Novartis Institutes for
BioMedical Research

Research Update

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President, NIBR

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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.

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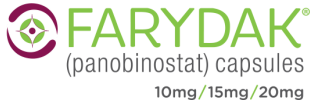
NIBR

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.

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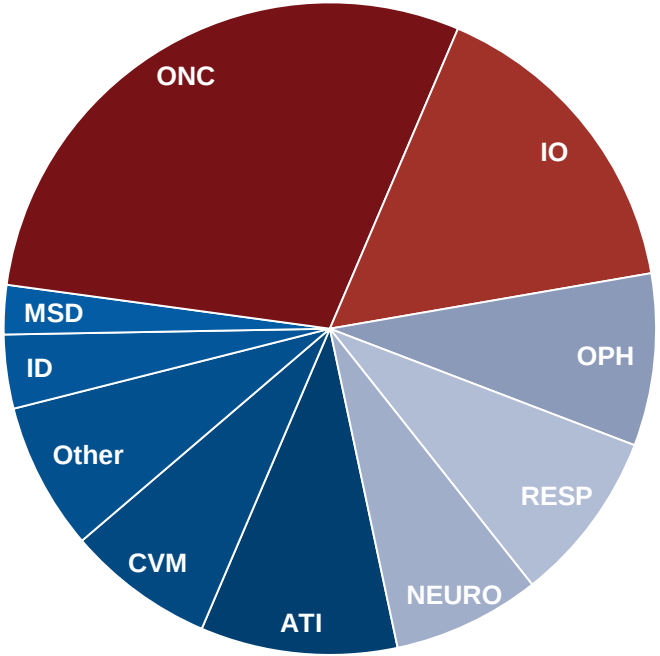
Organized around prevalent Disease Areas

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



Note: Distribution of ~90 New Molecular Entities at NIBR

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Agenda

1. NIBR 2.0
2. Oncology

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NIBR 2.0 Strategy

A next generation of therapeutics

NIBR 2.0 Strategy

1. Innovate the new science of therapeutics
2. Align with Development
3. Open the framework
4. Invest in our people
5. Rebuild & prioritize

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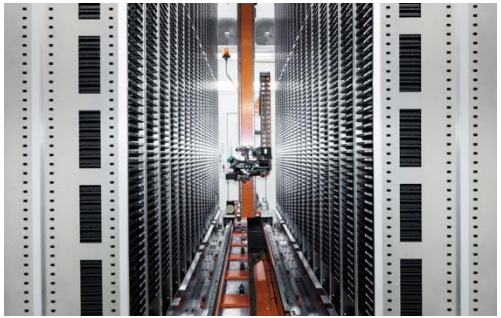
A Next-Gen DNA-Encoded Library (DEL) Platform

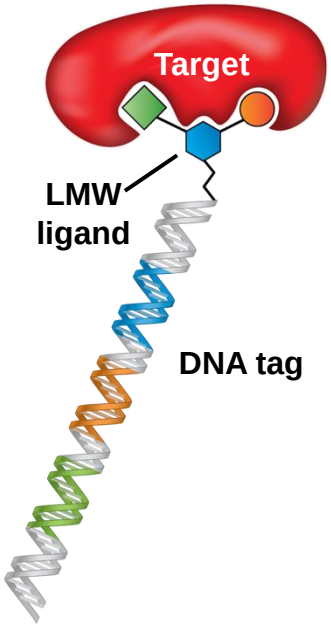
Screening on an unprecedented scale

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





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Targeted Protein Degradation

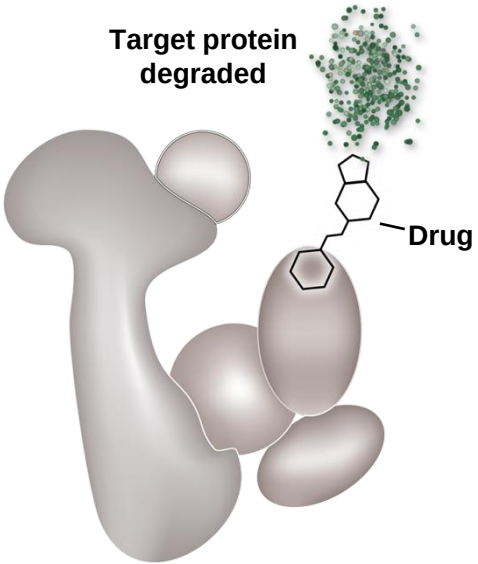
A new type of therapeutic

1. Innovate the new science of therapeutics

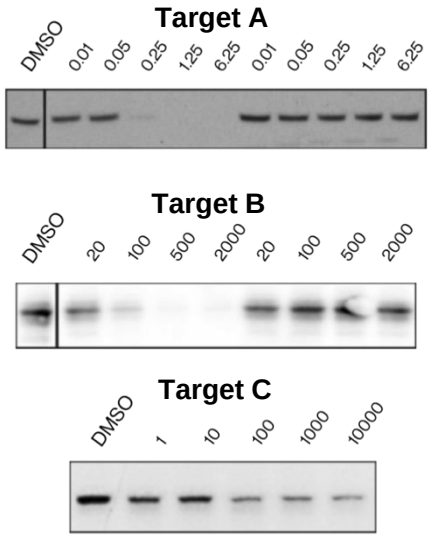
Drug molecules are typically directed to active sites of protein targets, disabling a single function of protein biomolecule

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



E3 complex



24 hr treatment of cancer cells

Source: NIBR in-house data Investigational. Efficacy & safety not yet established

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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)

