et al. Lancet 2015;386:1137–46
\textsuperscript{3} Mease P, et al. Oral presentation at the American College of Rheumatology (ACR) 2015 Annual Scientific Meeting, San Francisco, CA, USA.
...and inhibits progression of spinal structural damage in AS

~80% of patients achieve no progression of spinal structural damage at 2 years\(^1,2\)

![Graph showing cumulative probability of ΔmSASSS at Week 104 for secukinumab IV–75 mg (n = 82) and secukinumab IV–150 mg (n = 86).]

~80% of bio-naive patients achieve sustained clinical efficacy (ASAS20) through 1 year\(^3\)

In AS, Cosentyx® delivers rapid and clinically meaningful benefits\(^4\)

- Signs & symptoms
- Physical function

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\(^1\) Baraliakos X, et al. Late-breaking abstract 6L: American College of Rheumatology (ACR) Annual Meeting, November 2015, San Francisco, USA

\(^2\) Measured by X-ray


Longevity of response, low immunogenicity and high recapture of response with Cosentyx®

Key adverse events | Any secukinumab dose |
--- | --- |
Injection site reaction\(^1\) | <1% |
Immunogenicity\(^2\) | <1% |
Neutralizing antibodies with loss of efficacy\(^2\) | 0% |

- Long-term efficacy on skin and joints is a primary treatment goal for physicians and patients\(^3\)
- Cosentyx® demonstrates a high recapture of response (95%) following retreatment after withdrawal at week 52\(^4\)
- Lack of injection site reactions and no injection pain are important for patients\(^3\)

\(^1\) Poster published IPFA 2015; Langley et al. NEJM 2014
\(^2\) US product insert
\(^3\) Data on file
\(^4\) Based on PASI 75 (Blauvelt et al. Late Breaker Poster presentation, AAD 2015)
Cosentyx® is outpacing competitors in record time due to strong clinical profile across indications.

1 Total TRx data across indications and specialties incl. dermatologists and rheumatologists. (Source: NPA weekly data; data till week ending April 1, 2016)

2 Biologics segment defined as Humira®, Enbrel®, Simponi®, Stelara®, Cimzia®, Cosentyx®, Otezla®, infliximab (Source: IMS)

All trademarks are the property of their respective owners.
Cosentyx®: Approved in all major markets across three indications

Source: Novartis (Apr 2016). Note that only PsO and PsA are approved in Japan & Maylasia (not AS)
An extensive clinical program will generate data across indications

### Selection of Trials

<table>
<thead>
<tr>
<th>Psoriasis</th>
<th>Psoriatic Arthritis</th>
<th>Ankylosing Spondylitis</th>
<th>NrAxSpA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Registration and label expansion trials</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CLEAR (H2H superiority vs. Stelara®)</td>
<td>FUTURE 5 (X-ray)</td>
<td>Japan registration study</td>
<td>Registration study (EU, US, JP)</td>
</tr>
<tr>
<td><strong>CLARITY</strong> (H2H superiority vs. Stelara®)</td>
<td><strong>EXCEED 1</strong> (H2H superiority vs. Humira®)</td>
<td>China registration study</td>
<td></td>
</tr>
<tr>
<td>TRANSFIGURE (nail)</td>
<td></td>
<td></td>
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<tr>
<td>GESTURE (palmoplantar)</td>
<td></td>
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<tr>
<td>China registration study</td>
<td></td>
<td></td>
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<tr>
<td>Pediatric psoriasis</td>
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<tr>
<td><strong>Long-term data generation</strong></td>
<td></td>
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<tr>
<td>ERASURE (placebo)</td>
<td>FUTURE 1 (X-ray)</td>
<td>MEASURE 1 &amp; extension (X-ray)</td>
<td></td>
</tr>
<tr>
<td>FIXTURE (H2H superiority vs. Enbrel®)</td>
<td>FUTURE 2 (PFS)</td>
<td>MEASURE 2 (PFS)</td>
<td></td>
</tr>
<tr>
<td>SCULPTURE (FI vs. RAN)</td>
<td>FUTURE 3 (AI)</td>
<td>MEASURE 3 (300 mg)</td>
<td></td>
</tr>
<tr>
<td>STATURE (partial responders)</td>
<td>FUTURE 4 (load/no-load)</td>
<td>MEASURE 4 (load/no-load)</td>
<td></td>
</tr>
<tr>
<td><strong>Scientific insights and real world data</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>SIGNATURE: TNF-IR switch</td>
<td>Achilles (enthesitis)</td>
<td>STOPAIN (spinal pain)</td>
<td></td>
</tr>
<tr>
<td>PROSE: HRQOL outcomes</td>
<td>MAXimize (axial PsA)</td>
<td>ACHILLES (enthesitis)</td>
<td></td>
</tr>
<tr>
<td>GAIN: Bi-weekly maintenance for partial responders</td>
<td>Switch vs. Enbrel® (in TNF-IR)</td>
<td>SERRENA SPA NIS</td>
<td></td>
</tr>
<tr>
<td>OPTIMISE: Maintenance treatment optimization</td>
<td>ULTIMATE PDUS PsA study (imaging)</td>
<td>RWE (registry)</td>
<td></td>
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<tr>
<td>CORRONA: US Registry</td>
<td>Road to remission</td>
<td>Tight control</td>
<td></td>
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<tr>
<td></td>
<td>Early PsA</td>
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<tr>
<td></td>
<td>RWE (registry)</td>
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<tr>
<td></td>
<td>SERRENA AQUILLA (NIS)</td>
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</tbody>
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*All trademarks are the property of their respective owners
FI: fixed internal as needed, RAN: re-treatment as needed, PFS: pre-filled syringe, AI: auto-injector, NIS: non-interventional study, RWE: real world evidence*
Head-to-head superiority trials underway in three indications to potentially become standard of care

- Most comprehensive head-to-head program to date in psoriasis, PsA and AS
- Registration study to add potential NrAxSpA indication
- Trial read-outs may further enhance the Cosentyx® label
- Real world evidence supports clinical use cases e.g. early treatment and TNF naive

*CLEAR* 
assessing superiority vs. Stelara® at week 16\(^1\) & 52

*CLEARITY*
assessing superiority vs. Stelara® for US label

*EXCEED 1*
assessing superiority vs. Humira® in PsA

*SURPASS*
assessing superiority vs. Humira® in AS

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\(^1\) EU label includes 16 week superiority claim already; US label does not

All trademarks are the property of their respective owners.
Ilaris® received 3 FDA Breakthrough Therapy Designations for Periodic Fever Syndromes

Ilaris® CLUSTER trial

Ilaris® offers major therapeutic benefit for patients with TRAPS, HIDS and FMF

Ilaris® is effective and well tolerated

Submission completed in US, EU and JP

FDA breakthrough therapy designations received

Autoinflammatory conditions with recurrent attacks of high and disabling fever

Often accompanied by severe systemic inflammation and pain

No approved treatments for TRAPS and HIDS, and very limited options for FMF

FMF: Familial Mediterranean Fever
HIDS: Hyperimmunoglobulin D Syndrome, also called Mevalonate Kinase Deficiency (MKD)
TRAPS: Tumor Necrosis Factor Receptor Associated Periodic Syndrome
Targeting NASH – a chronic, progressive liver disease with no approved therapy – through FXR-agonism

### Pathophysiology of NASH

**Healthy Liver**

**Non-Alcoholic Fatty Liver (NAFL)**

**Non-Alcoholic Steatohepatitis (NASH)**

**De-Compensated Cirrhosis / Cancer**

- Liver inflammation +/- fibrosis, including cirrhosis
- Currently second leading cause of liver transplant in the US

### FXR agonism

Farnesoid X Receptor (FXR) is a nuclear hormone bile acid receptor expressed at high levels in the liver & intestine.

