Research Update

James Bradner, M.D.
President, NIBR
Disclaimer

This presentation contains forward-looking statements that can be identified by terminology such as "potential," "expected," "will," "planned," or similar expressions, or by express or implied discussions regarding potential new products, potential new indications for existing products, or regarding potential future revenues from any such products; potential shareholder returns or credit ratings; or regarding the potential outcome of the announced review of options being undertaken to maximize shareholder value of the Alcon Division; or regarding the potential financial or other impact on Novartis or any of our divisions of the significant reorganizations of recent years, including the creation of the Pharmaceuticals and Oncology business units to form the Innovative Medicines Division, the creation of the Global Drug Development organization and Novartis Operations (including Novartis Technical Operations and Novartis Business Services), the transfer of the Ophthalmic Pharmaceuticals products of our Alcon Division to the Innovative Medicines Division, the transfer of selected mature, non-promoted pharmaceutical products from the Innovative Medicines Division to the Sandoz Division, and the transactions with GSK, Lilly and CSL; or regarding the potential impact of the share buyback plan; or regarding potential future sales or earnings of the Novartis Group or any of its divisions; or by discussions of strategy, plans, expectations or intentions. You should not place undue reliance on these statements. Such forward looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward looking statements. There can be no guarantee that any new products will be approved for sale in any market, or that any new indications will be approved for any existing products in any market, or that any approvals which are obtained will be obtained at any particular time, or that any such products will achieve any particular revenue levels. Nor can there be any guarantee that the review of options being undertaken to maximize shareholder value of the Alcon Division will reach any particular results, or at any particular time. Neither can there be any guarantee that Novartis will be able to realize any of the potential strategic benefits, synergies or opportunities as a result of the significant reorganizations of recent years, including the creation of the Pharmaceuticals and Oncology business units to form the Innovative Medicines Division, the creation of the Global Drug Development organization and Novartis Operations (including Novartis Technical Operations and Novartis Business Services), the transfer of the Ophthalmic Pharmaceuticals products of our Alcon Division to the Innovative Medicines Division, the transfer of selected mature, non-promoted pharmaceutical products from the Innovative Medicines Division to the Sandoz Division, and the transactions with GSK, Lilly and CSL. Neither can there be any guarantee that shareholders will achieve any particular level of shareholder returns. Nor can there be any guarantee that the Group, or any of its divisions, will be commercially successful in the future, or achieve any particular credit rating or financial results. In particular, management’s expectations could be affected by, among other things: regulatory actions or delays or government regulation generally; the potential that the strategic benefits, synergies or opportunities expected from the significant reorganizations of recent years, including the creation of the Pharmaceuticals and Oncology business units to form the Innovative Medicines Division, the creation of the Global Drug Development organization and Novartis Operations (including Novartis Technical Operations and Novartis Business Services), the transfer of the Ophthalmic Pharmaceuticals products of our Alcon Division to the Innovative Medicines Division, the transfer of selected mature, non-promoted pharmaceutical products from the Innovative Medicines Division to the Sandoz Division, and the transactions with GSK, Lilly and CSL may not be realized or may take longer to realize than expected; the inherent uncertainties involved in predicting shareholder returns or credit ratings; the uncertainties inherent in the research and development of new healthcare products, including clinical trial results and additional analysis of existing clinical data; our ability to obtain or maintain proprietary intellectual property protection, including the ultimate extent of the impact on Novartis of the loss of patent protection and exclusivity on key products which commenced in prior years and will continue this year; safety, quality or manufacturing issues; global trends toward health care cost containment, including ongoing pricing and reimbursement pressures, such as from increased publicity on pharmaceuticals pricing, including in certain large markets; uncertainties regarding actual or potential legal proceedings, including, among others, actual or potential product liability litigation, litigation and investigations regarding sales and marketing practices, intellectual property disputes and government investigations generally; general economic and industry conditions, including uncertainties regarding the effects of the persistently weak economic and financial environment in many countries; uncertainties regarding future global exchange rates; uncertainties regarding future demand for our products; and uncertainties regarding potential significant breaches of data security or data privacy, or disruptions of our information technology systems; and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this presentation as of this date and does not undertake any obligation to update any forward-looking statements as a result of new information, future events or otherwise.
NIBR