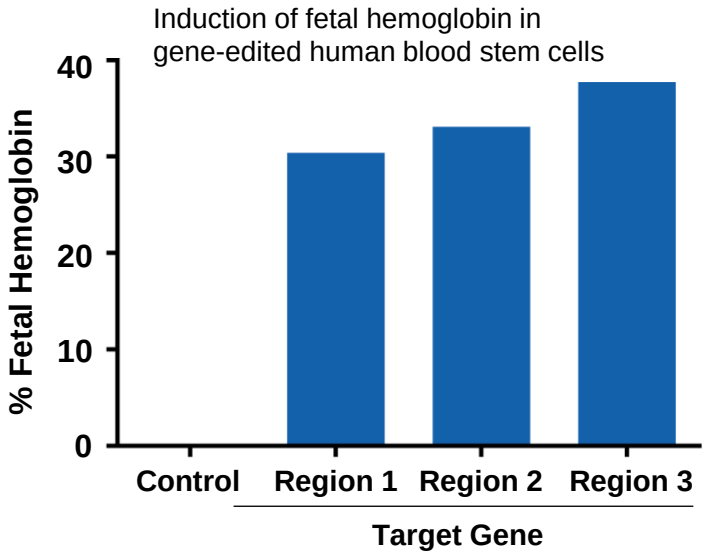
In collaboration with Intellia Therapeutics, evaluating utility of CRISPR/Cas9 for editing CART cells to treat cancer and human hematopoietic stem cells (HSC), *e.g.*, to potentially cure sickle cell and other blood disorders

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

CARIBOU BIOSCIENCES

Intellia THERAPEUTICS

Editing the Genome in Sickle Cell Disease



Source: NIBR in-house data Investigational. Efficacy & safety not yet established

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Aligning around Accelerated Drug Development

Seamless alignment of early and late development

2. Align with Development

- ✓ unmet medical need = $f^{\text{desperation}}(\text{population})$
- ✓ 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

✓ Completed ✓ In progress

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

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Open Innovation in Drug Discovery

Connectivity as a new priority in Research & Early Development

3. Open the framework

Scholars

Chemical Probes

Penn
University of Pennsylvania

ADURO BIOTECH

imi innovative medicines initiative

Partnerships

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NIBR

A unique research community

4. Invest in our people

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New Oncology Leadership

Developing the next wave of definitive cancer therapeutics

5. Rebuild & prioritize

Jeffrey Engelman
Oncology

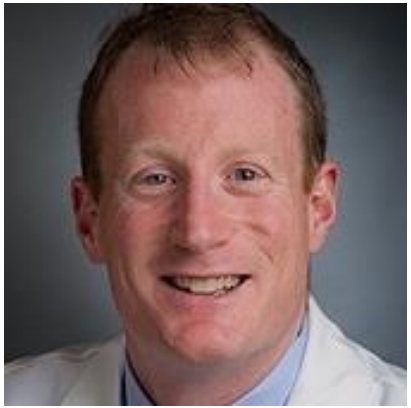
Mass. General Hospital (MGH)
Joined NIBR in June 2016

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

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Agenda

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2. Oncology

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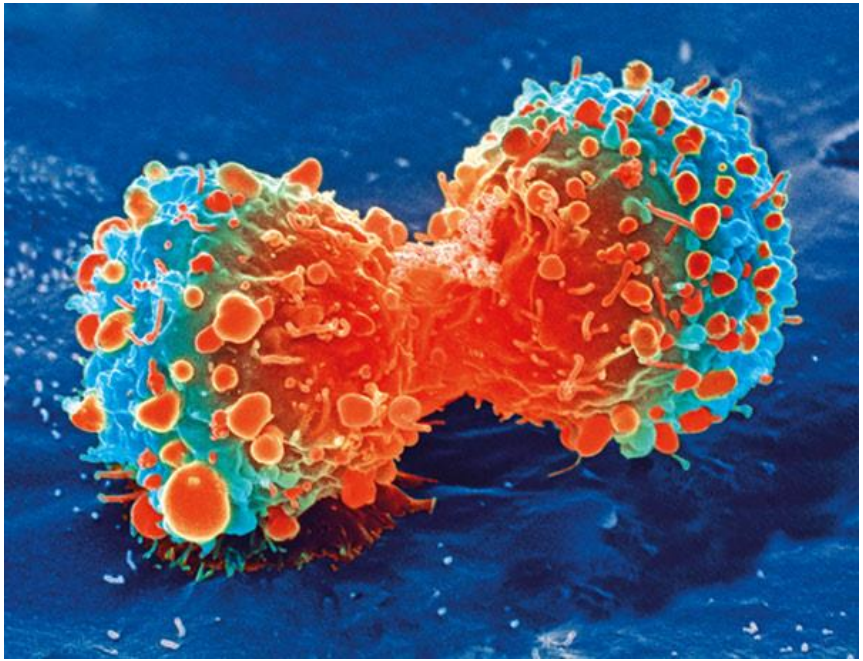
Immuno-Oncology (IO)