FXR agonism decreases inflammation, stellate cell activation and lipid accumulation in the liver

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1 Wong et al, Gastroenterology 2015; 148, 547-555
**LJN452: a potent, non-bile acid FXR agonist with a highly differentiated profile (early stage)**

### EFFICACY

<table>
<thead>
<tr>
<th>Effect</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti fibrotic</td>
<td>Strong effect in pre-clinical models</td>
</tr>
</tbody>
</table>
| NASH resolution | Strong effect in pre-clinical models of cholestasis & NASH  
- ~300 times more potent than OCA\(^1\) based on cellular assays\(^2\) |
| LDL-C | No elevation in obese / healthy volunteers (2 week treatment)  
- Non-Bile Acid derived FXR agonists do not elevate LDL-C in primates |

### SAFETY

<table>
<thead>
<tr>
<th>Effect</th>
<th>Description</th>
</tr>
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</table>
| Pruritus | Not expected (non Bile Acid)  
- No TGR5\(^3\) agonist activity |
| Structure | Non Bile Acid  
- Limited recirculation & systemic exposure (may improve safety profile) |

---

\(^1\) OCA: Obeticholic acid  
\(^2\) Internal data on file  
\(^3\) TGR5: the G protein-coupled bile acid receptor 1 (GPBAR1), may have positive effect of eliciting weight loss via gut hormone
Thrombosis / Stroke

Coronary Artery Disease

Heart Failure

Peripheral Arterial Disease

Hypertriglyceridemia

Metabolic Disorders

Cardio-Metabolic
It’s only the beginning: further approvals, launches and reimbursements for Entresto® to come

Q1 2016
>50 approvals

Q1 2017
>70 approvals expected

Approved
Launched
Launched & reimbursed
Entresto® performance...

Relative uptake (US and Europe)¹
% patient penetration

A slow start in the US...
- Promotional launch as of Jan 2016²
- 91% Medicare patients covered as of Apr 2016
- Share of voice recently expanded with FF and DTC effective Apr 2016

...while encouraging in EU
- A faster initial patient uptake
- CH/DE launched with:
  - Full launch
  - Full coverage of cardiologists and PCPs
  - Broad access from launch
- FR: restricted coverage and access only under Art. 48
- UK: NICE positive guidance³
- DE: IQWiG assessment supports “considerable benefit” for 100% of in-label population

¹ Monthly patient penetration calculated as number of patients on Entresto® divided by pool of HFrEF patients in country. Estimates based on sales (treated) and prevalence (pool). Data per April 29, 2016
² Restricted Product Insert (PI) launch only from July to December 2015 in the US
³ For a population more restricted than in the label
Novartis Entresto® given strong Class I recommendation in both US and EU heart failure guidelines, less than a year after regulatory approvals

- US guidelines now recommend Entresto as standard of care for HFrEF as an alternative to ACEs or ARBs; call for doctors to switch patients with mild to moderate symptoms to Entresto

- Updated guidelines from the European Society of Cardiology recommend Entresto instead of an ACE or ARB in patients fitting the PARADIGM-HF profile

- Guidance underscores the benefits of Entresto for patients to significantly reduce risk of death due to cardiovascular causes or heart failure hospitalization
### Novartis Entresto® given strong Class I recommendation in both US and EU heart failure guidelines, less than a year after regulatory approvals

#### US Guidelines from ACC/AHA

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B-R</td>
<td>In patients with chronic symptomatic HFrEF NYHA Class II or III who tolerate an ACE inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.</td>
</tr>
</tbody>
</table>

#### ESC Guidelines

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B</td>
<td>Sacubitril/valsartan is recommended as a replacement for an ACE-I to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACE-I, a beta-blocker and an MRA¹</td>
</tr>
</tbody>
</table>

¹ Patient should have elevated natriuretic peptides (plasma BNP ≥150 pg/mL or plasma NT-proBNP ≥600 pg/mL, or if HF hospitalization within the last 12 months, plasma BNP ≥100 pg/mL or plasma NT-proBNP ≥400 pg/mL) and able to tolerate enalapril 10 mg b.i.d.
Scaling up to deliver on Entresto® for appropriate patients in the US, and worldwide

1. Expand promotion and share of voice
   - Field force expanded by 50%
   - Evaluating timing for further PCP field force expansion
   - Launched “Tomorrow” direct to consumer campaign

2. Inform patients and practices about reimbursement process
   - Continue Entresto® Central¹ platform and CoverMyMeds¹ services as well as the distribution of blank plan specific PA forms directly to the HCP offices
   - Educate on office challenges with PA process and managed care issues, given most cardiology practices have limited experience with PA process; each payer issues its own PA²

3. Expand and execute the clinical program “FortiHFy”
   - Two pivotal trials with outcomes endpoints to support potential new indications (HFpEF 2019, HF post acute MI 2020)
   - Broaden data in HFrEF beyond PARADIGM population
   - Generate additional data regarding potential symptomatic / QoL benefits
   - Generate real world evidence

² Different insurers have different PAs for the same medicine (e.g. Entresto®); cardiology practices face various brands which recently launched and require PAs, like Entresto®, PCKS9s and Corlanor® (Corlanor® is a registered trademark of Biofarma)
FortiHFy: Generating further data in an extensive clinical program (selected examples)...