A powerful drug discovery and early development engine

Examples of Novartis drug approvals since 2002 with PoC in NIBR

Building on this legacy, we now organize around improving the return on R&D through innovation, prioritization and collaboration.
NIBR
Organized around prevalent Disease Areas

Autoimmunity, Transplantation & Inflammation
Cardiovascular & Metabolism
Infectious Diseases
Musculoskeletal
Neuroscience
Ophthalmology
Oncology
Immuono-Oncology
Respiratory Diseases

Note: Distribution of ~90 New Molecular Entities at NIBR
Agenda

1. NIBR 2.0
2. Oncology
NIBR 2.0 Strategy
A next generation of therapeutics

1. Innovate the new science of therapeutics
2. Align with Development
3. Open the framework
4. Invest in our people
5. Rebuild & prioritize
A Next-Gen DNA-Encoded Library (DEL) Platform

Screening on an unprecedented scale

1. Innovate the new science of therapeutics

Testing large collections of DNA-barcoded drug-like compound mixtures against proteins in rapid affinity screening experiments

Potential to deliver high impact medicinal chemistry starting points
Targeted Protein Degradation

A new type of therapeutic

1. Innovate the new science of therapeutics

Drug molecules are typically directed to active sites of protein targets, disabling a single function of protein biomolecule.

NIBR is innovating a new type of therapeutic agent that destroys all functions of a protein target immediately upon binding, irrespective of the site of binding.

We have initiated the assembly of a technology platform around so-called Targeted Protein Degradation to develop powerful new medicines across NIBR.

CRISPR as a Therapeutic Modality
Leveraging leadership in cell and regenerative medicine

1. Innovate the new science of therapeutics

CRISPR platform licensed from Caribou Biosciences for use as a research tool within NIBR to edit specific genetic loci (e.g., in mice and cultured cells)

In collaboration with Intellia Therapeutics, evaluating utility of CRISPR/Cas9 for editing CART cells to treat cancer and human hematopoietic stem cells (HSC), e.g., to potentially cure sickle cell and other blood disorders

Leverages Novartis’ cell and gene therapy expertise, including HSC expansion technology

Aligning around Accelerated Drug Development
Seamless alignment of early and late development

2. Align with Development

- ✓ unmet medical need = f(population)
- ✓ Expand cross-divisional representation into NIBR and Development decision boards
- ✓ Set clear expectations of behavior
- ✓ Identify joint spaces between NIBR and Development
- ✓ Reposition leaders where they are most effective
- ✓ Act decisively
- ✓ Talent-share programs with Development

Source: http://www.drincavo.com/knee-arthritis.html

Completed ✓ In progress
Open Innovation in Drug Discovery
Connectivity as a new priority in Research & Early Development

3. Open the framework
4. Invest in our people
Developing the next wave of definitive cancer therapeutics

5. Rebuild & prioritize

Jeffrey Engelman
Oncology
Mass. General Hospital (MGH)
Joined NIBR in June 2016

Glenn Dranoff
Immuno-Oncology
Dana-Farber Cancer Institute
Joined NIBR March 2015

Lilli Petruzzelli
Translational Clinical Onc.
University of Michigan
Joined NIBR in October 2014

Peter Hammerman
Oncology Translational Res.
Dana-Farber Cancer Institute
Joined NIBR September 2016
Agenda

1. NIBR 2.0
2. Oncology
A relatively small number of patients currently respond to immuno-oncology therapy options.

Even among responders, a significant number need to discontinue therapy due to adverse events.

Data emerging over the next 12-18 months from Novartis and competitor trials will inform the most impactful paths forward.