Opportunities and challenges



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

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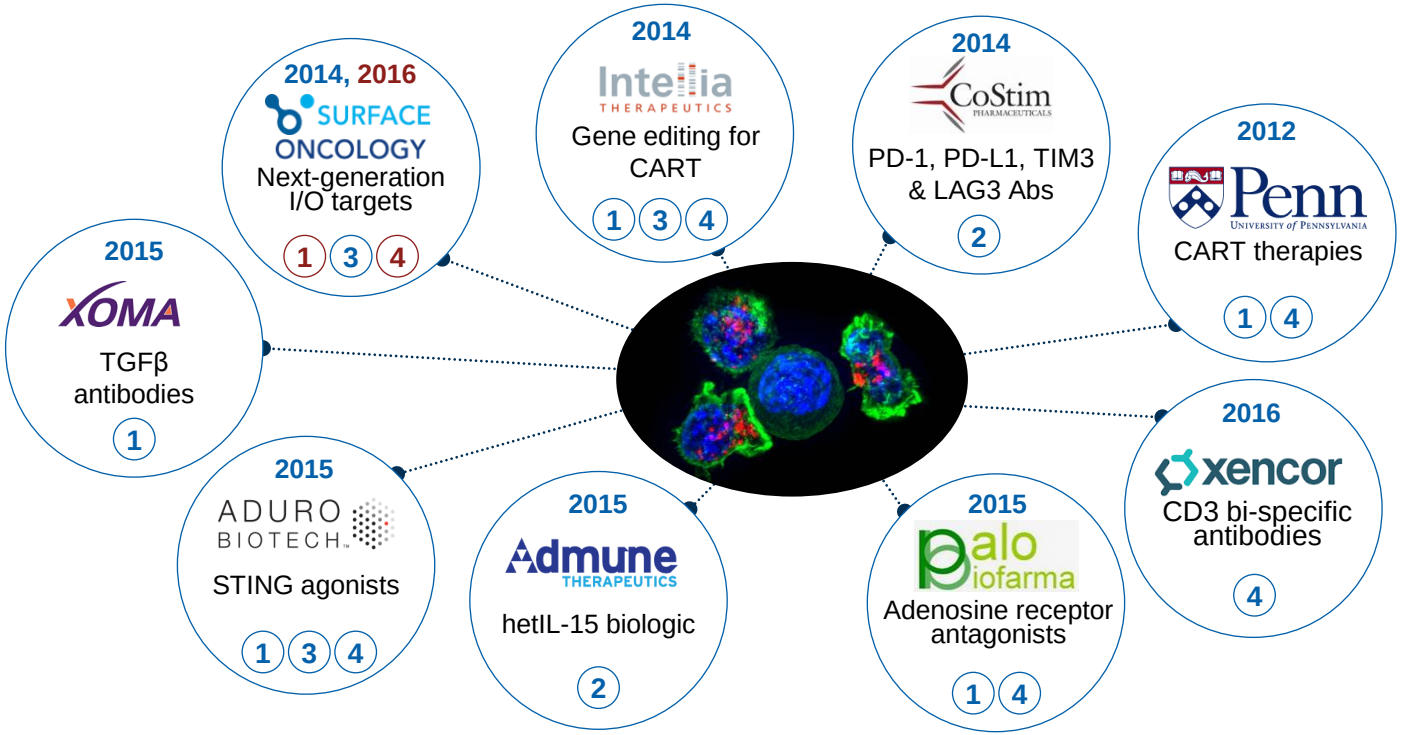
The Novartis Immuno-Oncology Pipeline

Jump-started by external innovation



1. License
2. Acquisition
3. Equity Investment
4. Collaboration

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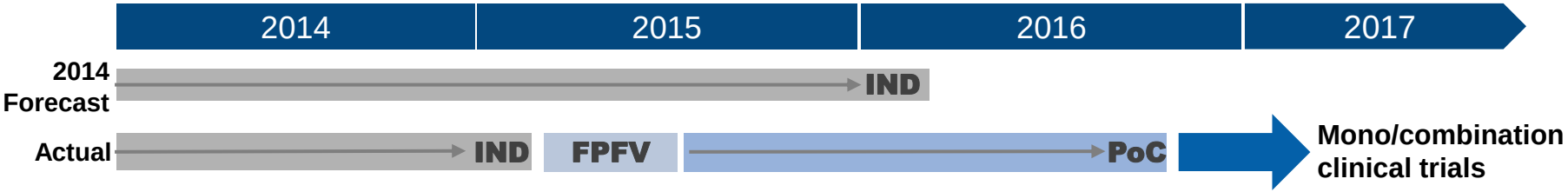
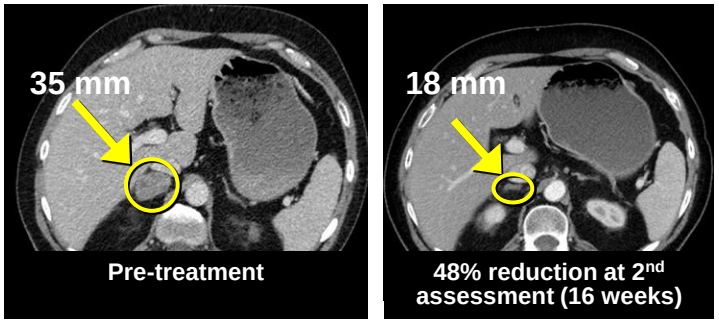
Accelerating the IO Portfolio

PDR001 Development Timeline

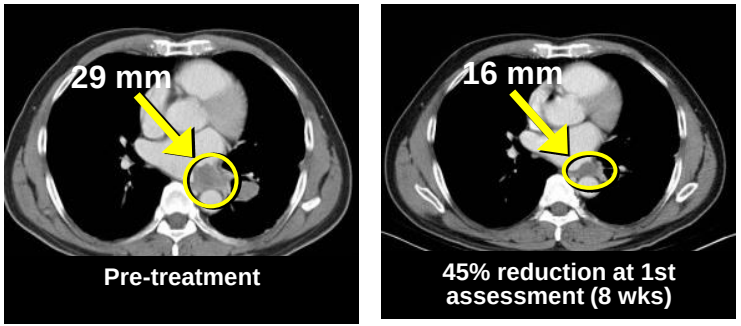


Initial PDR001 Responses



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

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The Novartis Immuno-Oncology Pipeline