With >40 ongoing / planned trials, with over 30,000 investigators¹
Expand clinical evidence in HF patients incl. in HFrEF “non-PARADIGM”

Generate additional data across different patient populations
Trials include
• PARAGON (HFpEF)
• PARADISE-HF (post acute MI)
• PARALLEL-HF (HFrEF Japan)
• TRANSITION (pre-/post-discharge)
• PIONEER-HF (pre-discharge)

Assess impact on symptoms and QoL (in HFrEF)
Trials including:
• PARASAIL (tolerability & HRQoL)

Drive mechanistic insights
Trials including:
• Exercise Capacity

Establish RWE² and Disease Management
Registries / Trials including:
• REPORT-HF (disease registry)
• CHAMP-HF (outpatient registry)
• GWTG-AHA registry (real world evidence)
• PARADIGM-HF OL extension
• Multiple Patient Program

¹ Novartis press release May 19, 2016
² RWE: Real World Evidence
### Selected key trials design and timing

<table>
<thead>
<tr>
<th>Clinicaltrials.gov</th>
<th>Trial</th>
<th>Trial description</th>
<th>Results expected</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT01920711</td>
<td>PARAGON</td>
<td><strong>HFrEF:</strong> Evaluation of the efficacy and safety of LCZ696 compared to valsartan, on morbidity and mortality in heart failure patients (NYHA Class II-IV) with preserved ejection fraction</td>
<td>2019/2020</td>
<td>4,600</td>
</tr>
<tr>
<td>TBD</td>
<td>PARADISE-HF</td>
<td><strong>Post acute MI:</strong> Prospective ARNI versus ACE inhibitor trial to determine superiority in reducing heart failure events after myocardial infarction</td>
<td>2020</td>
<td>4,650</td>
</tr>
<tr>
<td>NCT02468232</td>
<td>PARALLEL-HF</td>
<td><strong>HFrEF Japan:</strong> Evaluation of the efficacy and safety of LCZ696 compared to enalapril on morbidity and mortality in Japanese patients with chronic heart failure and reduced ejection fraction</td>
<td>2019</td>
<td>220</td>
</tr>
<tr>
<td>NCT02661217</td>
<td>TRANSITION</td>
<td><strong>Pre-/post-discharge:</strong> Comparison pre-discharge and post-discharge treatment initiation with LCZ696 in heart failure patients with reduced ejection-fraction hospitalized for an acute decompensation event (ADHF)</td>
<td>2019</td>
<td>1,000</td>
</tr>
<tr>
<td>NCT02554890</td>
<td>PIONEER-HF</td>
<td><strong>Pre-discharge:</strong> Comparison of sacubitril/valsartan versus enalapril on effect on NT-proBNP in patients stabilized from an acute heart failure episode</td>
<td>2018</td>
<td>736</td>
</tr>
<tr>
<td>NCT02595814</td>
<td>REPORT-HF</td>
<td><strong>Disease registry:</strong> Clinical characteristics, initial presentation, management, and outcomes of patients hospitalized with new-onset (first diagnosis) heart failure (HF) or decompensation of chronic HF are poorly understood worldwide. REPORT-HF is a global, prospective, and observational HF disease registry designed to characterize patient trajectories longitudinally during and following an index hospitalization for acute HF</td>
<td>2021</td>
<td>20,000</td>
</tr>
</tbody>
</table>
Entresto® has significant potential across indications, incl. post acute MI

Potentially eligible patients

Patient potential over time

- Post acute MI at risk of HF (planned filing 2020+)
  ~0.3m potential patients

- HFpEF (planned filing 2019)
  ~8.5m potential patients

- Approved in US and Europe
  - HFrEF, NYHA II-IV
  - CH only: QoL / symptom benefit
  ~8.5m potential patients

1 Potential patients are defined by the indications studied in the ongoing / planned trials in HFpEF and post acute MI. Potentially eligible population dependent on trial results and label. Current estimates are illustrative
2 Pivotal trials with outcomes endpoints to support new indications
3 Pending regulatory agreement
RELAX-AHF-2 and CANTOS trials are progressing

### RELAX-AHF-2 Trial

- **RLX030**
- **Placebo**

**Standard HF$^1$ therapy**

- Day 0
- Day 2
- Day 180

**Primary endpoints**

- Time to first CV$^1$ death during follow-up period (180 days)
- Time to first occurrence of worsening heart failure through Day 5

### CANTOS Trial

- 50mg ACZ885 + SoC
- 150mg ACZ885 + SoC
- 300mg ACZ885 + SoC
- Placebo + SoC

**End at 1400 events ~4.5 years average treatment**

#### Primary endpoint

- Time to first MACE$^1$ event which is a composite of CV death, non-fatal MI, and stroke

---

$^1$ CV: Cardiovascular; HF: Heart Failure; MACE: Major Adverse Cardiac Event
LIK066: Addressing underlying metabolic risks in the pandemics of Diabetes and Obesity

When given immediately prior to a meal, LIK066 reduced exogenous glucose appearance

Blocking reabsorption of filtered glucose by SGLT1 and SGLT2 in the kidney, results in increased loss of glucose through the urine

Inhibiting intestinal SGLT1 delays/reduces intestinal glucose absorption and stimulates distal L and K cells to release incretin hormones that reduce appetite and may enhance weight loss (GLP-1, PYY)

Positive PoC¹ data in obese / overweight patients expected to be disclosed later in 2016

¹ PoC: Proof of Concept study
Respiratory

- Asthma
- Idiopathic Pulmonary Fibrosis
- Cystic Fibrosis
- Pulmonary Arterial Hypertension
- COPD

Meet Novartis Management | May 24-25, 2016 | Investor Presentation
Ultibro® Breezhaler® is superior to Seretide® in reducing COPD exacerbations

**FLAME¹ study**  
Ultibro® Breezhaler® vs. Seretide®

- **Ultibro® Breezhaler® demonstrated consistent superiority over Seretide®**  
  - Regardless of patient’s disease severity or eosinophil levels

- **Exacerbation outcomes**  
  - Significantly reduced rate of moderate or severe exacerbations (17%)  
  - Significantly prolonged time to first moderate or severe exacerbation (22%)

- **Lung function**
- **Health-related quality of life (HRQoL)**

---

² Seretide® is a registered trademark of GlaxoSmithKline
Reducing severe exacerbations matters for COPD patients; it affects their QoL and their prognosis\(^1\)

**Mortality after first severe COPD exacerbation**

- 23% at 1 year\(^1\)
- ~70% at 7 years\(^1\)

**Mortality after first myocardial infarction (MI)**

- 8% STEMI\(^2\)
- 19% NSTEMI\(^2\)
- at 1 year\(^3\)
- 31% male
- 47% female at 7 years\(^4\)

---

\(^1\) Novartis press release May 15, 2016
\(^2\) STEMI: ST elevation myocardial infarction, NSTEMI: non-ST elevation myocardial infarction
QAW039 (fevipiprant) is a potent inhibitor of CRTh2-driven functional effects of PGD2 on effector cells

- An oral highly selective, reversible antagonist
  - High affinity for the CRTh2 receptor\textsuperscript{1-3}
- Shows slower receptor dissociation than other CRTh2 antagonists\textsuperscript{2}
  - Prolonged receptor occupancy may play an important role in clinical efficacy
- Inhibits CRTh2-driven functional effects of PGD\textsubscript{2} on effector cells\textsuperscript{4-7}
  - Prevents inflammatory cell migration
  - Decreases Th-2 cytokine (IL-4, IL-5 and IL-13) production
- Shows superior potency compared with other CRTh2 antagonists\textsuperscript{1-3}

