Meet Novartis Management
NIBR
May 31, 2017
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Key Messages

1. NIBR is a leading center of therapeutics discovery research, attracting top scientific talent (~6,000 associates) to 7 global research campuses. New leadership is in place with deep experience across therapeutic areas and modalities.

2. Integrated and aligned strategy in Research and Global Drug Development to optimize ~USD 8 billion\(^1\) of R&D spend. Robust research enterprise with broad and deep pipeline of ~90 new molecular entities spanning therapeutic areas addressing significant unmet need.

3. New technologies innovated and internalized for the next generation of therapeutics, including a renewed focus on our robust oncology portfolio.

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1. Excludes Alcon R&D of USD 0.5 bn in 2016
NIBR
A powerful drug discovery and early development engine

Examples of Novartis drug approvals with PoC in NIBR

Building on this legacy, we now organize around improving the return on R&D through innovation, prioritization and collaboration
NIBR
Responsive to the worldwide burden of disease

Distribution of ~90 New Molecular Entities at NIBR

- Oncology (ONC)
- Immuno-Oncology (IO)
- Ophthalmology (OPH)
- Respiratory Diseases (RESP)
- Neuroscience (NEURO)
- Autoimmunity, Transplantation & Inflammation (ATI)
- Cardiovascular & Metabolism (CVM)
- Infectious Diseases (ID)
- Musculoskeletal (MSD)
- Other
Agenda

NIBR 2.0

Oncology

Projects highlighted outside of 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
Advances in therapeutic discovery
New types of therapeutics

1. Innovate the new science of therapeutics

Next-Gen DNA-Encoded Library (DEL) platform
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

RNA-targeting splicing compounds
New mechanism demonstrates the feasibility of small molecule-mediated, sequence-selective splice modulation for a variety of diseases

Peptide discovery platform
Peptidream: Platform collaboration and technology transfer generate medicinal chemistry starting points to achieve orally available cyclic peptides and permeable low molecular weight compounds
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 CAR-T 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 = \( f(\text{population}) \)
✓ 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
Open innovation in drug discovery

Connectivity as a new priority in Research & Early Development

3. Open the framework

Scholars | Chemical Probes | Partnerships
NIBR
A unique research community

4. Invest in our people
## Portfolio prioritization

Improving collaboration & productivity of internal & external innovation

5. Rebuild and prioritize

<table>
<thead>
<tr>
<th>Evidence</th>
<th>Novelty</th>
<th>Competition</th>
<th>Strategic Imperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>RACE</td>
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<tr>
<td>GO</td>
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<tr>
<td>PACE</td>
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</tr>
<tr>
<td>RETIRE</td>
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<td></td>
</tr>
</tbody>
</table>

- **RACE**
  - Proceed as quickly as possible, may asymmetrically invest to progress more quickly
  - May have priority to “jump the queue”
  - Only in extreme cases would cross-portfolio resources need to be reviewed

- **GO**
  - Proceed at characteristic rapid, competitive pace
  - Follow traditional project plans and risk management practices
  - Cross-portfolio resources may be reviewed with minimal impact on timelines

- **PACE**
  - Proceed at typical pace, occasionally with more lean resource allocation pending demand
  - Resources may be gated on key go/no go decision points
  - Cross-portfolio resources may need to be reviewed
  - Project may be asked to return to Translation and Early Development (TED) for review at next major milestone

- **RETIRE**
  - Discontinue project, without expectation of development in indication
  - Resourced for agreed wind-down activities
Open innovation in drug discovery
Recent out-licensed deals and collaborations optimizing the portfolio

5. Rebuild and prioritize

Out-licensing of BEZ235 and BEZ235/RAD001 fixed-dose combination therapy for use in age-related disorders to a single-purpose spin-out

Out-licensing of HSC835\(^1\) for selected applications in hematopoietic stem cell transplantation

In-license and collaboration agreement for a type 1 diabetes program based on a novel antigen-specific immune tolerance induction platform