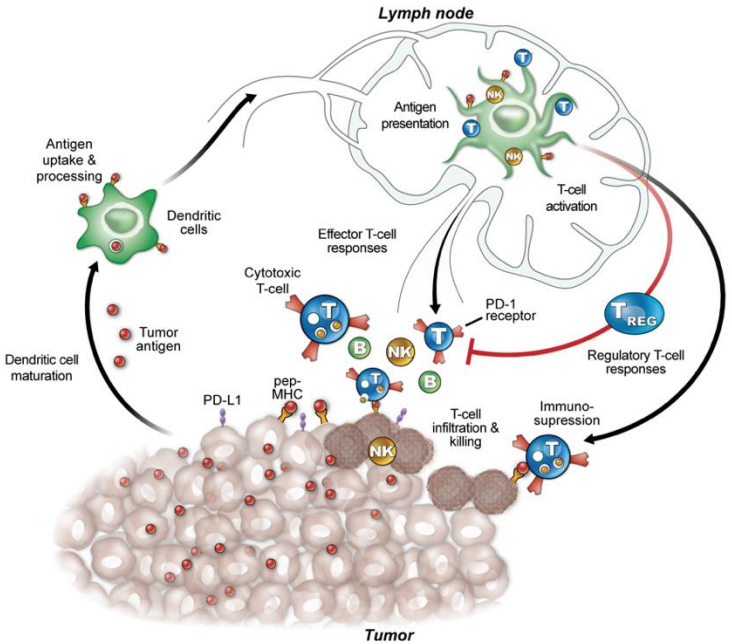
Prioritized by major mechanisms of immune escape

Immune Priming

STING
TIM-3
cMET
Porcupine

T-cell Engineering

CART	**Bi-specific Ab**
CD19	CD123
BCMA	CD20
CD123	
EGFRvIII	
Mesothelin	



T-Cell Modulation

IL-15	TEC
GITR	mTOR
IAP	

Tumor Environment

PD-1	CSF-1
PD-L1	CSF-1R
LAG-3	A_{2A} adenosine receptor
TIM-3	HDAC
TGF-β	MEK
IL-17	
IL-1	

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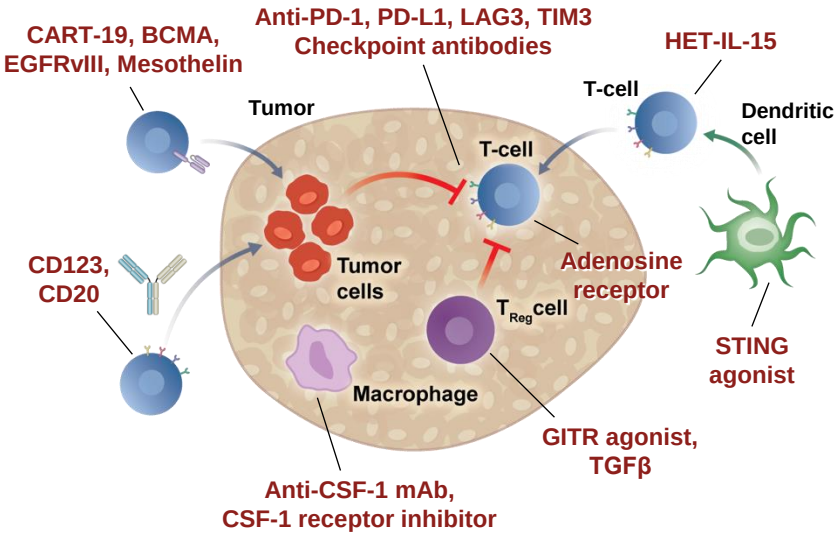
First-in-Class Potential in Clinical Investigation

A comprehensive pipeline focused on second-generation IO agents



	Target (Compound)	FIH Trial Initiated
Novel targets	CSF-1 (MCS110)	✓
	CSF-1R (BLZ945)	✓
	CART-19 (CTL019 / CTL119)	✓
	CART-BCMA (MCM998)	✓
	CART-EGFRvIII (LXF821)	✓
	CART-Mesothelin (NIU440)	2017
	CART-CD123 (MIH911)	✓
	Het IL-15 (NIZ985)	✓
	Adenosine receptor (NIR178)	✓
	TGFβ (NIS793)	2017
	STING (MIW815)[1]	✓
	GITR (GWN323)	✓
	CD123 x CD3 (SQZ622)[2]	✓
	CD20 x CD3 (THG338)[2]	✓
Checkpoint inhibitors	* PD-1 (PDR001)	✓
	PD-L1 (FAZ053)	✓
	LAG3 (LAG525)	✓
	TIM3 (MBG453)	✓

1. Collaboration / licensing with Aduro 2. Collaboration / licensing with Xencor
* Backbone of first-in-class combination strategies

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Potential First-in-Class Combination Therapies

20 exploratory IO combination studies expected by early 2017

	Target (Compound)	FIH Trial Initiated
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	2017
	IL-17 (CJM112) + PD-1	✓
	IL-1 (Ilaris®) + PD-1	✓
	TGFβ (NIS793) + PD-1	2017
	PD-L1 (FAZ053) + PD-1	✓
	STING (MIW815)[1] + PD-1	2017
IO with chemo	CSF-1 (MCS110) + carbo/gem	✓