\textsuperscript{1} Willard L et al. Eur Respir J 2014;44 (Suppl 58):P4072
\textsuperscript{2} Sykes D et al Mol Pharmacol 2016 DOI: 10.1124/mol.115.101832
\textsuperscript{3} Other anti-CRTh2 included in the analysis were QAV680, AZD-1981, QC-459 and BI-671800; tests were in-vitro
\textsuperscript{4} Barnes et al. Clin Exp Allergy 2012 42: 38-48
\textsuperscript{5} Gonem et al. ERS 2014
\textsuperscript{6} Berair ATS 2015
\textsuperscript{7} Stinson et al. J Allergy Clin Immunol 2015 135: 395-406
QAW039 (fevipiprant): Potential first-in-class CRTh2 antagonist for the treatment of asthma

- Potential to address patient segment with high unmet need
  - Small molecule with once daily oral administration
  - Effectively suppressed sputum eosinophils in Phase II study
  - Improved quality of life in same study
- Planned filing in 2019
- In addition, QVM149 and QMF149 started Ph III asthma programs ex-US

**Fevipiprant Phase III Program**

- GINA steps 4 and 5 standard-of-care asthma therapy
- Fevipiprant (QAW039) 150 mg
- Placebo
- Fevipiprant (QAW039) 450 mg
- Placebo

- Screening
- Baseline
- 2 - 6 week run-in
- 52 week double-blind treatment
- 4 week flu
- Interim analysis for futility
- End of study

**LUSTER-1 and LUSTER-2 trials are ongoing**

- 52-week trials including ~1,700 patients with severe asthma (GINA 4/5)
- Primary objective to evaluate effect on asthma exacerbations
Ophthalmology

- Uveitis
- Glaucoma
- Age-Related Macular Degeneration
- Diabetic Retinopathy
- Geographic Atrophy
- Dry Eye
Addressing strong unmet need in profitable and growing eye care segment

High unmet need
- 80% of global population lives with treatable eye diseases and conditions
- People are living longer

Profitable market
- USD 23 billion in ophthalmic pharmaceutical segment sales
- Strong profitability for companies at scale

Segment Growth
- +5% p.a. projected market growth
- Significant need for science- and technology-driven innovation

Sources: McKinsey & Company Press research; Market Scope; Evaluate Pharma; GIA (Global Industry Analysis)

1 Sx: Surgical, Ph: Pharmaceuticals, VC: Vision Care
Progressing the development of key late-stage assets in Ophthalmology

**OAP030**
- Anti-PDGF agent in development for the treatment of neovascular AMD
- 1-year topline results from ongoing pivotal trials expected in 2016
- Planned filing in 2017

**RTH258**
- Next generation anti-VEGF therapy based on single chain antibody fragment (scFv)
- Potential for longer duration of action and improved formulation options / less frequent dosing
- Pivotal trials ongoing, planned filing 2018

---

**Anti-PDGF/anti-VEGF combination therapy**

**Antibody size comparison**

AMD: age-related macular degeneration
PDGF: platelet-derived growth factor
VEGF: vascular endothelial growth factor

---

1 Also known as Fovista® (pegpleranib) and E10030. This product is being developed by Ophthotech Corp. Ophthotech has licensed ex-US commercialization rights to Novartis under a Licensing and Commercialization Agreement
Neuroscience

Alzheimer’s Disease

Migraine

Multiple Sclerosis

Muscle Wasting / Muscle Weakness

Neuropathic Pain
Selected development programs in Neuroscience

**Multiple sclerosis**
- Gilenya® pediatric RRMS
- BAF312 SPMS
- OMB157\(^1\) RMS

**Specialty neurology**
- AMG 334\(^3\) migraine prophylaxis
- EMA401 neuropathic pain

**Neuromuscular disease**
- BYM338\(^2\) Hip fracture recovery in Ph IIa/b
- Sarcopenia in Ph IIb

**Alzheimer’s disease**
- CAD106
- CNP520

---

\(^1\) OMB157 is also known as ofatumumab

\(^2\) Primary endpoint of Ph II/III in sporadic Inclusion Body Myositis (sIBM) was not met; data are under review

\(^3\) Licensed from Amgen for ex-US/Canada/Japan territories
OMB157: Potential for best-in-class anti-B-cell therapy for Multiple Sclerosis

World-class commercial and medical MS capabilities, Gilenya® is ex-US MS market leader

Established credibility in MS

Selective binding

Favorable safety profile

Potential for low immunogenicity

Subcutaneous dosing

Successful dose finding

Every 4 weeks subcutaneous application as maintenance therapy

Highly potent and specifically targets distinct epitope on the human CD20 molecule, both the large and small extracellular loops, expressed on B cells

Human IgG1 kappa (IgG1κ) monoclonal antibody, no mouse sequences - efficacy less likely to diminish on prolonged treatment

Improved management of effects on B-cells and low frequency of post-injection systemic reactions

Low dose of ofatumumab is expected to be as effective as other high dose anti-CD20 antibodies

Ph III trials expected to start in Q3-2016 with planned filing in 2019

Ph II MIRROR Study CSR, Novartis data on file

Ph II Bar-Or A et al., Presented at AAN, April 2014

Ph II Two Phase III trials with teriflunomide as active comparator in parallel

Note: OMB157 is also known as ofatumumab

Ruuls SR et al., Biotechnol J. 2008;3:1157-71

Ofatumumab investigational brochure. Novartis data on file

Sorensen PS et al., Neurology. 2014;82(7):573-81
Alzheimer's prevention: CNP520, a BACE-1 inhibitor co-developed with Amgen, completed Ph II

Inhibition of BACE-1, an enzyme involved in the processing of the amyloid precursor protein, intervenes early in the amyloid pathway and reduces levels of Aβ peptides

- Chronic BACE inhibitor treatment in animals stops further amyloid deposition, normalizes neurodegeneration markers, attenuates neuroinflammation and restores neuronal connectivity

- In AD animal models, CNP520 strongly reduces amyloid, while the undesirable effects observed with other BACE inhibitors were not seen

- CNP520 completed Phase IIa trial in Mar 2016

- A CNP520 cohort is expected to start in H2 2016 within the Alzheimer’s Prevention Study in collaboration with the Banner Alzheimer’s Institute and Amgen, pending regulatory approval
In 2016, CNP520 will be included in a trial enrolling pre-symptomatic patients with 2 copies of the high risk APOE 4 allele.
<table>
<thead>
<tr>
<th>Agenda</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overview</strong></td>
</tr>
<tr>
<td><strong>Pharmaceuticals Business Unit</strong></td>
</tr>
<tr>
<td><strong>Oncology Business Unit</strong></td>
</tr>
</tbody>
</table>
Executive summary

