Forward Looking Statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development of new products, including future clinical trial results and analysis of clinical data (including post-marketing data), decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates. There are additional risks that may cause actual results to differ materially from those contemplated by the forward-looking statements, such as the lack of commercial success of certain product candidates once approved, pricing pressures, both in the United States and abroad, including pharmaceutical reimbursement and pricing, the future approval and commercial success of therapeutic alternatives, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, changes in applicable laws or regulations, the impact of cost containment initiatives and subsequent changes thereto, as well as those risks and uncertainties discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2016. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.
Opening Remarks
- Olivier Brandicourt - Chief Executive Officer

Strategic Focus of Sanofi’s R&D Model 2.0
- Elias Zerhouni - President, Global R&D

Leading in Specialty Care
- Bill Sibold - EVP, Sanofi Genzyme

Building Immunology & Multiple Sclerosis
- Jorge Insuasty - SVP, Global Head of Development
- Frank Nestle - Global Head of Immunology & Inflammation Therapeutic Research Area

Sustaining Rare Disease
- Rand Sutherland - Therapeutic Area Head, Rare Disease Development

Q&A Session

Building Oncology
- Jorge Insuasty - SVP, Global Head of Development
- Yong-Jun Liu - SVP, Global Head of Research

Sustaining Diabetes & Cardiovascular
- Stefan Oelrich - EVP, Diabetes & Cardiovascular
- Klaus Henning Jensen - Therapeutic Area Head, Diabetes Development
- Jay Edelberg – VP, Global Cardiovascular Development

Sustaining Vaccines
- David Loew - EVP, Sanofi Pasteur
- John Shiver - SVP, Vaccines R&D

Closing Remarks
- Elias Zerhouni - President, Global R&D

Q&A Session
Olivier Brandicourt
Chief Executive Officer
Today We Will Focus on…

- Sustaining innovation in R&D
- Delivering outstanding launches
- Reshaping the portfolio
- Simplifying the organization
Sanofi Research and Development

<table>
<thead>
<tr>
<th>71</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>projects in development for NMEs or additional indications(^{(1)})</td>
<td>potential submissions in next 18 months</td>
</tr>
<tr>
<td>7</td>
<td>&gt;10</td>
</tr>
<tr>
<td>NME and Vaccine approvals since 2015(^{(2)})</td>
<td>pivotal study starts in next 12 months</td>
</tr>
</tbody>
</table>

\(^{(1)}\) Includes 4 Phase 1 products and 1 Phase 2 product for which Sanofi has opt-in rights but has not exercised these rights

\(^{(2)}\) Adlyxin®, Dengvaxia®, Dupixent®, Kevzara®, Praluent®, Soliqua™ /Suliqua™ 100/33, Toujeo®
R&D Transformation Has Resulted in R&D Productivity Above the Industry Average

2014-2016

- Advanced high-value development projects
- Robust launch pipeline
- Rigorous portfolio prioritization processes
- Further improved R&D organization efficiency
- Developed proprietary technology platforms
- Strengthened biologic capabilities
- Focused and fully aligned R&D with GBUs

R&D Productivity

New product sales/R&D spending\(^{(1)}\)

<table>
<thead>
<tr>
<th>Year</th>
<th>Industry average</th>
<th>SANOFI 2011</th>
<th>SANOFI 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^{(1)}\) KMR analysis: new product sales per year (products registered in the past 5 years) divided by R&D spend per year
Sanofi’s R&D Hub Model to Capture Innovation Through Cutting Edge Platform Technologies and Capabilities

<table>
<thead>
<tr>
<th>North America Hub</th>
<th>French Hub</th>
<th>German Hub</th>
<th>Asia-Pacific Hub</th>
<th>Partnered Tech</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Multi-Specifics</td>
<td>• Multi-Specifics</td>
<td>• Multi-Specifics</td>
<td>• Digital Hub</td>
<td>• BioNTech mRNA Mixture</td>
</tr>
<tr>
<td>• PRR Antibody Conjugates</td>
<td>• PRR Antibody Conjugates</td>
<td>• Peptides</td>
<td>• Ablynx Nanobodies</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• siRNA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Working across geographies, organizations and disciplines around the Hub model

Connecting with our biomedical ecosystem to generate value through networks
# A Focused and Commercially-Aligned R&D Organization

<table>
<thead>
<tr>
<th>Sanofi Genzyme</th>
<th>DCV</th>
<th>Sanofi Pasteur</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immunology &amp; MS</strong></td>
<td><strong>Oncology</strong></td>
<td><strong>Rare Disease</strong></td>
</tr>
<tr>
<td>dupilumab Asthma*</td>
<td>isatuximab MM</td>
<td>avalglucosidase alfa Pompe</td>
</tr>
<tr>
<td>dupilumab Nasal Polyps*</td>
<td>isatuximab+cemiplimab Solid tumors*</td>
<td>oilpudase alfa ASMD</td>
</tr>
<tr>
<td>dupilumab EoE*</td>
<td>cemiplimab CSCC*</td>
<td>patisiran hATTR amyloidosis*</td>
</tr>
<tr>
<td>dupilumab Food Allergies*</td>
<td>cemiplimab NSCLC*</td>
<td>fitusiran Hemophilia*</td>
</tr>
<tr>
<td>dupilumab Pediatric studies*</td>
<td>cemiplimab BCC*</td>
<td>venglustat Gaucher type 3</td>
</tr>
<tr>
<td>dupilumab COPD*</td>
<td>cemiplimab Cervical Cancer*</td>
<td>venglustat GBA-Parkinson’s</td>
</tr>
<tr>
<td>IL33(1) Asthma*</td>
<td>TGF-Beta mAb Solid tumors</td>
<td>venglustat ADPKD</td>
</tr>
<tr>
<td>IL33(1) COPD*</td>
<td>LAG3(2) Advanced Cancers**</td>
<td>Praluent® CV events reduction*</td>
</tr>
<tr>
<td>IL33(1) Atopic Dermatitis*</td>
<td>Anti-CA6(3) TNBC</td>
<td>sotagliflozin T1D*</td>
</tr>
<tr>
<td>sarilumab GCA</td>
<td>Anti-CEACAM5 ADC(4) Solid tumors</td>
<td>sotagliflozin T2D*</td>
</tr>
<tr>
<td>sarilumab PMR</td>
<td>SERD MBC</td>
<td>efpeglenatide T2D*</td>
</tr>
<tr>
<td>alemtuzumab PPMS</td>
<td></td>
<td>GLP-1/GCG(5) Obesity</td>
</tr>
<tr>
<td>BTK inhibitor* MS</td>
<td></td>
<td>GLP-1/GCG(5) NASH</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Development Priorities</th>
<th>DCV</th>
<th>Sanofi Pasteur</th>
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</thead>
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<tr>
<td>PRN2246</td>
<td>MenQuad TT</td>
<td><strong>Partnered assets</strong></td>
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<tr>
<td>RSV mAb(7)</td>
<td>RSV mAb(7)</td>
<td>RSV Vaccine</td>
</tr>
<tr>
<td>RSV Vaccine</td>
<td>RSV Vaccine</td>
<td>Fluzone® QIV HD</td>
</tr>
<tr>
<td>Fluzone® QIV HD</td>
<td>Fluzone® QIV HD</td>
<td>PR5i</td>
</tr>
</tbody>
</table>

*Partnered assets
**Opt-in rights product for which rights have not been exercised yet