We aim for a leadership position in oncology by leveraging our broad immuno-oncology and targeted therapy portfolios.
The Novartis Immuno-Oncology Pipeline
Jump-started by external innovation

- **2012**
  - **Penn CART therapies**
    - 1, 4

- **2014**
  - **Intellia Gene editing for CART**
    - 1, 3, 4
  - **CoStim PD-1, PD-L1, TIM3 & LAG3 Abs**
    - 2

- **2015**
  - **XOMA TGFβ antibodies**
    - 1
  - **ADURO BIOTECH STING agonists**
    - 1, 3, 4
  - **Admune Therapeutics hetIL-15 biologic**
    - 2
  - **paloBIOFARMA Adenosine receptor antagonists**
    - 1, 4

- **2016**
  - **xencor CD3 bi-specific antibodies**
    - 4

---

1. License
2. Acquisition
3. Equity Investment
4. Collaboration
Accelerating the IO Portfolio

PDR001 Development Timeline

<table>
<thead>
<tr>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forecast</td>
<td>IND</td>
<td>FPFV</td>
<td>PoC</td>
</tr>
</tbody>
</table>

Initial PDR001 Responses

56 year-old with squamous cell carcinoma of lung that progressed after platinum doublet
Source: Andrea Varga and Jean-Charles Soria, Gustave Roussy

57 year-old with BRAF wild-type melanoma metastatic to lung that progressed after dacarbazine
Source: Josh Lin, National Taiwan University Hospital

Investigational. Efficacy & safety not yet established

Pre-treatment
48% reduction at 2nd assessment (16 weeks)

Pre-treatment
45% reduction at 1st assessment (8 wks)
# The Novartis Immuno-Oncology Pipeline

Prioritized by major mechanisms of immune escape

## Immune Priming
- STING
- TIM-3
- cMET
- Porcupine

## T-cell Engineering
- **CART**
- **Bi-specific Ab**
- CD19
- CD123
- BCMA
- CD123
- EGFRvIII
- Mesothelin

## T-Cell Modulation
- IL-15
- TEC
- GITR
- mTOR
- IAP

## Tumor Environment
- PD-1
- CSF-1
- PD-L1
- CSF-1R
- LAG-3
- A2A adenosine receptor
- TIM-3
- HDAC
- TGF-β
- MEK
- IL-17
- IL-1
First-in-Class Potential in Clinical Investigation

A comprehensive pipeline focused on second-generation IO agents

### Novel targets

<table>
<thead>
<tr>
<th>Target (Compound)</th>
<th>FIH Trial Initiated</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF-1 (MCS110)</td>
<td>✓</td>
</tr>
<tr>
<td>CSF-1R (BLZ945)</td>
<td>✓</td>
</tr>
<tr>
<td>CART-19 (CTL019 / CTL119)</td>
<td>✓</td>
</tr>
<tr>
<td>CART-BCMA (MCM998)</td>
<td>✓</td>
</tr>
<tr>
<td>CART-EGFRvIII (LXF821)</td>
<td>✓</td>
</tr>
<tr>
<td>CART-Mesothelin (NIU440)</td>
<td>2017</td>
</tr>
<tr>
<td>CART-CD123 (MIH911)</td>
<td>✓</td>
</tr>
<tr>
<td>Het IL-15 (NIZ985)</td>
<td>✓</td>
</tr>
<tr>
<td>Adenosine receptor (NIR178)</td>
<td>✓</td>
</tr>
<tr>
<td>TGFβ (NIS793)</td>
<td>2017</td>
</tr>
<tr>
<td>STING (MIW815)*</td>
<td>✓</td>
</tr>
<tr>
<td>GITR (GWN323)</td>
<td>✓</td>
</tr>
<tr>
<td>CD123 x CD3 (SQZ622)*</td>
<td>✓</td>
</tr>
<tr>
<td>CD20 x CD3 (THG338)*</td>
<td>✓</td>
</tr>
</tbody>
</table>

### Checkpoint inhibitors

<table>
<thead>
<tr>
<th>Target (Compound)</th>
<th>FIH Trial Initiated</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-1 (PDR001)</td>
<td>✓</td>
</tr>
<tr>
<td>PD-L1 (FAZ053)</td>
<td>✓</td>
</tr>
<tr>
<td>LAG3 (LAG525)</td>
<td>✓</td>
</tr>
<tr>
<td>TIM3 (MBG453)</td>
<td>✓</td>
</tr>
</tbody>
</table>

---

1. Collaboration / licensing with Aduro
2. Collaboration / licensing with Xencor

* Backbone of first-in-class combination strategies
## Potential First-in-Class Combination Therapies