Oncology

• Further advances in oncology as new data continue to emerge

• Despite progress, there remains a major unmet medical need

• Novartis Oncology is the #2 oncology company in the world with a 15+ year track record of innovation and a large commercial footprint to bring assets to market quickly

• Our focus is on cancer types with high unmet need and potential for innovative / differentiated therapies

• Novartis is leveraging its established Targeted Therapy (TT) portfolio and proprietary technologies to understand the pathways in emergent resistance to eventually overcome them

• We have a broad and novel Immuno-Oncology (IO) portfolio and understanding of immune activation to combat cancer in novel ways (TT/IO and IO/IO)
A global leader in oncology

Update on selected pipeline programs

Back-up
A global leader in oncology with USD 13+ billion in sales and broad pipeline across TT and IO

USD 13.5\(^1\) billion in 2015 net sales in oncology positions Novartis as #2 globally

**22 approved medicines**
in solid tumors, hematology and rare diseases

**A broad pipeline**
with over 30 assets in development, in both IO and TT

**More than 10,000 oncology employees**
worldwide operating in 80+ countries

\(^1\) Based on Innovative Medicines Division sales per January 27, 2016 financial statements.
Apply TT/IO to our five focus areas...

Targeted Therapy
Small Molecules
Monoclonal Antibodies

Immuno-Oncology
Checkpoint Inhibitors
2nd Generation IO Targets
Adoptive Cell Therapy CART

Focus

Lung  Melanoma  Breast  RCC  Hematology

Built on our Targeted Therapy and Immuno-Oncology capabilities
...to drive the next generation of differentiated oncology therapies

1. Continue to innovate with TTs
   - File PKC412
   - File LEE011 (CDK 4/6)
   - Complete BYL019 (PI3K) pivotal studies
   - Next generation BCR-ABL inhibitor (ABL001)
   - Develop GSK assets in new indications

2. Advance our broad IO portfolio
   - PD-1, TIM3, LAG3 and PDL-1 checkpoint inhibitors
   - Second generation IO assets (STING, GITR, Het IL-15, TGFBeta, CSF-1, Adenosine receptor)
   - CAR-T platform

3. Develop new combination therapies
   - Address unmet market needs with TT/TT, TT/IO and IO/IO combinations
   - Move potential first-in-class combinations through clinic

4. Leverage R&D strength and global commercial footprint to quickly bring new assets to market
Continue to innovate with TT: Industry-leading early stage TT complements our IO and combination strategy

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Exemplary compounds</th>
<th>Target</th>
<th>PoC(^1) achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI3K/PTEN/AKT</td>
<td>BYL719</td>
<td>PI3Ka selective</td>
<td>✓</td>
</tr>
<tr>
<td>FGF</td>
<td>BGJ398</td>
<td>FGFR-1/2/3</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>FGF401</td>
<td>FGFR4 selective</td>
<td></td>
</tr>
<tr>
<td>RAS/RAF/MAPK</td>
<td>LXH254</td>
<td>CRAF (pan-RAF)</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>LTT462</td>
<td>ERK</td>
<td></td>
</tr>
<tr>
<td>ErbB/HER</td>
<td>EGF816(^2)</td>
<td>EGFR mut</td>
<td>✓</td>
</tr>
<tr>
<td>Apoptosis Regulation</td>
<td>LCL161</td>
<td>IAP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CGM097</td>
<td>P53/HDM2</td>
<td></td>
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<tr>
<td></td>
<td>HDM201</td>
<td>P53/HDM2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BCL201</td>
<td>BCL2</td>
<td></td>
</tr>
<tr>
<td>Epigenetic</td>
<td>MAK683</td>
<td>EED</td>
<td></td>
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<tr>
<td>Wnt</td>
<td>WNT974</td>
<td>Porcupine</td>
<td></td>
</tr>
<tr>
<td>Cell Cycle</td>
<td>LEE011</td>
<td>CDK4/6</td>
<td>✓</td>
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<tr>
<td>BCR/Abl</td>
<td>ABL001</td>
<td>Bcr/Abl allosteric</td>
<td>✓</td>
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<tr>
<td>C-MET</td>
<td>INC280</td>
<td>cMET</td>
<td>✓</td>
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<tr>
<td>PIM</td>
<td>PIM447</td>
<td>Pan-PIM</td>
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</tr>
<tr>
<td>IDH</td>
<td>IDH305</td>
<td>IDH-1</td>
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<tr>
<td>SERD</td>
<td>LSZ102</td>
<td>SERD</td>
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<td>GPCR</td>
<td>LXS196</td>
<td>PKC</td>
<td></td>
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<tr>
<td>ADC</td>
<td>PCA062</td>
<td>P-Cadherin ADC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HKT288</td>
<td>Cadhein-6 ADC</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) Proof-of-Concept  
\(^2\) EGF816 combo with INC280
Continue to innovate with TT: selected new targeted therapies with clinical entry anticipated in 2016

BRAF and KRAS mutant cancers

- LXH254: CRAF inhibitor
- LTT462: ERK inhibitor

Ovarian and renal cancers

- HKT288: Cadherin-6 ADC

Epigenetic modulation

- MAK683: EED inhibitor
While IO has advanced, there is a significant opportunity for Novartis to play

- CTLA-4 blockade induces impressive memory, but has low response rate and inflammatory toxicity
- PD-1/PD-L1 blockade shows broader activity than anti-CTLA-4 mAbs, but durability of responses remains to be fully determined
- CTLA-4 and PD-1 blockade both appear to require pre-existing anti-tumor immunity for clinical benefit, but most patients fail to manifest significant endogenous responses
- Key mechanistic aspects of protective tumor immunity remain poorly understood, complicating patient stratification, monitoring of response, and crafting of efficacious combination therapies
Advance IO: Rapidly progress twelve checkpoint and other novel targets through the clinic

Strong pipeline focused on second generation IO

<table>
<thead>
<tr>
<th>Target</th>
<th>FIH Trial Initiated</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>PD-L1</td>
<td>2016</td>
</tr>
<tr>
<td>LAG3</td>
<td>✓</td>
</tr>
<tr>
<td>TIM3</td>
<td>✓</td>
</tr>
<tr>
<td>CSF-1</td>
<td>✓</td>
</tr>
<tr>
<td>CART-19</td>
<td>✓</td>
</tr>
<tr>
<td>CART-BCMA</td>
<td>✓</td>
</tr>
<tr>
<td>Het IL-15</td>
<td>✓</td>
</tr>
<tr>
<td>Adenosine receptor</td>
<td>✓</td>
</tr>
<tr>
<td>TGFβ</td>
<td>2016</td>
</tr>
<tr>
<td>STING</td>
<td>✓</td>
</tr>
<tr>
<td>GITR</td>
<td>✓</td>
</tr>
</tbody>
</table>