EoE= Eosinophilic Esophagitis ; COPD= Chronic Obstructive Pulmonary Disease ; PPMS= Primary Progressive Multiple Sclerosis ; RRMS= Relapsing-Remitting Multiple Sclerosis ; MM= Multiple Myeloma ; CSCC= Cutaneous Squamous Cell Carcinoma ; NSCLC= Non-Small Cell Lung Cancer ; BCC= Basal Cell Carcinoma ; TNBC= Triple Negative Breast Cancer ; MBC= Metastatic Breast Cancer ; ASMD= Acid sphingo-myelinase deficiency ; ADPKD= Autosomal Dominant Polycystic Kidney Disease ; T1D= Type 1 Diabetes ; T2D= Type 2 Diabetes ; NASH= Nonalcoholic Steatohepatitis; HCM= Hypertrophic Cardiomyopathy
9 Potential Submissions\(^{(1)}\) for New Products or Additional Indications Over Next 18 Months

### Planned Submissions

**Q4 2017**
- **dupilumab**
  - sBLA, persistent, uncontrolled Asthma

**H1 2018**
- **sotagliflozin**
  - NDA, Type 1 Diabetes
- **cemiplimab**
  - BLA, metastatic CSCC
- **patisiran**
  - Submissions for hATTR amyloidosis in Brazil & Japan

**H2 2018**
- **Praluent**
  - sBLA, ODYSSEY CVOT
- **DUPIXENT**
  - Dupilumab
- **isatuximab**
  - BLA, RRMM
- **Men Quad TT**
  - 2\(^{nd}\) generation meningococcal ACYW conjugate vaccine

**H1 2019**
- **dupilumab**
  - sBLA, Nasal Polyps

---

(1) Number of submissions determined by first submission to a regulatory authority in a country; subsequent submissions to other global regulatory authorities are not included in the count of 9 potential submissions.
New Wave of Pivotal Study Starts Expected Over the Next 12 Months

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>dupilumab</strong>&lt;sup&gt;(1)&lt;/sup&gt;</td>
<td>COPD, Eosinophilic Esophagitis</td>
</tr>
<tr>
<td>Anti-IL4Rα mAb</td>
<td></td>
</tr>
<tr>
<td><strong>venglustat</strong>&lt;sup&gt;(2)&lt;/sup&gt;</td>
<td>Autosomal dominant polycystic kidney disease (ADPKD)</td>
</tr>
<tr>
<td>Oral GCS inhibitor</td>
<td></td>
</tr>
<tr>
<td><strong>SAR425899</strong></td>
<td>Obesity</td>
</tr>
<tr>
<td>GLP-1/GCR dual agonist</td>
<td></td>
</tr>
<tr>
<td><strong>efpeglenatide</strong>&lt;sup&gt;(3)&lt;/sup&gt;</td>
<td>Type 2 Diabetes</td>
</tr>
<tr>
<td>Once-weekly GLP-1RA</td>
<td></td>
</tr>
<tr>
<td><strong>isatuximab</strong>&lt;sup&gt;(4)&lt;/sup&gt;</td>
<td>1L MM SCT eligible, 1L MM SCT ineligible</td>
</tr>
<tr>
<td>Anti-CD38 mAb</td>
<td></td>
</tr>
<tr>
<td><strong>alemtuzumab</strong></td>
<td>Primary Progressive MS</td>
</tr>
<tr>
<td><strong>cemiplimab</strong>&lt;sup&gt;(1)&lt;/sup&gt;</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; line NSCLC</td>
</tr>
<tr>
<td><strong>mavacamten</strong>&lt;sup&gt;(4)&lt;/sup&gt;</td>
<td>Obstructive Hypertrophic Cardiomyopathy</td>
</tr>
</tbody>
</table>

COPD= Chronic Obstructive Pulmonary Disease; NSCLC= Non-Small Cell Lung Cancer

<sup>(1)</sup> Collaboration with Regeneron
<sup>(2)</sup> Phase 2/3 registrational study
<sup>(3)</sup> Collaboration with Hanmi
<sup>(4)</sup> Collaboration with Myokardia. Sanofi will lead ex-U.S. regulatory and commercial activities to mavacamten program where it has ex-U.S. commercialization rights
Financially Disciplined R&D Investments Based on Rigorous Prioritization Methodology

**R&D Investments (in €bn)**

<table>
<thead>
<tr>
<th>Year</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017e</th>
<th>2018e</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>4.8</td>
<td>5.3</td>
<td>5.2</td>
<td>5.5</td>
<td></td>
</tr>
</tbody>
</table>

**Efficiency frontier provides a comparative view of the total value creation for a given R&D investment**

Projects ranked from left to right in descending order of productivity.

- Projects in the *top right* corner estimated to have *lowest* productivity.
- Projects in the *bottom left* corner estimated to have *highest* productivity.

Cumulative Risk-Adjusted NPV (€m) vs. Cumulative Risk-Adjusted R&D Cost (€m)
Rigorous Candidate Selection Resulting in Probabilities of Success Above Industry Average in Later Stages

Projects discontinued at an early stage…

% projects discontinued by stage

<table>
<thead>
<tr>
<th>Year</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stopped in early stages</td>
<td>64%</td>
<td>36%</td>
<td>14%</td>
<td>86%</td>
<td>100%</td>
</tr>
</tbody>
</table>

...Higher probabilities of success in later stages

% probability of success by Phase (2014-2016)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Stopped in late stages</td>
<td>36%</td>
<td>86%</td>
<td>83%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

(1) KMR analysis
# Innovative Portfolio*(1)* Brings High Value to Patients

## Expected Phase in 2018

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3 / Pivotal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-PoC</td>
<td>Pre-PoC</td>
<td></td>
</tr>
</tbody>
</table>

## Post-PoC

<table>
<thead>
<tr>
<th>Potential New Treatment Options</th>
<th>Potential First or Best in Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>cemiplimab NSCLC monotherapy</td>
<td>dupilumab Asthma</td>
</tr>
<tr>
<td>efpeglenatide Type 2 Diabetes</td>
<td>cemiplimab SCC</td>
</tr>
<tr>
<td>sotagliflozin Type 2 Diabetes</td>
<td>sotagliflozin Type 1 Diabetes</td>
</tr>
<tr>
<td>MenQuadTT Meningitis</td>
<td>dupilumab Nasal Polyposis</td>
</tr>
<tr>
<td>isatuximab Multiple Myeloma</td>
<td>avalglucosidase alfa</td>
</tr>
<tr>
<td></td>
<td>fitusiran Hemophilia</td>
</tr>
<tr>
<td></td>
<td>dupilumab EoE</td>
</tr>
<tr>
<td></td>
<td>olipudase alfa</td>
</tr>
<tr>
<td></td>
<td>Praluent® CVOT</td>
</tr>
<tr>
<td></td>
<td>patisiran hATTR Amyloidosis</td>
</tr>
<tr>
<td></td>
<td>anti-IL33 mAb</td>
</tr>
</tbody>
</table>

## Pre-PoC

<table>
<thead>
<tr>
<th>Potential New Treatment Options</th>
<th>Potential First or Best in Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>alemtuzumab PPMS</td>
<td>cemiplimab Advanced BCC</td>
</tr>
<tr>
<td>anti-LAG-3 mAb Solid Tumors</td>
<td>venglustat GBA-Parkinson’s</td>
</tr>
<tr>
<td>isatuximab combo Solid Tumors</td>
<td>anti-IL33 mAb Asthma</td>
</tr>
<tr>
<td>anti-TGFβ mAb Solid Tumors</td>
<td>venglustat Gaucher Type 3</td>
</tr>
<tr>
<td></td>
<td>anti-IL33 mAb COPD</td>
</tr>
<tr>
<td></td>
<td>venglustat ADPKD</td>
</tr>
<tr>
<td></td>
<td>mavacamten Cardiomyopathy</td>
</tr>
<tr>
<td></td>
<td>SERD Breast Cancer</td>
</tr>
<tr>
<td></td>
<td>GLP-1/GCG Obesity</td>
</tr>
<tr>
<td></td>
<td>RSV mAb</td>
</tr>
<tr>
<td></td>
<td>MYK-491 Dilated Cardiomyopathy</td>
</tr>
<tr>
<td>dupilumab COPD</td>
<td></td>
</tr>
</tbody>
</table>