20 exploratory IO combination studies expected by early 2017

<table>
<thead>
<tr>
<th>Target (Compound)</th>
<th>FIH Trial Initiated</th>
</tr>
</thead>
<tbody>
<tr>
<td>IO / IO</td>
<td></td>
</tr>
<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>✓</td>
</tr>
<tr>
<td>Adenosine R (NIR178) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>Het IL-15 (NIZ985) + PD-1</td>
<td>2017</td>
</tr>
<tr>
<td>IL-17 (CJM112) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>IL-1 (Ilaris®) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>TGFβ (NIS793) + PD-1</td>
<td>2017</td>
</tr>
<tr>
<td>PD-L1 (FAZ053) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>STING (MIW815) + PD-1</td>
<td>2017</td>
</tr>
<tr>
<td>IO with chemo</td>
<td></td>
</tr>
<tr>
<td>CSF-1 (MCS110) + carbo/gem</td>
<td>✓</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Target (Compound)</th>
<th>FIH Trial Initiated</th>
</tr>
</thead>
<tbody>
<tr>
<td>IO with targeted agent²</td>
<td></td>
</tr>
<tr>
<td>cMET (INC280) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>Porcupine (WNT974) + PD-1</td>
<td>2017</td>
</tr>
<tr>
<td>HDAC (Farydak®) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>mTOR (Afinitor®) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>IAP inh (LCL161) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>MEK (Trametinib) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>TEC (EGF816) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>B/CRAF (LXH254) + PD-1</td>
<td>✓</td>
</tr>
</tbody>
</table>

1. Collaboration / licensing with Aduro
2. Excludes IO targeted agent partner studies

---

19 | R&D Update | January 25, 2017 | Novartis Investor Presentation
## A Pipeline of Early Stage Targeted Therapies

Single agent and combination studies in Early Development

### Monotherapy

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Target (Compound)</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>FGF</td>
<td>FGFR-1/2/3 (BGJ398)</td>
<td>Bladder, Cholang.</td>
</tr>
<tr>
<td></td>
<td>FGFR4 selective (FGF401)</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>RAS/RAF/MAPK</td>
<td>pan-RAF (LXH254)</td>
<td>NSCLC</td>
</tr>
<tr>
<td></td>
<td>ERK (LTT462)</td>
<td>NSCLC</td>
</tr>
<tr>
<td>EGFR</td>
<td>EGFR mut (EGF816)</td>
<td>NSCLC</td>
</tr>
<tr>
<td>Apoptosis Regulation</td>
<td>P53/HDM2 (HDM201)</td>
<td>AML</td>
</tr>
<tr>
<td></td>
<td>BCL2 (BCL201)</td>
<td>R/R CLL, NHL</td>
</tr>
<tr>
<td>Epigenetic</td>
<td>EED (MAK683)</td>
<td>DLBCL, NPC</td>
</tr>
<tr>
<td>Wnt</td>
<td>Porcupine (WNT974)</td>
<td>Pancreatic, CRC</td>
</tr>
<tr>
<td>BCR-ABL</td>
<td>BCR-ABL allosteric (ABL001)</td>
<td>CML</td>
</tr>
<tr>
<td>PIM</td>
<td>Pan-PIM (PIM447)</td>
<td>AML</td>
</tr>
<tr>
<td>IDH</td>
<td>IDH-1 (IDH305)</td>
<td>IDH1 mut. cancers (AML, Glioma, etc.)</td>
</tr>
<tr>
<td>SERD</td>
<td>SERD (LSZ102)</td>
<td>Breast Cancer</td>
</tr>
<tr>
<td>GPCR</td>
<td>PKC (LXS196)</td>
<td>Uveal Melanoma</td>
</tr>
<tr>
<td>ADC</td>
<td>P-Cadherin ADC (PCA062)</td>
<td>PCAD, H&amp;N, Esoph, Ovarian, RCC</td>
</tr>
<tr>
<td></td>
<td>Cadherin-6 ADC (HKT288)</td>
<td></td>
</tr>
</tbody>
</table>