	Target (Compound)	FIH Trial Initiated
IO with targeted agent[2]	cMET (INC280) + PD-1	✓
	Porcupine (WNT974) + PD-1	2017
	HDAC (Farydak®) + PD-1	✓
	mTOR (Afinitor®) + PD-1	✓
	IAP inh (LCL161) + PD-1	✓
	MEK (Trametinib) + PD-1	✓
	TEC (EGF816) + PD-1	✓
	B/CRAF (LXH254) + PD-1	✓

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

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A Pipeline of Early Stage Targeted Therapies

Single agent and combination studies in Early Development

Monotherapy

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

Combinations

Targeted
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

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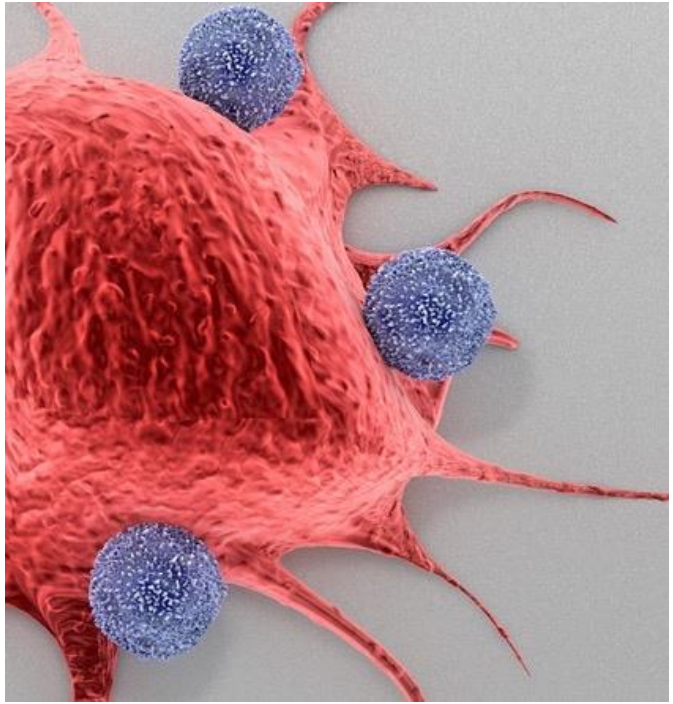
Cell-based Immunotherapy Anticipated to Reach Regulatory Consideration in 2017

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



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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

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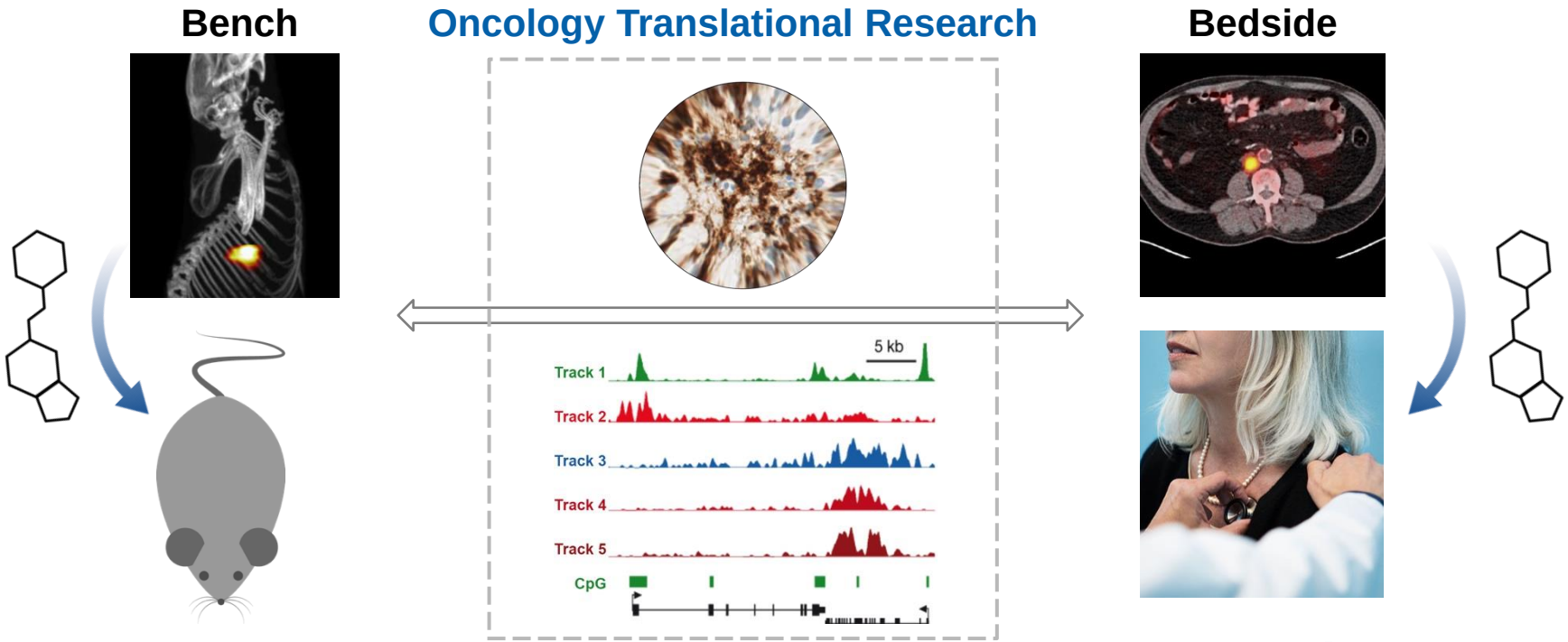
Oncology Translational Research