*(1) Products in graphic include selected R&D pipeline projects and do not reflect the entirety of Sanofi's clinical development portfolio*

*(2) Proof of concept based on competitor data*

**Partnered products:** cemiplimab, dupilumab, anti-IL33 mAb, (Regeneron); anti-LAG3 (Regeneron product for which Sanofi has opt-in right); sotagliflozin (Lexicon); efpeglenatide (Hanmi); fitusiran, patisiran (Alnylam); mavacamten, MYK-491 (Myokardia) - Sanofi may have limited or shared rights on some of these products.
Strategic Priorities in R&D to Drive a Leading Pipeline of Innovative Molecules

R&D Priorities

- **Execute** to deliver late-stage pipeline with financially disciplined investments
- **Accelerate** research productivity
- **Drive** portfolio to at least two-thirds internally developed
- **Advance** Sanofi’s proprietary research platforms
Elias Zerhouni
President, Global R&D

Strategic Focus of Sanofi’s R&D Model 2.0
Sanofi is a Science-Driven Company

Scientific Publications

<table>
<thead>
<tr>
<th>Year</th>
<th>Total</th>
<th>Sanofi R&amp;D</th>
<th>Nature, Science, Cell(1)</th>
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<tr>
<td>2010</td>
<td>477</td>
<td>7</td>
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<tr>
<td>2011</td>
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<td>2012</td>
<td>747</td>
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<tr>
<td>2013</td>
<td>805</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>2014</td>
<td>832</td>
<td>15</td>
<td>19</td>
</tr>
<tr>
<td>2015</td>
<td>886</td>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>2016</td>
<td>885</td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

% Pipeline First in Class Projects

- First in class: 65%
- Follower: 35%

Scientific Approach to R&D: A Different Vision

- Deeper understanding of molecular networks and pathways through translational medicine
- Scientific evidence indicates most diseases will require combination of therapies to achieve success
- Molecules attacking multiple points in disease pathway may result in efficacy in several diseases or improved risk/benefit in single disease

“Dream Molecules”
One Drug, Multiple Targets, Diverse Diseases

Disease 1
Disease 2
Disease 3

Multi-targeted Ab, Peptide or Drug

Disease Symptoms
Sanofi R&D Key Strategies

Therapeutic Modalities
- small molecules ➔ biologics

Mode of Action
- mono-targeting ➔ multi-targeting

Technology Platforms
- licensing ➔ proprietary
Majority of Pipeline Now Biologics, Vaccines or Novel Technologies

• More specificity, less off target toxicity
• Possible multi-functionality in one molecule
• Shorter development cycle time, higher probability of success
• Opportunity for diverse modalities (e.g. mRNA)
• Challenges to entry of biosimilars

% of Pipeline by Molecule Type

- Biologics & Vaccines: 50%
- Novel Technologies: 22%
- Small molecules: 28%
Leading Technology Platforms

Addressing Multiple Disease Targets with Single Complex Molecules

- Multispecific Antibodies (bi- & tri-specific)
- siRNA Conjugates
- Trigonal Peptides
- PRR Antibody Conjugates
- BioNTech mRNA Mixture
- Ablynx Nanobodies®

PRR = Pattern Recognition Receptor
Proprietary Tri-specific Antibody\(^{(1)}\) Demonstrated Unprecedented Potency for HIV-1 in Pre-Clinical Study

A Breakthrough Proof of Technical Concept in Science\(^{(2)}\)

One antibody binds to 3 different epitopes

- VRC01Fab
- CODV-Fab
- PGDM1400

\[ 10E8v4 \quad F_v \]

Tri-specific broadly neutralizing HIV antibodies mediate potent SHIV protection in macaques


\(^{(1)}\) Collaboration between Sanofi and NIH; expected to enter Phase 1 in Q4 2018

\(^{(2)}\) Xu, L. et al. Science, 2017
A Robust R&D Pipeline in 6 Therapeutic Areas

- Immunology
- Multiple Sclerosis & Neurology
- Oncology
- Rare Disease
- DCV
- Vaccines and Infectious Diseases
R&D Organization Built on Strong Capabilities with Addition of New Talent

Head of R&D
E. Zerhouni

R&D Operations
J. Zhang

Regulatory Affairs
H. Malone

Research
Y.J. Liu

Development
J. Insuasty

Chief Scientific Officer
G. Nabel

Sanofi Pasteur R&D
J. Shiver

Diabetes
P. Larsen

Immunology
F. Nestle

Rare Disease
S. Cheng

Diabetes
K. Henning Jensen

Immunology
C. Antoni

Rare Disease
R. Sutherland

Neuroscience
R. Balice-Gordon

Oncology
L. Debussche

Cardiovascular
A. Muslin

Neuroscience
E. Wallstroem

Oncology
J. Lager

Cardiovascular
J. Edelberg

SANOFI
# What We Will Cover Today (1/2)

<table>
<thead>
<tr>
<th>Specialty Care</th>
<th>Bill Sibold</th>
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<tbody>
<tr>
<td><strong>Immunology</strong></td>
<td></td>
</tr>
<tr>
<td>• Realize the potential of dupilumab</td>
<td>Jorge Insuasty</td>
</tr>
<tr>
<td>• Next wave of Immunology</td>
<td>Frank Nestle</td>
</tr>
<tr>
<td><strong>Rare Disease</strong></td>
<td></td>
</tr>
<tr>
<td>• Vision and ambition in Rare Disease</td>
<td>Rand Sutherland</td>
</tr>
<tr>
<td>• Venglustat</td>
<td></td>
</tr>
<tr>
<td>• Patisiran and fitusiran</td>
<td></td>
</tr>
<tr>
<td>• Avalglucosidase-alfa</td>
<td></td>
</tr>
<tr>
<td>• Olipudase-alfa</td>
<td></td>
</tr>
<tr>
<td><strong>Oncology</strong></td>
<td></td>
</tr>
<tr>
<td>• Vision and ambition in Oncology</td>
<td>Jorge Insuasty</td>
</tr>
<tr>
<td>• Immuno-Oncology: Anti PD-1</td>
<td></td>
</tr>
<tr>
<td>• Isatuximab Multiple Myeloma and beyond</td>
<td>Yong-Jun Liu</td>
</tr>
<tr>
<td>• Next wave in Oncology</td>
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</tbody>
</table>
What We Will Cover Today (2/2)

### Diabetes & Cardiovascular

<table>
<thead>
<tr>
<th>Topic</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes strategy</td>
<td>Stefan Oelrich</td>
</tr>
<tr>
<td>GLP-1/GCG dual agonist</td>
<td>Klaus Henning Jensen</td>
</tr>
<tr>
<td>Sotagliflozin</td>
<td></td>
</tr>
<tr>
<td>Efpeglenatide</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Jay Edelberg</td>
</tr>
</tbody>
</table>

### Vaccines

<table>
<thead>
<tr>
<th>Topic</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vision and ambition in Vaccines</td>
<td>David Loew</td>
</tr>
<tr>
<td>Flu</td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td></td>
</tr>
<tr>
<td>RSV vaccine</td>
<td>John Shiver</td>
</tr>
</tbody>
</table>
Bill Sibold
Executive Vice President,
Sanofi Genzyme

SANOFI

Leading in Specialty Care
Driving Growth in Specialty Care Across 4 Franchises

Sanofi Genzyme Specialty Care Franchises

**Immunology**
- **Dupixent** (dupilumab)
- **Kezara** (santilumab)

Execute on launches and expand fast growing immunology franchise into disease areas with high unmet need.