### Combinations

<table>
<thead>
<tr>
<th>Targeted</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCR-ABL (ABL001) + TKI in CML</td>
</tr>
<tr>
<td>EGFR (EGF816) + cMET (INC280) in NSCLC</td>
</tr>
<tr>
<td>cRAF (LXH254) + Mekinist® in NSCLC</td>
</tr>
<tr>
<td>cRAF (LXH254) + ERK (LTT462) in NSCLC</td>
</tr>
<tr>
<td>Pan-PIM (PIM447) + FLT3 (PKC412) in AML</td>
</tr>
<tr>
<td>SERD (LSZ102) + PI3K (BYL719) in Breast Cancer</td>
</tr>
<tr>
<td>SERD (LSZ102) + CDK4/6 (LEE011) in Breast Cancer</td>
</tr>
</tbody>
</table>
Pediatric ALL filing on CTL019 expected in early 2017

DLBCL filing of CTL019 expected in H2 2017

Integration of the Cell & Gene Therapy Unit into broader Novartis organization

Increased investment at NIBR in CART manufacturing sciences

Cell-based Immunotherapy Anticipated to Reach Regulatory Consideration in 2017
Continued Leadership in CART Therapy
Near-term CTL019 filing and a strong development pipeline

Near-term: CTL019

**Relapsed / Refractory Pediatric and Young Adult Acute Lymphoblastic Leukemia (r/r ped ALL)**
Global clinical trial:
- Enrollment completed
- Primary endpoint met:
  - Overall response rate (CR+CRi) 82%
- Planned FDA filing in early 2017

**Relapsed / Refractory Diffuse Large B-Cell Lymphoma (r/r DLBCL)**
Global clinical trial:
- Fully enrolled: 80 patients in US and EU
- Primary endpoint: ORR; secondary endpoints include duration of response and overall survival

Potential future prospects

**Second-generation CARTs**
- CTL119 in adult ALL and CLL
- BCMA in multiple myeloma
- Combinations (e.g., CTL019 + checkpoint inhibitor)
- CD123 in acute myeloid leukemia
- Mesothelin in adenocarcinoma
- EGFRvIII in glioblastoma

**Next Generation of CARTs**
- Regulated CARTs
- Gene editing using CRISPR for allogeneic CARTs
Oncology Translational Research
A state-of-the-art laboratory to understand and to guide cancer drug development
### IO Monotherapy

- **Novel targets**
  - CSF-1 (MCS110)
  - CSF-1R (BLZ945)
  - CART-19 (CTLN19/119)
  - CART-BDMA (MCM998)
  - CART-EGFRvill (LXF821)
  - CART-Mesothelin (NIU440)
  - CART-CD123 (MIH911)
  - Het IL-15 (NIZ985)
  - Adenosine receptor (NIR178)
  - TGFβ (NIS793)
  - STING (MIW815)
  - GITR (GWN323)
  - CD123 x CD3 (SQZ622)
  - CD20 x CD3 (THG338)

- **Check-point inhibitors**
  - PD-1 (PDR001)
  - PD-L1 (FAZ053)
  - LAG3 (LAG525)
  - TIM3 (MBG453)

### IO Combinations

- **IO / IO**
  - LAG3 (LAG525) + PD-1
  - TIM3 (MBG453) + PD-1
  - GITR (GWN323) + PD-1
  - CSF-1 (MCS110) + PD-1
  - Adenosine R (NIR178) + PD-1
  - Het IL-15 (NIZ985) + PD-1
  - IL-17 (CJM112) + PD-1
  - IL-1 (Ilaris®) + PD-1
  - TGFβ (NIS793) + PD-1
  - PD-L1 (FAZ053) + PD-1
  - STING (MIW815) + PD-1
  - CSF-1 (MCS110) + carbo/gem

- **IO / chemo**
  - cMET (INC280) + PD-1
  - Porcypine (WNT974) + PD-1
  - HDAC (Farydak®) + PD-1
  - mTOR (Afinitor®) + PD-1
  - IAP inh (LCL161) + PD-1
  - MEK (Trametinib) + PD-1
  - TEC (EGR816) + PD-1
  - B/CRAF (LXH254) + PD-1