\(^1\) magenta compound MGTA-456
Agenda

NIBR 2.0

Oncology

Projects highlighted outside of Oncology
# 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>
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<tbody>
<tr>
<td>FGF</td>
<td>FGFR-1/2/3 (BGJ398)</td>
<td>Bladder, Chloang.</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>SHP2</td>
<td>SHP2 (TNO155)</td>
<td>NSCLC, H&amp;N</td>
</tr>
<tr>
<td>Apoptosis Regulation</td>
<td>P53/HDM2 (HDM201)</td>
<td>AML</td>
</tr>
<tr>
<td></td>
<td>BCL2 (BCL201)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>R/R CLL, NHL</td>
</tr>
<tr>
<td></td>
<td>MCL1 (MIK665)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>MM, NHL, AML</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>AML</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>
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</table>

1. Collaboration / licensing with Servier

## Combinations

<table>
<thead>
<tr>
<th>Target (Compound)</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) + MEK (Mekinist&lt;sup&gt;®&lt;/sup&gt;) 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 (Kisqali&lt;sup&gt;®&lt;/sup&gt;) in Breast Cancer</td>
</tr>
</tbody>
</table>
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>CAR-T-19 (CTL019 / CTL119)</td>
<td>✓</td>
</tr>
<tr>
<td>CAR-T-BCMA (MCM998)</td>
<td>✓</td>
</tr>
<tr>
<td>CAR-T-EGFRvIII (LXF821)</td>
<td>✓</td>
</tr>
<tr>
<td>CAR-T-Mesothelin (NIU440)</td>
<td>✓</td>
</tr>
<tr>
<td>CAR-T-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>✓</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>
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</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

22 exploratory IO combination studies in 2017

<table>
<thead>
<tr>
<th>Target (Compound)</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>✓</td>
</tr>
<tr>
<td>CSF-1R (BLZ945) + PD-1</td>
<td>2017</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>✓</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>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>cMET (INC280) + PD-1</td>
<td>✓</td>
</tr>
<tr>
<td>Porcupine (WNT974) + PD-1</td>
<td>✓</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 (Mekinist®) + 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>
<tr>
<td>FGFR4 (FGF401) + PD-1</td>
<td>2017</td>
</tr>
</tbody>
</table>

1. Collaboration / licensing with Aduro
2. Excludes IO targeted agent partner studies
## IO and TT projects advancing to development

6 IO studies and 2 Targeted Therapy agents in Phase 2/3

<table>
<thead>
<tr>
<th>Target</th>
<th>Indication</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IO Agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD-1 + Tafinlar® + Mekinist®</td>
<td>Melanoma</td>
<td>Enrolling Phase III ¹</td>
</tr>
<tr>
<td>PD-1 + chemo</td>
<td>Lung cancer</td>
<td>FPFV Planned (Q2 2017)</td>
</tr>
<tr>
<td>PD-1 single agent</td>
<td>Neuroendocrine tumors (NET)</td>
<td>Enrolling Phase II</td>
</tr>
<tr>
<td>PD-1 + regorafenib</td>
<td>Colorectal cancer (3rd-line)</td>
<td>FPFV Planned (Q3 2017)</td>
</tr>
<tr>
<td>PD-1 + bevacizumab + mFOLFOX6</td>
<td>Colorectal cancer (1st-line)</td>
<td>FPFV Planned (Q3 2017)</td>
</tr>
<tr>
<td>PD-1 + sorafenib</td>
<td>Hepatocellular carcinoma (HCC)</td>
<td>Enrolling Phase IB</td>
</tr>
<tr>
<td><strong>Targeted Agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EGFR (EGF816) / INC280 Combo</td>
<td>Non-small Cell Lung Cancer</td>
<td>Enrolling Phase IB/II expansion</td>
</tr>
<tr>
<td>BCR-ABL (ABL001)</td>
<td>Chronic myeloid leukemia (3rd-line)</td>
<td>Phase III study start in Q3 2017</td>
</tr>
</tbody>
</table>

¹. Safety Run-In (Part I)
**CAR-T therapy**
Expanding the scope of CAR-T cells beyond CTL019

B-cell Maturation Antigen (BCMA)-specific chimeric antigen receptor T cells (CAR-T-BCMA) for multiple myeloma: clinical response

Potential future prospects

**CD19 Target**
- CTL019 DLBCL: FDA Breakthrough Therapy designation, planned filing in US and EU in H2 2017
- CTL019 in adult ALL
- CTL119 in CLL
- Combinations (e.g. CTL019 + checkpoint inhibitor)