**Multiple Sclerosis**
- **Aubagio** (teriflunomide)
- **Lemtrada**

Continue to drive growth in a competitive market and strengthen portfolio.

**Oncology**
- **Jevtana** (cabazitaxel)
- **Mozobil** (plerixafor injection)
- **Thymoglobulin**

Prepare for launch opportunities with cemiplimab and isatuximab and optimize legacy brands.

**Rare Disease**
- **Cerezyme**
- **Cerdelga**
- **Myozyme**

Sustain RD leadership through patient focus and product differentiation and prepare for launches.
Strong U.S. Dupixent® Launch Outperforming Analogs

**Total Dupixent® Prescribers**
Growing prescriber breadth

- April: 1,700
- July: 5,232
- Oct: 7,197

**Weekly TRx Since Launch**

- DUPIXENT® (dupilumab)
- Cosentyx®
- Taltz®
Dupilumab Clinical Program Focused on Population with Uncontrolled Persistent Asthma

Nearly 20% of diagnosed asthma patients have severe persistent disease

Asthma patients by disease severity 2016 (all ages)

U.S. Patient Population

Diagnosed 25.5m

Severe Persistent Population 4.9m

Uncontrolled/ Biologics Eligible 1.0m

Current Biologics Treated ~9%

Global Launch Opportunities in Multiple Diseases to Realize the Full Potential of a ‘Pipeline in a Product’

- Dupilumab expected to be a key growth driver with significant commercial potential in multiple diseases
- Building a portfolio of opportunities around one compound
  - Launch of new indications over time
  - Geographic roll-out in global markets
  - Penetration into adult, adolescent and pediatric populations
  - Expansion in combination use

Growth Opportunities across Diseases, Geographies and Demographics

- ILLUSTRATIVE
  - COPD
  - Allergies
  - Eosinophilic Esophagitis
  - Nasal Polyposis
  - Asthma
  - Atopic Dermatitis (AD)

(1) If approved in indications by applicable Health Authority
Well-Positioned in the Growing Segments of the Market

Building on a Successful MS Franchise

And Driving the Transition Towards Oral and High Efficacy Therapies\(^{(1)}\)

Multiple Sclerosis Sales by Category of Product

- Injectables
- Orals
- High-efficacy
- Other

\(^{(1)}\) Source: eValuatePharma
Leveraging our Strength in Multiple Sclerosis

- Alemtuzumab
  - High unmet need in PPMS with limited treatment options
  - Pilot studies in SPMS and RRMS demonstrated prevention of disability progression
    - 1 year post alemtuzumab treatment, 33/36 SPMS patients had maintained pre-treatment EDSS
- BTK inhibitor - PRN2246
  - Recent licensing agreement signed with Principia for global rights to a potentially best-in-class brain penetrant oral BTK inhibitor

Alemtuzumab Impact on Disability in RRMS and SPMS Patients\(^{(1)}\)

<table>
<thead>
<tr>
<th>Change in EDSS</th>
<th>Pre 1 year</th>
<th>0 to 6</th>
<th>6 to 12</th>
<th>12 to 24</th>
<th>24 to 36</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>RRMS</td>
<td>p&lt;0.1</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>SPMS</td>
<td>p&lt;0.01</td>
<td>p&lt;0.001</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

Alemtuzumab Phase 3 in PPMS targeting 1,200 patients expected to start in H1 2018

Alemtuzumab is marketed under the brand name Lemtrada\(^{(2)}\) in RRMS. BTK= Bruton’s Tyrosine Kinase; RRMS= Relapsed Refractory Multiple Sclerosis; PPMS= Primary Progressive Multiple Sclerosis; SPMS= Secondary Progressive Multiple Sclerosis; EDSS= Expanded Disability Status Scale

\(^{(1)}\) The Principia transaction remains subject to customary regulatory approvals and has not yet closed. Under the terms of the agreement Sanofi will develop PRN2246 oral treatment that shows promise in multiple sclerosis (MS) and, potentially, other central nervous system (CNS) disease.

Sanofi’s Strong Commitment to Oncology Expected to Begin to Deliver in 2018

- 6 Pre-clinical programs enter Phase 1
- 14 New proof of concept indications
- 4 Potential proof of concept study readouts
  - Isatuximab: 4 MM
  - Cemiplimab*: 3 NSCLC, 1 BCC, 1 Cervical Cancer
- 9 Pivotal studies ongoing or planned
  - Cemiplimab* CSCC: U.S., EU
- 3 BLA/MAA submissions
  - Cemiplimab* CSCC
  - Isatuximab RRMM: U.S.
- 1 U.S. launch

NSCLC= Non-Small Cell Lung Cancer; BCC= Basal Cell Carcinoma; CSCC= Cutaneous Squamous Cell Carcinoma; RRMM= Relapsed Refractory Multiple Myeloma; MDS= Myelodysplastic Syndrome; AML= Acute Myeloid Leukemia; *cemiplimab partnered with Regeneron

(1) Subject to U.S. FDA approval
Jorge Insuasty
Senior Vice President,
Global Head of Development

Building a Competitive Position in Immunology
Realize the potential of dupilumab
## A Fast Growing Portfolio of the Innovative Pipeline Assets Across Multiple Therapeutic Areas

### 2018 Immunology Development Pipeline

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Registration</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAR439794 TLR4 agonist Peanut Allergy</td>
<td>SAR156597 IL4/IL13 bi-specific mAb Systemic Scleroderma</td>
<td>sarilumab Anti-IL6R mAb Systemic Juvenile Arthritis</td>
<td>dupilumab Anti-IL4Rα mAb COPD</td>
</tr>
<tr>
<td>GZ389988 TRKA antagonist Osteoarthritis</td>
<td>Sarilumab Anti-IL33 mAb Asthma</td>
<td>dupilumab Anti-IL4Rα mAb Atopic Dermatitis 12–17y</td>
<td>dupilumab Anti-IL4Rα mAb Asthma 12y+</td>
</tr>
<tr>
<td>sarilumab Anti-IL6R mAb Polyarticular Juvenile Idiopathic Arthritis</td>
<td>Sarilumab Anti-IL33 mAb Eosinophilic Esophagitis</td>
<td>dupilumab Anti-IL4Rα mAb Atopic Dermatitis 6–11y</td>
<td>dupilumab Anti-IL4Rα mAb Eosinophilic Esophagitis</td>
</tr>
<tr>
<td>Sarilumab Anti-IL33 mAb Asthma</td>
<td>dupilumab Anti-IL4Rα mAb Copd</td>
<td>sarilumab Anti-IL6R mAb Polymyalgia Rheumatica</td>
<td>sarilumab Anti-IL6R mAb Giant Cell Arteritis</td>
</tr>
<tr>
<td>Sarilumab Anti-IL33 mAb COPD</td>
<td>dupilumab Anti-IL4Rα mAb Nasal Polyposis</td>
<td>sarilumab Anti-IL6R mAb Polyarticular Juvenile Idiopathic Arthritis</td>
<td>approved</td>
</tr>
<tr>
<td>dupilumab Anti-IL4Rα mAb Asthma 6-11y</td>
<td>dupilumab Anti-IL4Rα mAb Asthma 12y+</td>
<td>sarilumab Anti-IL6R mAb Polyarticular Juvenile Idiopathic Arthritis</td>
<td><em>Kevzara®</em> Anti-IL6R mAb Rheumatoid Arthritis</td>
</tr>
<tr>
<td>dupilumab Anti-IL4Rα mAb Grass Allergy</td>
<td><em>Dupixent®</em> Anti-IL4Rα mAb Asthma 6-11y</td>
<td>dupilumab Anti-IL4Rα mAb Asthma 12y+</td>
<td><em>Dupixent®</em> Anti-IL4Rα mAb Atopic Dermatitis</td>
</tr>
</tbody>
</table>