A state-of-the-art laboratory to understand and to guide cancer drug development



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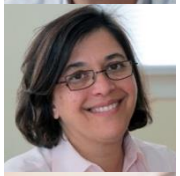
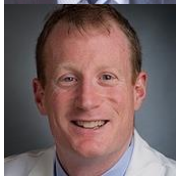
Bringing the Best Minds and Medicines Together to Deliver Definitive Cancer Therapies



IO Monotherapy

Novel targets	CSF-1 (MCS110)
	CSF-1R (BLZ945)
	CART-19 (CTL019/119)
	CART-BCMA (MCM998)
	CART-EGFRvIII (LXF821)
	CART-Mesothelin (NIU440)
	CART-CD123 (MIH911)
	Het IL-15 (NIZ985)
	Adenosine receptor (NIR178)
	TGFβ (NIS793)
	STING (MIW815)
	GITR (GWN323)
	CD123 x CD3 (SQZ622)[2]
	CD20 x CD3 (THG338)[2]
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[1]
IO/ chemo	CSF-1 (MCS110) + carbo/gem
IO/ targeted agent	cMET (INC280) + PD-1
	Porcupine (WNT974) + PD-1
	HDAC (Farydak®) + PD-1
	mTOR (Afinitor®) + PD-1
	IAP inh (LCL161) + PD-1
	MEK (Trametinib) + PD-1
	TEC (EGF816) + PD-1
	B/CRAF (LXH254) + PD-1

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FGF	FGFR-1/2/3	Bladder, Chloang.
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	ERK	NSCLC
EGFR	EGFR mut	NSCLC
Apoptosis Regulation	P53/HDM2	AML
	BCL2	R/R CLL, NHL
Epigenetic	EED	DLBCL, NPC
Wnt	Porcupine	Pancreatic, CRC
BCR-ABL	BCR-ABL allosteric	CML
PIM	Pan-PIM	AML
IDH	IDH-1	AML
SERD	SERD	Breast Cancer
GPCR	PKC	Uveal Melanoma
ADC	P-Cadherin ADC	PCAD, H&N, Esoph,
	Cadherin-6 ADC	Ovarian, RCC

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

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

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Selected other programs in clinical investigation

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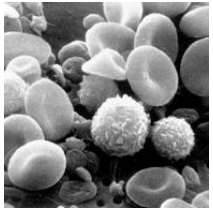
Autoimmunity & Transplant Immunology

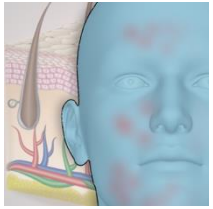
Programs in clinical investigation

Sjögren's Syndrome
VAY736: anti-BAFF-R Ab
CFZ533: anti-CD40 Ab

Acute Graft v Host Disease
KRP203: S1PR Agonist

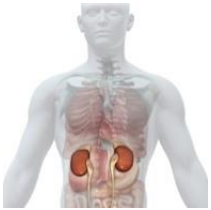


Inflammatory Acne
CJM112: anti-IL-17 Ab



Hidradenitis Suppurativa
CJM112: anti-IL-17 Ab

Kidney Transplant Rejection
CFZ533: anti-CD40 Ab



Sarcoidosis
ACZ885 (Ilaris®): anti-IL-1β Ab

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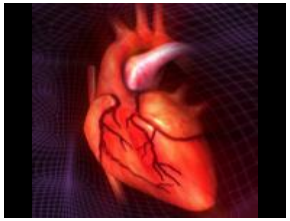
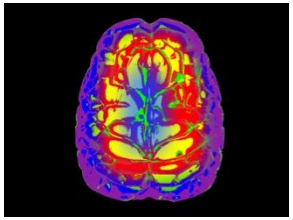
Cardiovascular and Metabolism

Programs in clinical investigation

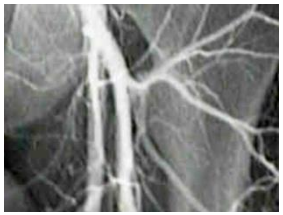
Heart Failure
CLR235: Heart contractility agent



Stroke Prevention
MAA868: Anti-thrombotic



Peripheral Arterial Disease
ACZ885: Anti-IL-1β



Weight Loss
LIK066: SGLT1/2 Inhibitor

Resistant Hypertension
LHW090: NEP Inhibitor

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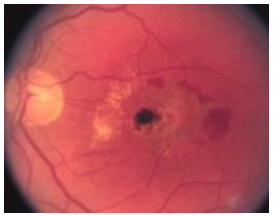
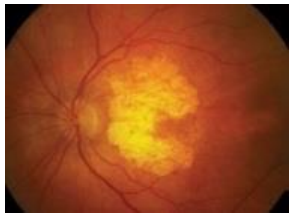
Ophthalmology & Regenerative Medicine

Programs in clinical investigation

Wet AMD
RTH258: High-potency scFv VEGFi

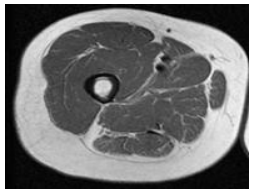


Dry AMD
Combinations of complement inhibitors

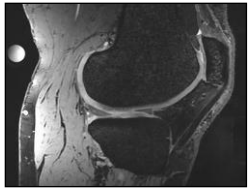


Diabetic Retinopathy
LKA651: Anti-erythropoietin ivt

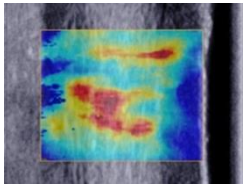
Sarcopenia
BYM338: Anti-ActRII Ab



Cartilage Injury
LNA043: Chondrogenesis inducer



Tendon Injury
Tendon repair promotion



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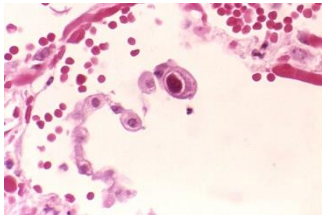
Infectious & Respiratory Diseases