**Other targets**
- BCMA in multiple myeloma
- CD123 in acute myeloid leukemia
- Mesothelin in adenocarcinoma
- EGFRvIII in glioblastoma

**Next Generation of CAR-Ts**
- Regulated CAR-Ts
- Gene editing using CRISPR for allogeneic CAR-Ts

Oncology Translational Research

A state-of-the-art laboratory to understand and to guide cancer drug development
Bringing the best minds and medicines together to deliver definitive cancer therapies

**IO Monotherapy**

### Novel targets

- CSF-1 (MCS110)
- CSF-1R (BLZ945)
- CAR-T-19 (CTL019/119)
- CAR-T-BCMA (MCM998)
- CAR-T-EGFRvlll (LXF821)
- CAR-T-Mesothelin (NIU440)
- CAR-T-CD123 (MIH911)
- Het IL-15 (NIZ985)
- Adenosine receptor (NIR178)
- TGFB (NIS793)
- STING (MIW815)
- GITR (GWN323)
- CD123 x CD3 (SOZ622)
- CD20 x CD3 (THG338)
- PD-1 (PDR001)
- PD-L1 (FAZ053)
- LAG3 (LAG525)
- TIM3 (MBG453)

### Check-point inhibitors

- CSF-1R (BLZ945)
- CAR-T-19 (CTL019/119)
- CAR-T-BCMA (MCM998)
- CAR-T-EGFRvlll (LXF821)
- CAR-T-Mesothelin (NIU440)
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**IO Combinations**

- LAG3 (LAG525) + PD-1
- TIM3 (MBG453) + PD-1
- GITR (GWN323) + PD-1
- CSF-1 (MCS110) + PD-1
- CSF-1R (BLZ945) + PD-1
- Adenosine R (NIR178) + PD-1
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- IL-17 (CJM112) + PD-1
- IL-1 (Ilaris®) + PD-1
- TGFB (NIS793) + PD-1
- PD-L1 (FAZ053) + PD-1
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- CSF-1 (MCS110) + carbo/gem
- cMET (INC280) + PD-1
- Porcupine (WNT974) + PD-1
- HDAC (Farydak®) + PD-1
- mTOR (Afinitor®) + PD-1
- IAP inh (LCL161) + PD-1
- MEK (Mekinist®) + PD-1
- TEC (EGF816) + PD-1
- B/CRAF (LXH254) + PD-1
- FGFR4 (FGF401) + PD-1

**Targeted Monotherapy**

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<td>MM, NHL, AML</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 allostereic (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>AML</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>

**Targeted Combos**

- BCR-ABL (ABL001) + TKI in CML
- EGFR (EGF816) + cMET (INC280) in NSCLC
- cRAF (LXH254) + MEK (Mekinist®) in NSCLC
- cRAF (LXH254) + ERK (LTT462) in NSCLC
- Pan-PIM (PIM447) + FLT3 (PKC412) in AML
- SERD (LSZ102) + PI3K (BLY719) in Breast Cancer
- SERD (LSZ102) + CDK4/6 (Kisqali®) in Breast Cancer
Agenda

NIBR 2.0

Oncology

Projects highlighted outside of Oncology
NIBR
Responsive to the worldwide burden of disease

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

Note: Projects between sPoC and PoC, excludes post-PoC.
# Autoimmunity & transplant immunology

## Programs in clinical investigation

<table>
<thead>
<tr>
<th>Condition</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sjögren's Syndrome</strong></td>
<td>VAY736: anti-BAFF-R Ab</td>
</tr>
<tr>
<td></td>
<td>CFZ533: anti-CD40 Ab</td>
</tr>
<tr>
<td><strong>Acute Graft v Host Disease</strong></td>
<td>KRP203: S1PR Agonist</td>
</tr>
<tr>
<td><strong>Inflammatory Acne</strong></td>
<td>CFZ533: anti-CD40 Ab</td>
</tr>
<tr>
<td><strong>Hidradenitis Suppurativa</strong></td>
<td>CJM112: anti-IL-17 Ab</td>
</tr>
<tr>
<td><strong>Kidney Transplant Rejection</strong></td>
<td>CFZ533: anti-CD40 Ab</td>
</tr>
<tr>
<td><strong>Sarcoidosis</strong></td>
<td>ACZ885 (Ilaris®): anti-IL-1β Ab</td>
</tr>
</tbody>
</table>
CFZ533: non-B cell depleting anti-CD40 Ab for immune-mediated diseases