Potential first-in-class
★ Target  ★ Indication
Develop new combination therapies: 16 combination exploratory IO studies expected in 2016

### IO / IO

<table>
<thead>
<tr>
<th>Target</th>
<th>FIH Trial Initiated</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAG3 (LAG525) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>TIM3 (MBG453) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>GITR (GWN323) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>CSF-1 (MCS110) + PD-1</td>
<td>2016</td>
</tr>
<tr>
<td>Adenosine R (NIR178) NSCLC + PD-1</td>
<td>2016</td>
</tr>
<tr>
<td>Het IL-15 + PD-1</td>
<td>2016</td>
</tr>
<tr>
<td>IL-17 + PD-1</td>
<td>2016</td>
</tr>
<tr>
<td>IL-1 + PD-1</td>
<td>2016</td>
</tr>
<tr>
<td>CSF-1 (MCS110) + carbo/gem in TNBC</td>
<td>✓</td>
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### IO with targeted agent

<table>
<thead>
<tr>
<th>Target</th>
<th>FIH Trial Initiated</th>
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<tr>
<td>INC280 (cMet) + PD-1</td>
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</tr>
<tr>
<td>WNT974 (Porcupine) + PD-1</td>
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</tr>
<tr>
<td>Panobinostat + PD-1</td>
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<tr>
<td>Everolimus + PD-1</td>
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<tr>
<td>LCL161 (IAP inh) + PD-1</td>
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<tr>
<td>MEK + PD-1</td>
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<tr>
<td>EGFR + PD-1</td>
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</table>

★ Potential first-in-class
Continue leadership in Cell & Gene Therapy with near-term CTL019 and future development pipeline

<table>
<thead>
<tr>
<th>Near term: CTL019</th>
<th>Potential future prospects</th>
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<tbody>
<tr>
<td>Relapsed / Refractory Pediatric Acute Lymphoblastic Leukemia (r/r ped ALL)</td>
<td>CART</td>
</tr>
<tr>
<td>Global clinical trial:</td>
<td>• BCMA in multiple myeloma</td>
</tr>
<tr>
<td>• Enrollment completed</td>
<td>• CD123 in acute myeloid leukemia</td>
</tr>
<tr>
<td>• Primary endpoint ORR (CR+CRi) at 6 months</td>
<td>Next Generation of CARTs</td>
</tr>
<tr>
<td>• Planned FDA filing by early 2017</td>
<td>• Regulated CARTs</td>
</tr>
<tr>
<td>Relapsed / Refractory Diffuse Large B-Cell Lymphoma (r/r DLBCL)</td>
<td>• Gene editing using CRISPR for allogeneic CARTs</td>
</tr>
<tr>
<td>Global clinical trial:</td>
<td>• Combination strategies (e.g., CART + checkpoint inhibitors)</td>
</tr>
<tr>
<td>• Recruiting in US and EU</td>
<td>FCR001</td>
</tr>
<tr>
<td>• Primary endpoint ORR (PR+CR); secondary endpoints include OS, DOR, PFS</td>
<td>Facilitating cell therapy to induce tolerance, being developed in mismatch living donor kidney transplant, reducing or eliminating need for re-transplants</td>
</tr>
<tr>
<td></td>
<td>HSC835</td>
</tr>
<tr>
<td></td>
<td>Expanded umbilical cord blood stem cells being developed in hematologic malignancies</td>
</tr>
</tbody>
</table>
CTL019: Reprogrammed patient specific T-cells could help fight CD19+ B-cell cancers in r/r disease\(^1\)

1. Patient relapse or refractory to prior therapy
2. Patient's T cells harvested at apheresis center
3. Patient's T cells transferred to Morris Plains
4. CTL019 controlled before quality release
5. CTL019 packaged and cryopreserved (reprogrammed T cells)
6. Modified T cells expanded and harvested
7. T cells activated and transduced with lentiviral vector
8. CTL019 infused into patient and CRS\(^2\) monitoring
9. Patient disease state evaluated +28 days after infusion
10. CTL019 cells transferred to infusion center

\(^1\) In patients with relapsed/refractory disease
\(^2\) CRS: Cytokine Release Syndrome, a common side effect of CART therapies, which may require hospitalization
A global leader in oncology

Update on selected pipeline programs

Back-up
MONALEESA-2 Ph III trial of LEE011 stopped for efficacy in HR+/HER2- advanced breast cancer

Pivotal Phase III trial of LEE011 (ribociclib), a CDK4/6 inhibitor, in combination with letrozole vs. letrozole alone in post-menopausal women with HR+/HER2- advanced breast cancer who had received no prior therapy in the metastatic setting

- The MONALEESA-2 independent Data Monitoring Committee recently recommended that the trial be stopped early as it met the primary efficacy endpoint at the pre-planned interim analysis.
- LEE011 (ribociclib) in combination with letrozole demonstrated a clinically meaningful improvement in progression-free survival (PFS) compared to letrozole alone in post-menopausal women who had received no prior therapy for advanced breast cancer.
- Full results of MONALEESA-2 will be presented at an upcoming medical congress; Novartis is initiating discussions with regulatory authorities worldwide.
LEE011, a CDK4/6 inhibitor, demonstrates promising activity in breast cancer in combination with letrozole

Preliminary response and clinical benefit rates in ongoing Phase I in 1st line treatment, post-menopausal women

- ORR 39% (11/28 patients); CBR\(^1\) 79%
- Mean exposure of 8.8+ months (ongoing)

3 Phase III trials of LEE011 in HR+/HER2-advanced breast cancer:

**MONALEESA-2 (post-menopausal)**
- 1st line in combination with letrozole
- Trial stopped for clinically meaningful improvement in PFS at interim analysis; US and EU filing planned for Q3 2016

**MONALEESA-3 (post-menopausal)**
- 1st/2nd line post AI in combination with fulvestrant
- Final data expected H2 2017; potential filing early 2018

**MONALEESA-7 (pre-menopausal)**
- 1st line in combination with tamoxifen/NSAI and goserelin
- Final data H1 and potential filing H2 2018

6 patients with non-measurable disease or unconfirmed data were excluded

Novartis data on file
\(^1\) CBR: Clinical benefit rate
Novartis is leading the way in advancing CML treatment

**Evolution of Treatment Goals**

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Hematologic or Cytogenetic Response</td>
<td>MMR</td>
<td>Prevent progression to AP/BP</td>
<td>MR4.5</td>
<td>Treatment free remission?</td>
<td>Cure?</td>
</tr>
</tbody>
</table>

**Treatment Landscape**

- Glivec®, a Novartis targeted therapy
- Tasigna®, a Novartis 2nd Generation TKI (and others)
- ABL001, a potential 1st allosteric BCR-ABL inhibitor
- Potential combination therapies, incl. ABL001