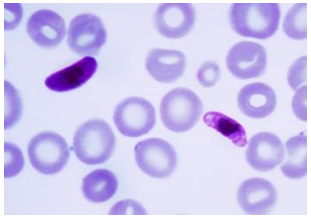
Programs in clinical investigation

Gram-negative Bacterial Infections
LYS228: Novel antibiotic

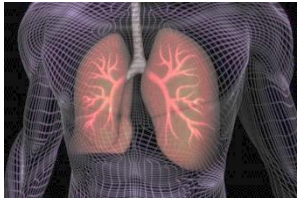
Congenital Cytomegalovirus
CSJ148: Anti-CMV



Malaria
KAF156: *P. falciparum*



COPD
QBW251: CFTR Potentiator



Cystic Fibrosis
QBW251: CFTR Potentiator

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Neuroscience

Programs in clinical investigation

Spinal Muscular Atrophy
LMI070: RNA Splicing Modulator

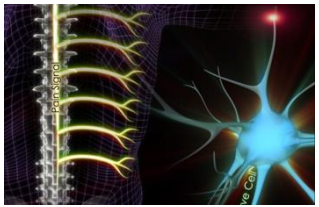
Alzheimer's Disease
CNP520: BACE Inhibitor

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



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Appendix
Research

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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

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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

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Novartis Institutes for BioMedical Research (NIBR)

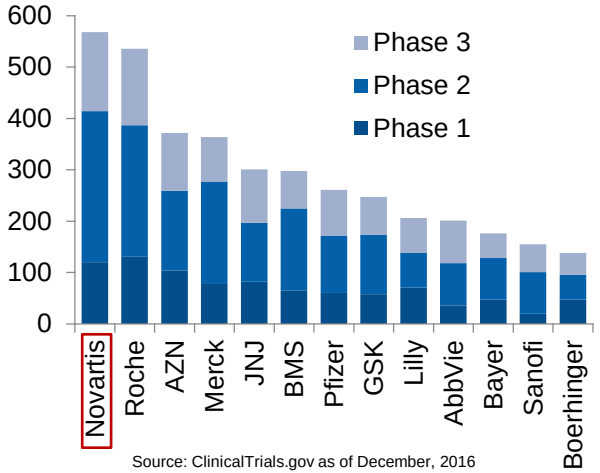
Drug discovery and early development

~6,000

Scientists /
7 sites globally

>500

Ongoing clinical trials (NIBR & GDD)



Source: ClinicalTrials.gov as of December, 2016

~400

Research projects

~90

New Molecular Entities

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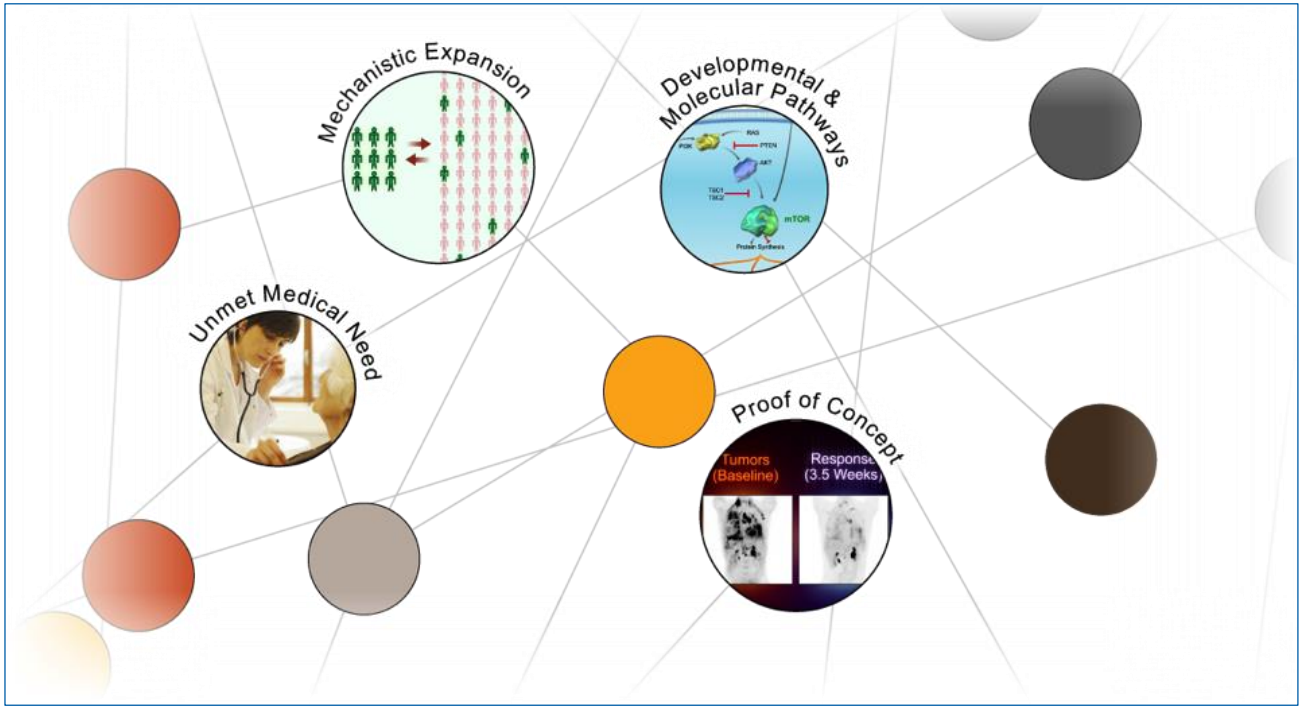
NIBR v1.0 – Pathways of Unmet Medical Need