### Targeted Monotherapy

<table>
<thead>
<tr>
<th>Pathway</th>
<th>Target</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>FGFR</td>
<td>FGFR1/2/3</td>
<td>Bladder, Chloang, Solid tumors</td>
</tr>
<tr>
<td>RAS/RAF/MAPK</td>
<td>pan-RAF</td>
<td>NSCLC</td>
</tr>
<tr>
<td>EGFR</td>
<td>EGFR mut</td>
<td>NSCLC</td>
</tr>
<tr>
<td>Apoptosis</td>
<td>PS3/HDM2</td>
<td>AML</td>
</tr>
<tr>
<td>Regulation</td>
<td>BCL2</td>
<td>R/R CLL, NHL</td>
</tr>
<tr>
<td>Epigenetic</td>
<td>EED</td>
<td>DLBCL, NPC</td>
</tr>
<tr>
<td>Wnt</td>
<td>Porcypine</td>
<td>Pancreatic, CRC</td>
</tr>
<tr>
<td>BCR-ABL</td>
<td>BCR-ABL allosteric</td>
<td>CML</td>
</tr>
<tr>
<td>PIM</td>
<td>Pan-PIM</td>
<td>AML</td>
</tr>
<tr>
<td>IDH</td>
<td>IDH-1</td>
<td>AML</td>
</tr>
<tr>
<td>SERD</td>
<td>SERD</td>
<td>Breast Cancer</td>
</tr>
<tr>
<td>GPCR</td>
<td>PKC</td>
<td>Uveal Melanoma</td>
</tr>
<tr>
<td>ADC</td>
<td>P-Cadherin ADC</td>
<td>PCAD, H&amp;N, Esoph, Ovarian, RCC</td>
</tr>
</tbody>
</table>

### Targeted Combos

- BCR-ABL (ABL001) + TKI in CML
- EGFR (EGF816) + cMET (INC280) in NSCLC
- cRAF (LXH254) + Mekinist in NSCLC
- cRAF (LXH254) + ERK (LTT462) in NSCLC
- Pan-PIM (PIM447) + FLT3 (PKC412) in AML
- SERD (LSZ102) + PI3K (BYL719) in Breast Cancer
- SERD (LSZ102) + CDK4/6 (LEE011) in Breast Cancer
Selected other programs in clinical investigation
<table>
<thead>
<tr>
<th>Autoimmunity &amp; Transplant Immunology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Programs in clinical investigation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sjögren's Syndrome</td>
<td>VAY736: anti-BAFF-R Ab, CFZ533: anti-CD40 Ab</td>
</tr>
<tr>
<td>Acute Graft v Host Disease</td>
<td>KRP203: S1PR Agonist</td>
</tr>
<tr>
<td>Inflammatory Acne</td>
<td>CJM112: anti-IL-17 Ab</td>
</tr>
<tr>
<td>Hidradenitis Suppurativa</td>
<td>CJM112: anti-IL-17 Ab</td>
</tr>
<tr>
<td>Kidney Transplant Rejection</td>
<td>CFZ533: anti-CD40 Ab</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>ACZ885 (Ilaris®): anti-IL-1β Ab</td>
</tr>
</tbody>
</table>
Cardiovascular and Metabolism

Programs in clinical investigation

Heart Failure
CLR235: Heart contractility agent

Stroke Prevention
MAA868: Anti-thrombotic

Peripheral Arterial Disease
ACZ885: Anti-IL-1β

Weight Loss
LIK066: SGLT1/2 Inhibitor

Resistant Hypertension
LHW090: NEP Inhibitor
### Ophthalmology & Regenerative Medicine

**Programs in clinical investigation**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry AMD</td>
<td>Combinations of complement inhibitors</td>
</tr>
<tr>
<td>Wet AMD</td>
<td>RTH258: High-potency scFv VEGFi</td>
</tr>
<tr>
<td>Diabetic Retinopathy</td>
<td>LKA651: Anti-erythropoietin ivt</td>
</tr>
<tr>
<td>Sarcopenia</td>
<td>BYM338: Anti-ActRII Ab</td>
</tr>
<tr>
<td>Cartilage Injury</td>
<td>LNA043: Chondrogenesis inducer</td>
</tr>
<tr>
<td>Tendon Injury</td>
<td>Tendon repair promotion</td>
</tr>
</tbody>
</table>

*Images of ocular and musculoskeletal conditions are included.*
Infectious & Respiratory Diseases