**ABL001 Overview**

- Potent, specific inhibitor of BCR-ABL
- Distinct allosteric MOA developed to have activity against BCR-ABL mutations conferring resistance to TKIs, such as Glivec®
- Potential to prevent emergence of resistances in combination with Tasigna® (pre-clinical)

**Program Update**

- Early clinical evidence suggests ABL001 is well-tolerated
- This data also shows that ABL001 is active in heavily-treated CML patients that are resistant to or intolerant of prior TKIs
- Ph I clinical assessment of ABL001 single agent and combinations with other TKIs ongoing

---

1 ASH 2014 presentation, Wylie, abstract #398
2 ASH 2015 presentation, Ottman, abstract #138
AP/BP: Accelerate Phase/Blast Phase; MMR: Major Molecular Response; TKI: Tyrosine Kinase Inhibitor
BYL719 shows preferential antitumor activity in PIK3CA mut BC patients in combination with fulvestrant

Phase I study in heavily pre-treated patients

Preferential antitumor activity seen in breast cancer patients with mutated PIK3CA vs wild type

- PIK3CA mut (response rate 27% and mPFS 9 months) vs. PIK3CA non-mutant (response rate 0% and mPFS 5 months)

Additional studies are ongoing in earlier HR+ HER2- breast cancer patients

- Phase II study in neoadjuvant early breast cancer
- Phase III study of fulvestrant ± BYL719 (SOLAR-1) in 1st/2nd line HR+ breast cancer
Jakavi® demonstrates promising efficacy in GvHD patients

- Novartis recently licensed Jakavi® from Incyte for GvHD ex-US
- Up to 80% of patients with HSCT develop GvHD
- JAK1/2 signaling is a key pathway leading to inflammation and tissue damage in GvHD
- Promising efficacy results include high ORR and OS in both acute and chronic SR GvHD


Jakavi® is in-licensed from Incyte Corp. Ex-US for hematology, oncology, and GvHD indications

1 ORR was 81.5%; 6-months OS was 79.0% and 97.4% in acute and chronic SR GvHD respectively (Leukemia 2015)

Before ruxolitinib 3 weeks after ruxolitinib
MIW815: A STING agonist for enhancing immune response to tumors

STING agonist (cyclic dinucleotides) injection into tumors eliminates both injected and non-injected tumors

MIW815 (collaboration with Aduro) effectively “immunizes” the mouse to tumors

Investigational; efficacy & safety not yet established

Treated and contralateral CT26 tumor growth

First in Human (FIH) anticipated Q2 2016
A global leader in oncology

Update on selected pipeline programs

Back-up
One of the largest clinical development programs in Oncology

With an extensive network of trial sites and physician partners

500+
Active and planned trials

35,000+
Patients planned or currently enrolled in clinical trials

95,000+
Targeted enrollment in 600+ ongoing third-party studies
TT and IO mechanisms and Novartis capabilities in each area

### TT
- **Platform**: TT
- **Mechanism**: Block major oncogenic pathways

### IO
- **Platform**: IO
- **Mechanism**: Overcome pathways of immune escape

#### Novartis capabilities
- Industry leading pipeline and experience with TTs
- Technical and clinical experience w/ TTs in largest segments (lung, breast, heme, RCC, melanoma)
- Relationships with key KOLs and centers (academic and clinical)
- New leadership from Jeff Engelman who will start June 1, 2016
- Broad IO portfolio diversified beyond checkpoint inhibitors
- 6 assets that are potentially first-in-class as monotherapy and 11 as combinations
- Dedicated IO team led by Glenn Dranoff

World-class R&D to accelerate winning combinations to market
Novartis quickly ramped up in IO with a number of key deals and partnerships

- **2012**
  - Penn
  - CART therapies

- **2014**
  - Intellia Therapeutics
  - Gene editing for CART
  - CoStim Pharmaceuticals
  - PD-1, PD-L1, TIM3 & LAG3 Abs

- **2015**
  - ADURO Biotech
  - STING agonists
  - Surface Oncology
  - Next-generation I/O targets
  - Admune Therapeutics
  - hetIL-15 biologic
  - Palo Pharma
  - Adenosine receptor antagonists
  - XOMA
  - TGFβ antibodies

1. License
2. Acquisition
3. Equity Investment
4. Collaboration
### Planned filings 2016 to ≥2020

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<tr>
<th>Year</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>2019</th>
<th>≥ 2020</th>
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<tbody>
<tr>
<td>LEE011 + ltz&lt;sup&gt;b&lt;/sup&gt;</td>
<td>PKC412</td>
<td>ASM&lt;sup&gt;a&lt;/sup&gt;</td>
<td>OAP030&lt;sup&gt;c&lt;/sup&gt;</td>
<td>LCI699</td>
<td>BAF312</td>
</tr>
<tr>
<td>HR+, HER2 (postmenopausal)</td>
<td>Afinitor&lt;sup&gt;c&lt;/sup&gt;</td>
<td>TSC&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Cushing’s disease</td>
<td>Testorol®&lt;sup&gt;TM&lt;/sup&gt;</td>
<td>Testorol®&lt;sup&gt;TM&lt;/sup&gt;</td>
</tr>
<tr>
<td>adv. BCL-2 line</td>
<td>Tafinlar®&lt;sup&gt;d&lt;/sup&gt; + Mekinist®&lt;sup&gt;d&lt;/sup&gt;</td>
<td>BRAT&lt;sup&gt;d&lt;/sup&gt; v690+ NSCLC&lt;sup&gt;d&lt;/sup&gt;</td>
<td>RTH258</td>
<td>KAF156</td>
<td>ASB183</td>
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<td>Arzerra&lt;sup&gt;dc&lt;/sup&gt;</td>
<td>Tasigna&lt;sup&gt;dc&lt;/sup&gt;</td>
<td>Chronic lymphocytic leukemia</td>
<td>Fat翰®&lt;sup&gt;i&lt;/sup&gt;</td>
<td>BKM120</td>
<td>OAX567</td>
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<tr>
<td>CLL (relapse)</td>
<td>CMK&lt;sup&gt;dc&lt;/sup&gt; treatment free remission</td>
<td>Cosentyx®&lt;sup&gt;dc&lt;/sup&gt;</td>
<td>nArkSp&lt;sup&gt;dc&lt;/sup&gt;</td>
<td>Malaria</td>
<td>QGE031</td>
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<tr>
<td>Votrient®&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Arzerra&lt;sup&gt;dc&lt;/sup&gt;</td>
<td>NHIL&lt;sup&gt;j&lt;/sup&gt; (refractory)</td>
<td>Entresto™&lt;sup&gt;TM&lt;/sup&gt; Heart failure</td>
<td>Malaria</td>
<td>CSUM&lt;sup&gt;dc&lt;/sup&gt;</td>
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<tr>
<td>Renal cell carcinoma (adjuvant)</td>
<td>CTL019</td>
<td>LEE011+ fulv HR+, HER2 (postmenopausal)</td>
<td>CAD106</td>
<td>Solid tumors</td>
<td>VAY736</td>
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<tr>
<td>LARI™&lt;sup&gt;TM&lt;/sup&gt;</td>
<td>DBLCL&lt;sup&gt;j&lt;/sup&gt;</td>
<td>HR+, HER2 (premenopausal)</td>
<td>Tafinlar®+ Mekinist®&lt;sup&gt;d&lt;/sup&gt;</td>
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<td>Cushing’s disease</td>
<td>Gilenya®&lt;sup&gt;k&lt;/sup&gt;</td>
<td>Lucentis&lt;sup&gt;®&lt;/sup&gt;</td>
<td>Jakavi®&lt;sup&gt;TM&lt;/sup&gt; GIVID&lt;sup&gt;i&lt;/sup&gt;</td>
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<td>BYM338</td>
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<td>Tafinlar®&lt;sup&gt;d&lt;/sup&gt; + Mekinist®&lt;sup&gt;d&lt;/sup&gt;</td>
<td>ROP&lt;sup&gt;TM&lt;/sup&gt;</td>
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<td>QMF149</td>
<td>Entresto™&lt;sup&gt;TM&lt;/sup&gt; Heart failure</td>
<td>PIM447</td>
<td>Hematologic tumors</td>
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<td>AXK&lt;sup&gt;TM&lt;/sup&gt; + NSCLC&lt;sup&gt;TM&lt;/sup&gt; (1st line, treatment naive)</td>
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<td>Sarcopenia</td>
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<td>New molecule</td>
<td>New indication</td>
<td>New formulation</td>
<td>New molecule</td>
<td>New indication</td>
<td>New formulation</td>
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**Combination Abbreviations:**
- fulv: fulvestrant
- ltz: letrozole
- tmx: tamoxifen
- gsn: goserelin
- NSAI: Non-steroidal aromatase inhibitor