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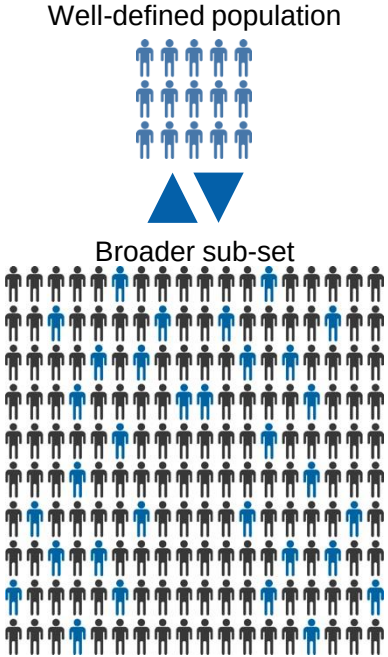
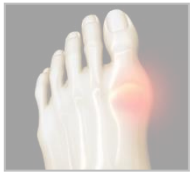
NIBR v1.0 – Pathways of Unmet Medical Need



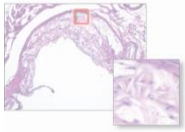
CAPS
<0.020 Million*

Systemic Juvenile Idiopathic Arthritis (SJIA)
0.075 million*

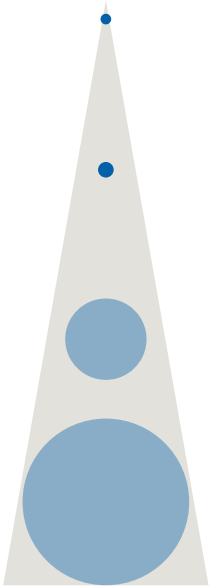
Gout
20 Million*



Atherosclerosis[2]
130 Million*



ILARIS® (canakinumab) [1]



1. Ilaris is approved for the symptomatic treatment of refractory acute gouty arthritis in the EU
* Global prevalence estimates.

2. Investigational. Image from *Latz, et al., Nature, Vol 464|29 April 2010*

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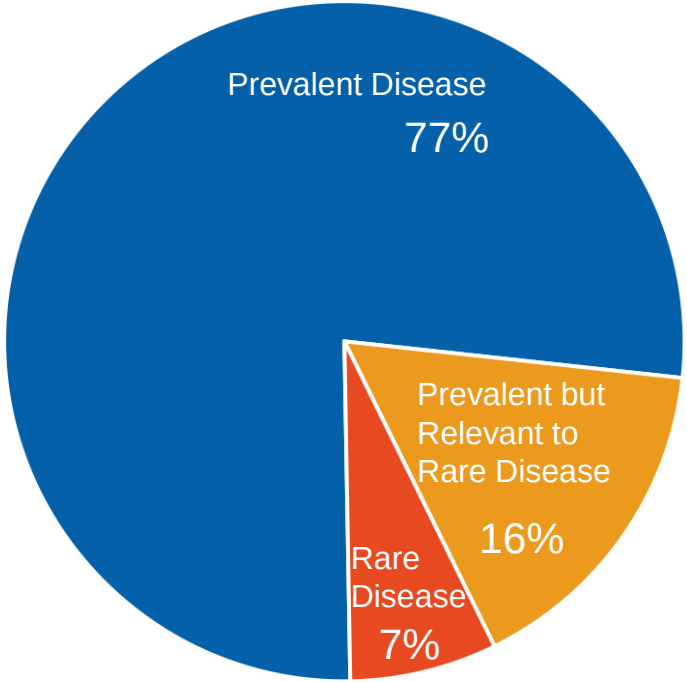
NIBR

Organized around prevalent Disease Areas

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

Projects by Disease Prevalence



Note: Projects between sPoC and PoC, excludes post-PoC.

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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

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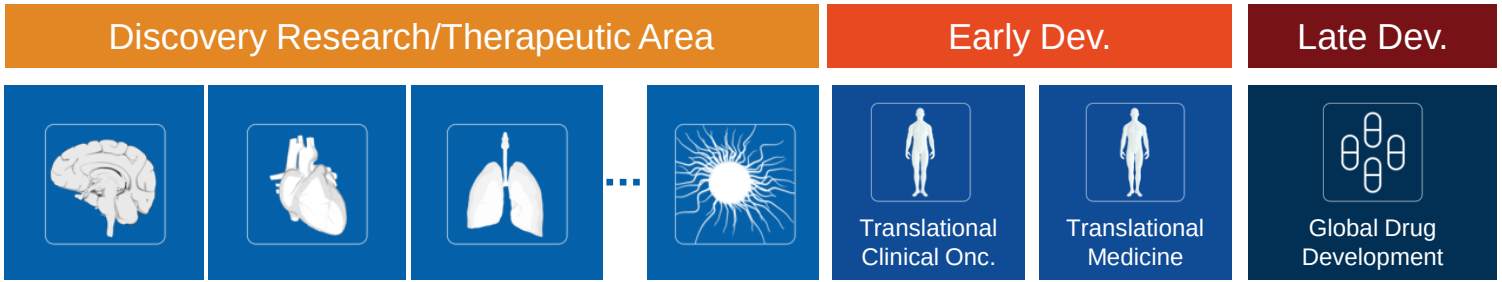
Aligning around Accelerated Drug Development

Strategic restructuring in 2016 as a step-wise evolution for speed and agility

2. Align with Development



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