Programs in clinical investigation

**Gram-negative Bacterial Infections**
LYS228: Novel antibiotic

**Congenital Cytomegalovirus**
CSJ148: Anti-CMV

**Malaria**
KAF156: P. falciparum

**COPD**
QBW251: CFTR Potentiator

**Cystic Fibrosis**
QBW251: CFTR Potentiator
Neuroscience

Programs in clinical investigation

**Spinal Muscular Atrophy**
LMI070: RNA Splicing Modulator

**Alzheimer’s Disease**
CNP520: BACE Inhibitor

**Migraine**
AMG 334: Anti-CGRP
AMG 301: Novel Inhibitor

**Sleep Disorders**
LML134: Novel Antagonist

**Secondary Progressive MS**
BAF312: S1P1 Modulator

**Neuropathic Pain & Addiction**
AFQ056: mGluR5 Antagonist
Appendix

Research
NIBR 2.0 – Executive Summary

An optimized growth engine

- NIBR is a well-established center of basic and translational research, which attracts top scientific talent (~6,000 scientists) to 7 global research campuses

- New leadership is in place with deep experience across therapeutic areas and modalities

- Integrated approach to drug discovery fully aligned with Global Drug Development to optimize ~$8 billion\(^1\) of R&D spend

- Robust research enterprise with broad and deep pipeline of ~90 new molecular entities spanning therapeutic areas with significant unmet needs

- New technologies innovated and internalized for the next generation of therapeutics

- Focus today will be to provide an update on our robust oncology portfolio

---

1. Excludes Alcon R&D of USD 0.5 bn in 2016
NIBR 2.0 – Executive Summary
A renewed focus on Oncology

• New leadership recruited from leading cancer centers

• Innovating and advancing 31 molecular entities in oncology

• A rapidly curated, clinical-stage immuno-oncology “IO” portfolio with 18 checkpoint and novel IO targets studied across 37 monotherapy and combination trials

• Organized around leading edge translational research, guided by a state-of-the-art Oncology Translational Research laboratory

• Empowered by 16 unique targeted therapeutics in early clinical development at NIBR

• Comprehensive mechanistic-based approaches to cancer therapeutics
Novartis Institutes for BioMedical Research (NIBR)

Drug discovery and early development

~6,000
Scientists / 7 sites globally

~400
Research projects

>500
Ongoing clinical trials (NIBR & GDD)

~90
New Molecular Entities

Source: ClinicalTrials.gov as of December, 2016
NIBR v1.0 – Pathways of Unmet Medical Need
Well-defined population

Broader sub-set

**Well-defined population**

**Broader sub-set**

CAPS

<0.020 Million*

Systemic Juvenile Idiopathic Arthritis (SJIA)

0.075 million*

Gout

20 Million*

Atherosclerosis^2

130 Million*

1. Ialiris is approved for the symptomatic treatment of refractory acute gouty arthritis in the EU

* Global prevalence estimates.
NIBR
Organized around prevalent Disease Areas

Autoimmunity, Transplantation & Inflammation
Cardiovascular & Metabolism
Infectious Diseases
Musculoskeletal
Neuroscience
Ophthalmology
Oncology
Immuo-Oncology
Respiratory Diseases

Projects by Disease Prevalence

Prevalent Disease 77%
Prevalent but Relevant to Rare Disease 16%
Rare Disease 7%

Note: Projects between sPoC and PoC, excludes post-PoC.
Chemical Biology & Therapeutics

A new discovery engine

1. Innovate the new science of therapeutics

A new discovery engine
The Chemical Biology mindset

Maximize adjacencies
Create centers of excellence, eradicate siloes

A culture of drug hunting
A heightened sense of urgency

Ruthless prioritization
Enterprise-level thinking

Innovation and partnership
Connect to the innovator
Aligning around Accelerated Drug Development
Strategic restructuring in 2016 as a step-wise evolution for speed and agility

2. Align with Development

- Discovery Research/Therapeutic Area
  - Global Discovery Chemistry
  - NIBR Biologics Center
  - PK Sciences
  - Pre-Clinical Safety

- Early Dev.
  - Translational Clinical Onc.
  - Translational Medicine

- Late Dev.
  - Global Drug Development
  - Translational Research & Dev.
  - Biologics Technical Dev. & Mfg.
  - Biostatistics

NIBR
Global Drug Development (GDD)