- **Ongoing**
- **First patient scheduled in 2018**

**Sanofi** *Dupixent®/ dupilumab, Kevzara®/ sarilumab, anti-IL33 mAb: partnered with Regeneron*
Development Program Confirms Dupilumab’s Value Proposition in Multiple Immune-Mediated Diseases

1. Comprehensive clinical program across several diseases in the Type 2 spectrum
2. First biologic to demonstrate positive clinical data in AD, Asthma, NP, EoE<sup>(1)</sup>
3. New studies to be initiated in patients with multiple co-morbidities
4. New studies to be initiated in COPD and allergic indications
5. Large safety database with established profile for continuous therapy

<sup>(1)</sup> Dupilumab is under clinical investigation for Asthma, NP and EoE and its safety or efficacy for these uses has not been evaluated by any regulatory authority
Dupilumab Clinical Trial Program Planned to Expand across 7 Indications including Pediatric Patients in Asthma and AD

Expected timeline

2016 2017 2018 2019

Atopic Dermatitis
(6-<18y)
(12-<18y)
(6-<12y)
(6m-<6y)

Asthma
(adults/adolescents)
(6-<12y)
(6m-<6y)

Nasal Polyposis

Eosinophilic Esophagitis

COPD

Peanut Allergy

Grass Allergy

Potential timeline molecular drugs

- Phase 3
- Part A / PK
- Part B / Ph 3

Potential U.S. submission

Potential EU submission
Dupilumab Being Evaluated as First-in-Class Dual Inhibitor of IL4/IL13 in Key Type 2 Conditions

- **Atopic Dermatitis**
  - Breakthrough therapy in moderate-to-severe AD
  - First-in-class biologic treatment

- **Asthma**
  - Efficacy in 3 pivotal trials
  - Largest Phase 3 program of a biologic therapy in asthma

- **Nasal Polyposis**
  - Positive Proof of Concept data
  - No currently approved biologic
  - Phase 3 fully enrolled

- **Eosinophilic Esophagitis**
  - Positive Proof of Concept data
  - No currently approved biologic

---

dupilumab
Atopic Dermatitis: >2,500 Patient Development Program

### Adult Patients

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-week monotherapy(^{(1)})</td>
<td>4-week concomitant TCS(^{(1)})</td>
<td>SOLO 1 &amp; 2</td>
</tr>
<tr>
<td>Drug-drug interactions(^{(2)})</td>
<td>12-week monotherapy(^{(1)})</td>
<td>16-week monotherapy(^{(7)})</td>
</tr>
<tr>
<td></td>
<td>16-week monotherapy dose-ranging(^{(3)})</td>
<td>CHRONOS</td>
</tr>
<tr>
<td></td>
<td>EXPLORE: 16-week monotherapy biopsy/biomarkers(^{(4)})</td>
<td>52-week concomitant TCS(^{(8)})</td>
</tr>
<tr>
<td></td>
<td>EVALUATE: 16-week vaccine interaction (Tdap and MPSV4)(^{(5,6)})</td>
<td>SOLO-CONTINUE</td>
</tr>
<tr>
<td></td>
<td></td>
<td>36-week monotherapy(^{(9)})</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CAFÉ: 16-week concomitant TCS in cyclosporine-experienced patients(^{(6,10)})</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Open-label extension(^{(11)})</td>
</tr>
</tbody>
</table>


\(^{(2)}\) ClinicalTrials.gov (NCT02647086).


\(^{(5)}\) ClinicalTrials.gov (NCT02210780).


\(^{(9)}\) ClinicalTrials.gov (NCT02395133).

\(^{(10)}\) ClinicalTrials.gov (NCT02755649). Accessed February 2017

\(^{(11)}\) ClinicalTrials.gov (NCT01949311).
Higher Disease Burden of Atopic Dermatitis in Pediatrics

- Manifestations similar to adults, pruritus remains the cardinal symptom
- 1-year prevalence ~10% of U.S. pediatric population\(^1\)
  - 1-2% of these pediatric AD patients have severe disease\(^2,3,4\)
- Onset of disease for majority of children is about 5 years old

Similar Disease Manifestation in Children

(1) Shaw et al., J In Derm, Eczema Prevalence in the United States; Data from the 2003 National Survey of Children’s Health, 2011, 131, 67-73
(6) Weinberg et al. Successful Treatment of Severe Atopic Dermatitis in a Child and an Adult With the T-Cell Modulator efalizumab; Arch Dermatol. 2006; 142(5):555-558
Proof of Concept Suggests Efficacy in Children and Adolescents with Atopic Dermatitis

Results Consistent with Adult Population\(^1\)

**EASI\(^2\) scores in children**

(6 -11 years)

<table>
<thead>
<tr>
<th>Week</th>
<th>Mean % change from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-100</td>
</tr>
<tr>
<td>2</td>
<td>-63.4%</td>
</tr>
<tr>
<td>4</td>
<td>-76.2%</td>
</tr>
<tr>
<td>6</td>
<td>-80%</td>
</tr>
<tr>
<td>8</td>
<td>-85%</td>
</tr>
<tr>
<td>10</td>
<td>-90%</td>
</tr>
<tr>
<td>12</td>
<td>-95%</td>
</tr>
<tr>
<td>14</td>
<td>-100%</td>
</tr>
</tbody>
</table>

**Mean % change from baseline**

- dupilumab 4 mg/kg
- dupilumab 2 mg/kg

**EASI\(^2\) scores in adolescents**

(12-17 years)

<table>
<thead>
<tr>
<th>Week</th>
<th>Mean % change from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-100</td>
</tr>
<tr>
<td>2</td>
<td>-50.9%</td>
</tr>
<tr>
<td>4</td>
<td>-63.4%</td>
</tr>
<tr>
<td>6</td>
<td>-76.2%</td>
</tr>
<tr>
<td>8</td>
<td>-85%</td>
</tr>
<tr>
<td>10</td>
<td>-90%</td>
</tr>
<tr>
<td>12</td>
<td>-95%</td>
</tr>
<tr>
<td>14</td>
<td>-100%</td>
</tr>
</tbody>
</table>

**Mean % change from baseline**

- dupilumab 4 mg/kg
- dupilumab 2 mg/kg

Registralional studies initiated in age-groups ranging from 6 months to 17 years old

The safety and efficacy of dupilumab in pediatric AD patients has not been evaluated by any regulatory authority

\(^1\) Phase 2a, open-label, ascending-dose, sequential-cohort trial among atopic dermatitis patients failing TCS

\(^2\) EASI score is a tool used to measure the extent (area) and severity of atopic eczema (Eczema Area and Severity Index)
Inadequately Controlled Asthma Represents a Significant Unmet Medical Need and Economic Burden

Asthma

• Asthma is a common chronic disease that leads to significant health and economic burden for patients and their families

• Despite existing therapies 5% to 10% of patients suffer from severe\(^1\) forms

• Estimated direct and indirect economic burden of asthma
  • $56bn in the U.S.\(^4\)
  • €34bn in the EU\(^5\)

5%-10% of U.S. asthma population with severe disease\(^1\) accounts for 50% of all asthma costs\(^2,3\)

U.S. asthma severe patient population

U.S. asthma related costs

Estimated annual per-patient direct costs for this population are $16,154 to $32,308\(^3\)

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(1) Defined by hospitalization, ER visits, and/or requirement for systemic corticosteroids
(4) AAAAI; www.aaaai.org/about-aaaai/newsroom/asthma-statistics
(5) ERS White Book; www.erswhitebook.org/chapters/the-economic-burden-of-lung-disease
Dupilumab in Asthma - IL4/IL13 as Key Type 2 Cytokines that May Have Broad Effects on Type 2 Inflammation