Exemplary programs in clinical investigation – autoimmunity, transplantation & inflammation

CFZ533 potently disrupts B cell activation in non-human primates (germinal centers)

Control (intact)  Treated (disrupted)

Currently in clinical studies for:
Primary Sjögren’s syndrome
Allograft prevention in renal transplantation
Graves’ disease
Myasthenia Gravis
Others planned

CFZ533 suppresses antibody response in first-in-human study

Currently in proof-of-concept studies

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
MAA868: anti-FXI mAb for treatment of thromboembolic diseases

Exemplary programs in clinical investigation – cardiovascular and metabolism

FXI is important for thrombosis but plays a minor role in hemostasis

FXI inhibition has potential of providing efficacy but with a reduced bleeding risk compared to other anticoagulants

MAA868 shows sustained anticoagulant activity in a pre-clinical model

Single subcutaneous dose doubles coagulation time (aPTT ↑ by ~2x) and inversely lowers free FXI for >30 days

Source: NIBR in-house data. Investigational. Efficacy & safety not yet established  CD = catalytic domain.

Next steps: start of Ph 2b dose range finding study
LHW090: Neprilysin (NEP) inhibitor for resistant hypertension

Exemplary programs in clinical investigation – cardiovascular and metabolism

Patients with resistant hypertension have blood pressure above goal despite concurrent use of 3 anti-hypertensive agents of different classes, and have a ~ 4-fold increased risk for cardiovascular events

NEP inhibitor attenuated Blood Pressure response when used in combination with 3 drugs in a pre-clinical model

![Graph showing blood pressure response](image)

Next steps: start of Ph 2b dose range finding study

Source: NIBR in-house data. Investigational. Efficacy & safety not yet established. ¹ Pierdomenico et al., AJH, 2005
Regenerative medicine & ophthalmology
Programs in clinical investigation

NASH/Primary Biliary Cholangitis
LJN452: Farnesoid X Receptor agonist

Sarcopenia
BYM338: Anti-ActRII Ab

Cartilage Injury
LNA043: Chondrogenesis inducer

Tendon Injury
Tendon repair promotion

Wet AMD
RTH258: High-potency scFv VEGFi

Dry AMD
Combinations of complement inhibitors

Diabetic Retinopathy
LKA651: Anti-erythropoietin ivt
LJN452: an effective Farnesoid X Receptor (FXR) Agonist for liver repair

Exemplary programs in clinical investigation – liver repair

Significant improvement in fibrosis compared to Ocaliva®, in a pre-clinical model of Primary Biliary Cholangitis (PBC)

Nonalcoholic Steatohepatitis (NASH) is projected to be the leading cause of liver transplant by 2020. LJN452 improves fibrosis and fatty liver in a pre-clinical model of NASH

Next steps: complete ongoing Ph 2 studies in 2018

Source: NIBR in-house data. Investigational. Efficacy & safety not yet established. 1. Picro sirius red staining 2. Mayo Clinic | Ocaliva® is a registered trademark of Intercept Pharmaceuticals, Inc
LNA043: Chondrogenesis inducer for cartilage repair

Exemplary programs in clinical investigation – musculoskeletal diseases

There are currently no drug therapies for cartilage degenerative diseases or acute cartilage injuries, and surgery provides insufficient outcomes.

Intra-articular injection of LNA043 promotes hyaline cartilage repair in pre-clinical models.

Next steps: currently in Ph 1 study, proceeding to Ph II

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 301: Novel Inhibitor

- Sleep Disorders
  LML134: Novel Antagonist

- Treatment-resistant Depression
  NR2B Negative Allosteric Modulator

- Neuropathic Pain & Addiction
  AFQ056: mGluR5 Antagonist
Summary

• NIBR is a leading center of therapeutics discovery research

• Robust research enterprise with broad and deep pipeline of ~90 new molecular entities

• New technologies for the next generation of therapeutics, including a renewed focus on our robust oncology portfolio