1. Breast cancer
2. Acute myeloid leukemia
3. Tuberculosis complex
4. Chronic lymphocytic leukemia
5. Choroidal neovascularization (CNV) secondary to conditions other than macular degeneration and pathologic myopia
6. Aggressive systemic mastocytosis
7. Non-small cell lung cancer
8. Chronic myeloid leukemia
9. Long-acting release
10. Neurovascular age-related macular degeneration
11. Secondary prevention of cardiovascular events
12. Non-Hodgkin’s lymphoma
13. Diffuse large B-cell lymphoma
14. Multiple sclerosis
15. Non-radiographic axial spondyloarthritis
16. Secondary progressive multiple sclerosis
17. Preserved ejection fraction
18. Graft-Versus-Host Disease
19. Retinopathy of prematurity
20. Relapsing multiple sclerosis
21. Non-alcoholic steatohepatitis
22. Chronic spontaneous urticaria / Inducible urticaria
23. Diabetic macular edema

---

**a)** AMG 334 is not included in this view. AMG 334 is part of the global collaboration with Amgen to commercialize and develop neuroscience treatments.

**b)** Submission anticipated late 2016 or early 2017.


**e)** Submitted in EU in Q1 2016.

**f)** Also known as Fovista<sup>®</sup> (pegpleranib) and E10030. This product is being developed by Ophthotech Corp. Ophthotech has licensed ex-US commercialization rights to Novartis under a Licensing and Commercialization Agreement.

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# Pipeline of key projects in confirmatory development

## Phase I / II

<table>
<thead>
<tr>
<th>Project</th>
<th>Disease Area</th>
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<tbody>
<tr>
<td>ABL001</td>
<td>CML¹</td>
</tr>
<tr>
<td>INC280</td>
<td>NSCLC²</td>
</tr>
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<td>INC280</td>
<td>Solid tumors</td>
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<td>ASB183</td>
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<td>BYM338</td>
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<td>BYM338</td>
<td>Sarcoma</td>
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<td>DLBCL¹</td>
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<td>QEO31</td>
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<td>HSC835</td>
<td>Stem cell transplantation</td>
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## Phase III / Pivotal

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<td>TSC1 seizures</td>
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<tr>
<td>BYL719</td>
<td>Hip fracture</td>
</tr>
<tr>
<td>BYL719 + fulv HR+ HER2(+) postmenopausal Adv. BC² 2nd line</td>
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<tr>
<td>CTL019</td>
<td>Pediatric acute lymphoblastic leukemia</td>
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<tr>
<td>LEE011 + Itz HR+ HER2(+) postmenopausal Adv. BC² 1st line</td>
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<td>LEC999</td>
<td>Cushing’s disease</td>
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<td>OAP030(3)</td>
<td>nAMD²</td>
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<td>RLX030</td>
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<td>RTH258</td>
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<tr>
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<td>GILENYA</td>
<td>Pediatric MS¹</td>
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<td>JAKAVI</td>
<td>Early myelofibrosis</td>
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<td>PKC412</td>
<td>AML¹</td>
</tr>
<tr>
<td>LEE011 + Itz HR+ HER2(+) postmenopausal Adv. BC¹ 1st line</td>
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<td>LEE011 + Itz HR+ HER2(+) postmenopausal Adv. BC¹ 2nd line</td>
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<tr>
<td>ZYKADIA</td>
<td>BRAF V600+ Melanoma (adjuvant)</td>
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<tr>
<td>VOTRIENT</td>
<td>Renal cell carcinoma (adjunct)</td>
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<td>LUENTIS</td>
<td>Cushing’s disease</td>
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## In Registration

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<td>CNV²</td>
</tr>
<tr>
<td>VOFIq®️</td>
<td>BRAF V600+ Melanoma (adjuvant)</td>
</tr>
</tbody>
</table>

## Abbreviations:

- fulv  fulvestrant
- itz  letrozole
- tmx  tamoxifen
- gsn  goserelin
- NSAI  Non-steroidal aromatase inhibitor

---

1. Chronic myeloid leukemia
2. Non-small cell lung cancer
3. Non-alcoholic steatohepatitis
4. Chronic spontaneous urticaria / Inducible urticaria
5. Diffuse large B-cell lymphoma
6. Graft-Versus-Host Disease
7. Relapsing multiple sclerosis
8. Secondary progressive multiple sclerosis
9. Breast cancer
10. Neovascular age-related macular degeneration
11. Acute myeloid leukemia
12. Secondary prevention of cardiovascular events
13. Tuberculous sclerosis complex
15. Non-radiographic axial spondyloarthritis
16. Preserved ejection fraction
17. Multiple sclerosis
18. Retinopathy of prematurity
19. Aggressive systemic mastocytosis
20. Diabetic macular edema
21. Long-acting release
22. Neuroendocrine tumors
23. Chronic lymphocytic leukemia
24. Choroidal neovascularization (CNV) secondary to conditions other than macular degeneration and pathologic myopia

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