- Type 2 inflammation in asthma involves a range of cytokines and mediators
- IL4/IL13 with unique roles as key drivers of Type 2 mediated asthma
- Type 2 asthma encompasses much more than eosinophilic changes alone
- IL13 mAbs have not been successful in Phase 3 development in asthma

IL4 and IL13 Play Key Roles in Type 2 Inflammation

- **IL4**
  - TH2 cell differentiation (1)
- **IL13**
  - Goblet cell hyperplasia (2)
  - Mucus overproduction (2)
  - Collagen deposition (2)
  - Airway smooth muscle effects (2)
- **IL5**
- B-cell isotype switching and IgE production (2)

Eosinophil chemotaxis (recruitment) to inflamed lung tissue and promotion of tissue eosinophilia (3,4)
Risk of exacerbation

A Comprehensive Asthma Clinical Development Program Conducted in a Broad Patient Population

**Adult & Adolescent Patients**

<table>
<thead>
<tr>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pivotal</strong></td>
<td><strong>Pivotal</strong></td>
</tr>
<tr>
<td>DRI12544(^{(1)})</td>
<td><strong>QUEST(^{(3)})</strong></td>
</tr>
<tr>
<td>Adults, Dose ranging – Pivotal</td>
<td>Adults and adolescents (12+ years)</td>
</tr>
<tr>
<td>24 weeks, N=776</td>
<td>52 weeks, N=1,902</td>
</tr>
<tr>
<td><strong>EXPEDITION(^{(2)})</strong></td>
<td><strong>VENTURE(^{(4)})</strong></td>
</tr>
<tr>
<td>Adults, Exploratory (airway inflammation)</td>
<td>Adults and adolescents (12+ years) with severe steroid dependent asthma</td>
</tr>
<tr>
<td>12 weeks, N=42</td>
<td>24 weeks, N=210</td>
</tr>
<tr>
<td><strong>TRAVERSE(^{(5)})</strong></td>
<td><strong>TRAVERSE(^{(5)})</strong></td>
</tr>
<tr>
<td></td>
<td>Open-label extension study</td>
</tr>
<tr>
<td></td>
<td>up to 108 weeks, N=2,287</td>
</tr>
</tbody>
</table>

---

1. Wenzel S et al. Lancet 2016; Phase 2b dose-ranging trial
2. clinicaltrials.gov (NCT02573233) accessed Nov 1st 2017
3. clinicaltrials.gov (NCT02573233) accessed Nov 1st 2017
4. clinicaltrials.gov (NCT02528214) accessed Nov 1st 2017
5. clinicaltrials.gov (NCT02573233) accessed Nov 1st 2017
Dupilumab in Asthma Pivotal Trial Program: Reduced Exacerbations in Overall Population

**Dose Ranging Study**
Moderate-to-severe asthma

- Placebo: 0.90
- 200 mg Q2W: 0.27
- 300 mg Q2W: 0.27

**QUEST**
Moderate-to-severe asthma

- Placebo: 0.87
- 200 mg Q2W: 0.46
- Placebo: 0.97
- 300 mg Q2W: 0.52

**VENTURE**
OCS dependent asthma

- Placebo: 1.60
- 300 mg Q2W: 0.65

The safety and efficacy of dupilumab in asthma patients have not been evaluated by any regulatory authority. Most common adverse event was injection site reaction, which was more frequent in the dupilumab dose groups than placebo. Other common adverse events more common with dupilumab than placebo were upper respiratory tract infection, headache, nasopharyngitis and bronchitis. Incidence of infections and of serious adverse events was balanced across treatment groups.
Dupilumab Demonstrated Rapid and Sustained Improvement of Lung Function

The safety and efficacy of dupilumab in asthma patients have not been evaluated by any regulatory authority.

(1) The overall rates of adverse events, deaths, infections, conjunctivitis, herpes and discontinuations were comparable between the dupilumab and placebo groups. Injection site reactions were more common in the dupilumab groups (17% of dupilumab patients vs 8% for placebo patients).
Dupilumab Reduced OCS, Exacerbations and Improved Lung Function in Severe Steroid-Dependent Asthma Population

**VENTURE Study: Overall Patient Population at Week 24**

- **Reduction in maintenance OCS use**
  - Placebo: -42%
  - Dupilumab 300 mg Q2W: -70%

- **% of patients achieved zero OCS use**
  - Placebo: 25%
  - Dupilumab 300 mg Q2W: 48%

- **Reduction in exacerbations**
  - Placebo: 1.60
  - Dupilumab 300 mg Q2W: 0.65
  - Reduction: -59%

- **Improvement in FEV1 (L)**
  - Placebo: 0.01
  - Dupilumab 300 mg Q2W: 0.22
  - Improvement: +0.22

- Safety and tolerability profile consistent with previous studies

**Notes:**
- OCS = Oral Corticosteroids; FEV1 = Forced expiratory volume
- The safety and efficacy of dupilumab in asthma patients have not been evaluated by any regulatory authority.
Dupilumab Demonstrated Efficacy Across Broad Population and Independent of Eosinophilic Phenotype

Consistent Reduction in Risk of Exacerbation and Improvement in Lung Function

Exacerbations relative reduction vs placebo at week 24

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>≥150 eos</th>
<th>≥300 eos</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative reduction</td>
<td>-64 to -69%</td>
<td>-72 to -73%</td>
<td>-71 to -81%</td>
</tr>
<tr>
<td></td>
<td>-59%</td>
<td>-56 to -60%</td>
<td>-66 to -67%</td>
</tr>
<tr>
<td></td>
<td>-58%</td>
<td>-58%</td>
<td>-71%</td>
</tr>
</tbody>
</table>

FEV1 Δ LS mean vs placebo (L) at week 24

<table>
<thead>
<tr>
<th></th>
<th>DRI (range of 200mg and 300mg Q2W)</th>
<th>QUEST (range of 200mg and 300mg Q2W)</th>
<th>VENTURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.16 to 0.20</td>
<td>0.16 to 0.14</td>
<td>0.18 to 0.23</td>
<td>0.21 to</td>
</tr>
<tr>
<td>0.20</td>
<td>0.20</td>
<td>0.23</td>
<td>0.26</td>
</tr>
<tr>
<td>0.19 to 0.14</td>
<td>0.17</td>
<td>0.15</td>
<td>0.24</td>
</tr>
<tr>
<td>0.22</td>
<td>0.22</td>
<td>0.22</td>
<td>0.32</td>
</tr>
</tbody>
</table>

The safety and efficacy of dupilumab in asthma patients has not been evaluated by any regulatory authority.
## Dupilumab’s Profile Demonstrated in Pivotal Asthma Program Suggests Key Differentiation in Competitive Class

<table>
<thead>
<tr>
<th>Biologics in asthma</th>
<th>dupilumab</th>
<th>benrazilumab</th>
<th>mepolizumab</th>
<th>reslizumab</th>
<th>omalizumab</th>
<th>tezepelumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism of action</td>
<td>✓ Dual inhibitor IL4/IL13</td>
<td>Anti-IL5R</td>
<td>Anti-IL5</td>
<td>Anti-IL5</td>
<td>Anti-IgE</td>
<td>Anti-TSLP</td>
</tr>
<tr>
<td>Population studied</td>
<td>✓ All comers/biomarkers unrestricted</td>
<td>Eosinophilic phenotype</td>
<td>Eosinophilic phenotype</td>
<td>Eosinophilic phenotype</td>
<td>High IgE</td>
<td>All comers/biomarkers unrestricted</td>
</tr>
<tr>
<td>Efficacy in Type 2 co-morbidities</td>
<td>✓ Atopic Dermatitis</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a(1)</td>
</tr>
<tr>
<td>✓ PoC in EoE, NP</td>
<td>In office by HCP, Q4W first 3 doses, then Q8W</td>
<td>In office by HCP, Q4W</td>
<td>In office by HCP, Q4W</td>
<td>In office by HCP, Q2W or Q4W</td>
<td>TBD</td>
<td></td>
</tr>
<tr>
<td>Dosing &amp; Administration</td>
<td>✓ At-home administration, Q2W</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

The safety and efficacy of dupilumab in asthma patients has not been evaluated by any regulatory authority.

(1) As per Amgen Q3 2017 earnings call, tezepelumab Phase 2a study in atopic dermatitis failed to report statistical significance on its primary endpoint.
Safety Database Supports Profile for Continuous Therapy

- No imbalance in serious infection or malignancy (1)
- Update from asthma indication ongoing

6,500+ patients on dupilumab in development program

~4,000 patients with exposure to dupilumab for >1 year

23 clinical trials completed in clinical program

12 clinical trials initiated and currently ongoing

(1) Most common adverse reactions (incidence ≥1%): injection site reactions, conjunctivitis, blepharitis, oral herpes, keratitis, eye pruritus, other herpes simplex virus infection, dry eye
High Unmet Medical Need in Patients with Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

- CRSwNP a prevalent and persistent disease
- CRSwNP affects 2-4% of adults\(^{(2)}\)
  - 30-70% overlap rate with asthma\(^{(3)}\)
- Symptoms (nasal blockage and congestion, loss of smell, facial pressure and pain) lead to reduced productivity, sleep and quality of life
- Standard of care: Intranasal steroid use, followed by functional endoscopic sinus surgery
  - Annual number of functional endoscopic sinus surgery procedures ~250K in U.S. and EU5
  - Recurrence post surgery in >50% of patients

---

(1) Endoscopic images from a healthy person and patient with severe CRSwNP. Source: Schleimer RP. Annu Rev Pathol 2017;12:331–357
(3) Ref: Alobid 2011b; Dietz de Loos 2013; Bachert 2010; Promsopa 2016; Hakansson 2015
Dupilumab Improved Endoscopic, Radiographic and Patient Reported Measures in PoC study

The safety and efficacy of dupilumab in patients with NP has not been evaluated by any regulatory authority. Safety profile consistent with previous studies. Most common AEs were injection site reactions, nasopharyngitis, oropharyngeal pain, epistaxis, headache and dizziness. MFNS= Mometasone Furoate Nasal spray; LS= Least Squares; SE= Standard Error

(1) NPS= Nasal Polyps Score; Bilateral score range 0–8 (0 = no polyps, 4 = large polyps causing complete obstruction of the inferior nasal cavity)
(2) Individual results did vary

<table>
<thead>
<tr>
<th>Improvement in Nasal Endoscopy NPS(1)</th>
<th>Treatment with dupilumab (CT scan)(2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LS Mean Change in NPS(1) (± SE)</strong></td>
<td><strong>Baseline Lund-Mackay score 18</strong></td>
</tr>
<tr>
<td>placebo/ MFNS</td>
<td>Disease occupied 89%</td>
</tr>
<tr>
<td>-0.3 (± 0.3)</td>
<td></td>
</tr>
<tr>
<td>dupilumab/ MFNS</td>
<td><strong>End of treatment Lund-Mackay score 9</strong></td>
</tr>
<tr>
<td></td>
<td>Disease occupied 44%</td>
</tr>
<tr>
<td>-1.9 (± 0.3)</td>
<td></td>
</tr>
<tr>
<td>-1.6; P = 0.0009</td>
<td></td>
</tr>
</tbody>
</table>

~50% improvement in sinus patency

Phase 3 fully enrolled with read-out expected in H2 2018
Eosinophilic Esophagitis (EoE): A Type 2 Inflammation of the Esophagus with Limited Treatment Options

- Chronic allergic inflammatory disease localized to the esophagus
- Symptoms of esophageal dysfunction and histology resulting from eosinophilic inflammation
- Treatment options limited to diet changes, proton-pump inhibitors, corticosteroids and surgery (dilation)
- ~150K patients in the U.S.\(^{(1)}\)
  - Rising incidence
  - Approximately 60% with co-morbidities
  - >40% with family history of atopy or allergies\(^{(2)}\)

\(^{(2)}\) Mohammad AA et al., Journal of the American Academy of Dermatology, 2017; 76(3):559-560
\(^{(3)}\) Reprinted from Gastroenterology, 147(6), Dellon ES, Liacouras CA, Advances in clinical management of eosinophilic esophagitis, 1238–1254, Copyright (2014), with permission from Elsevier
Dupilumab Improved Symptoms, Endoscopy and Histology Measurements in Moderate-to-Severe EoE in PoC study

Primary Endpoint (Subjective)
Dupilumab significantly reduced Straumann Dysphagia Instrument SDI PRO score at week 10

Secondary Endpoint (Objective)
Significant reduction in overall peak esophageal intraepithelial eosinophils at week 12

- There were no new significant safety concerns in this trial. Higher rates of injection site reactions were observed on dupilumab versus placebo

Start of Phase 3 expected in H2 2018

The safety and efficacy of dupilumab in patients with EoE has not been evaluated by any regulatory authority
Dupilumab, by Blocking the IL4/IL13 Pathway, Potentially Addresses the Burden of Co-Morbidities Effectively

- Co-morbidities represent large burden for patients suffering from immune-mediated diseases
- Addressing co-morbidities in dupilumab development program is a key differentiator
- Start of clinical program evaluating co-morbidities planned for 2018

Co-Morbid History of Patients in dupilumab Studies

<table>
<thead>
<tr>
<th>Condition</th>
<th>Atopic Dermatitis SOLO 1 &amp; 2 CHRONOS</th>
<th>Asthma Phase 2 &amp; QUEST</th>
<th>Nasal Polyposis PoC</th>
<th>Eosinophilic Esophagitis PoC</th>
</tr>
</thead>
</table>

Dupilumab is under clinical investigation for Asthma, NP and EoE and its safety or efficacy for use in co-morbidities has not been evaluated by any regulatory authority.
## Dupilumab to Start Phase 3 Program in COPD in 2018

### Large unmet need for new treatment options in COPD

- Estimated market of ~€16bn in 2025\(^{(1)}\)
- Despite existing therapies a large subset of patients still experience severe exacerbations
- Significant need for a new MoA
  - Approximately 2m patients in the U.S. at risk despite inhaled triple therapy\(^{(2)}\)
  - Penetration of biologics by 2025 ~10-15%

### Compelling rationale for dupilumab development program in COPD

- Unmet need to prevent exacerbation and to improve pulmonary function
  - No approved biologics to date
- Type 2 inflammation plays a key role in a group of COPD patients and is associated with decreased lung function\(^{(3)}\)
- Leverage robust efficacy and safety data to build COPD development program for dupilumab

---

\(^{(1)}\) Estimated global sales of advanced therapies (biologics and orals)

\(^{(2)}\) Adelphi COPD DSP

\(^{(3)}\) Asthma–COPD Overlap. Clinical Relevance of Genomic Signatures of Type 2 Inflammation in Chronic Obstructive Pulmonary Disease Am J Respir Crit Care Med. 2015 Apr 1; 191(7): 758–766
IL33 mAb\(^{(1)}\): Potential for Broader Spectrum of Immune Modulation in Atopic Dermatitis, Asthma and COPD

IL33 is a proinflammatory cytokine released by damaged epithelial cells in response to insults such as allergens, pathogens and smoke\(^{(2)}\).

IL33 signaling initiates and amplifies downstream inflammatory pathways characteristic of both Type 1 and Type 2 inflammation\(^{(2)}\).

- Target identified and validated by human genetics\(^{(3)}\)
- Major opportunity in monotherapy and in combination
  - Building on the benefit of dupilumab in AD, as well as potentially asthma and COPD

\(^{(1)}\) Collaboration with Regeneron
\(^{(2)}\) Cayrol and Girard, 2014
\(^{(3)}\) Regeneron Genetics Center validated that LOF mutations in IL33 decrease the risk of asthma by greater than 50%
## IL33 mAb\(^{(1)}\) as Monotherapy and in Combination with Dupilumab: Clinical Development Program

### Phase 1 Program

<table>
<thead>
<tr>
<th>Phase 1 in Healthy Adults</th>
<th>IL33 administered intravenously or subcutaneously</th>
<th>Completed</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Phase 1b in Adult Patients with Moderate Asthma</th>
<th>Studies safety, tolerability, pharmacokinetics of multiple ascending doses of IL33</th>
<th>Started Q1 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1b in Mild Allergic Asthma Patients (BAC)</td>
<td>Studies effects of IL33, dupilumab and combined IL33/dupilumab on inflammatory signature after bronchial allergen challenge (BAC)</td>
<td>Started Q3 2017</td>
</tr>
</tbody>
</table>

### Phase 2 Program

<table>
<thead>
<tr>
<th>Phase 2b in Atopic Dermatitis</th>
<th>Planned to start H1 2018</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Proof of Concept in COPD</th>
<th>Planned to start H2 2018</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Proof of Concept in Asthma</th>
<th>Planned to start H1 2018</th>
</tr>
</thead>
</table>
# LCM Opportunity in Overlapping Conditions with a Strong IL6 Signature

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
<th>Prevalence</th>
<th>Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Giant Cell Arteritis(1)</strong></td>
<td>- Chronic vasculitis of medium and large vessels&lt;br&gt;- Occurs in the elderly, mostly women&lt;br&gt;- Symptoms: jaw claudication, visual symptoms including blindness, arm claudication&lt;br&gt;- IL6 level correlate with severity&lt;br&gt;- 50% have PMR-type symptoms</td>
<td>&gt;228K patients in the U.S.(2); Prevalence varies across ex-U.S. markets(3)</td>
<td>Offering IL6 efficacy with less frequent dosing</td>
</tr>
<tr>
<td><strong>Polymyalgia Rheumatica(1)</strong></td>
<td>- Inflammatory syndrome in the elderly, mostly women&lt;br&gt;- Characterized by symmetrical proximal (shoulder &amp; hip girdle) aching and stiffness&lt;br&gt;- IL6 levels correlate with severity&lt;br&gt;- 10 to 30% develop GCA within 1 year&lt;br&gt;- Corticosteroid are current preferred treatment option</td>
<td>At least 711K patients in the U.S.(2); Prevalence varies across ex-U.S. markets(3)</td>
<td>To become 1st biologic therapy indicated for PMR</td>
</tr>
</tbody>
</table>

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(1) Potential area for further study  
Frank Nestle
Global Head of Immunology & Inflammation Research Therapeutic Area

Building a Competitive Position in Immunology
Next wave in Immunology
Sanofi’s Vision to Discover Breakthrough Medicines in Immunology

Sanofi is developing precision immune therapies

Precision Immunology

Multi-pathway targeting

Accelerating discovery of impactful patient treatments

Patients with immunological disease

Atopic Dermatitis
Asthma
Systemic Lupus Erythematosus
Rheumatoid Arthritis
Type 1 Diabetes
Multiple Sclerosis

Interrogate at single cell level

Medicine

Develop breakthrough precision immune therapies
Discovering Transformative Immunology Medicines

Going beyond the current paradigm of single cytokine blockade

**Multi-pathway modulation**
- Bi-specific antibodies
- Tri-specific antibodies

**Targeted cell depletion and modulation**
- aCXCR3
- CXCR3+ cell, NK cell, Macrophage

**Master Regulators**
- Autoantibody
- CD40L
Targeted Cell Depletion in Dermatology and Type 1 Diabetes

SAR440241 - Anti-CXCR3
Targeted T-cell Depletion

Depletion of Epidermal T-cells by anti-CXCR3 in Vitiligo Model

Durable Reversal of Hyperglycemia in NOD Diabetes Model

Clinical Candidate
aCXCR3

Autoimmune Lymphocyte
NK cell, Macrophage

Reduction in Vitiligo Score\(^{(1)}\)

Diabetes Reversal

Potential clinical indications:
T1D, Vitiligo, Psoriasis

---

Next Key Master Regulator in Immunology: CD40L

α-CD40L mAb

Autoantibody

CD40L

MHC Class I

MHC Class II

B-cell

TCR

CD4+ T-cell

CD40L Expression on Single Immune Cells

CD40LG

AMP Consortium Phase 1 Data - single cell RNA seq

CD40L

SAR441344 α-CD40L

Inactivated Fc Region

FcγRIIA

No Platelet Activation

Potential clinical Indications:
MS, SLE

AMP Consortium; MS= Multiple Sclerosis; SLE= Systemic Lupus Erythematosus
Global License Agreement with Principia for Brain-Penetrant BTK Inhibitor

Rationale of BTK Inhibition in MS\(^{(1)}\)

- B-Cell maturation
- Proliferation (NF-κB)
- Autoantibody production
- Cytokine Secretion

B-Cells

BCR activation

CNS Microglia

Immune complex activation

- Microglial activation
- Pro-inflammatory cytokine secretion (e.g., TNFα, IL1β, IL6)

Differentiation of PRN2246 vs Other BTKi and Current High-Efficacy Treatments

<table>
<thead>
<tr>
<th>Current high-efficacy DMTs</th>
<th>Other BTKi</th>
<th>PRN2246</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-Cell modulation (not depletion)</td>
<td>☒</td>
<td>☑</td>
</tr>
<tr>
<td>Oral</td>
<td>☒</td>
<td>☑</td>
</tr>
<tr>
<td>Significant drug levels in the brain</td>
<td>☒</td>
<td>☒</td>
</tr>
<tr>
<td>Potential to modulate CNS innate immunity</td>
<td>☒</td>
<td>☒</td>
</tr>
</tbody>
</table>

The Principia transaction remains subject to customary regulatory approvals and has not yet closed. Under the terms of the agreement Sanofi will develop PRN2246 oral treatment that shows promise in multiple sclerosis (MS) and, potentially, other central nervous system (CNS) disease.

BTK= Bruton’s Tyrosine Kinase; BCR= B-Cell Receptor

Multi-Pathway Modulation: Collaboration with Ablynx

Ablynx: A Leading Biologics Platform

- Up to 8 programs focused on immune-mediated inflammatory diseases
- Multiple drug targets in a single molecule
- Proven success:
  - >45 programs
  - >2,000 patients and volunteers treated with Nanobodies®

Deal signed with Ablynx:
July 2017

Potential Indications:
Asthma/COPD, RA, AD, Psoriasis

Ablynx Nanobody®
- Nano to pico-molar affinities
- Able to bind and block challenging targets
- Multiple administration routes
- Simple to manufacture

AD = Atopic Dermatitis; COPD = Chronic Obstructive Pulmonary Disease; RA = Rheumatoid Arthritis;
Over 30 Years of Innovation in Rare Disease

**Mission**
Discover and develop transformative therapies for rare diseases with well-defined mechanisms and high unmet need

**Ambition**
Expand leadership by:
- Sustaining innovation in LSD treatments
- Strategically expanding into related conditions through Rare Disease Therapeutic Areas

- **Fabry Disease**
  - Rare Nephrology
- **Gaucher Disease**
  - Rare Hematology
- **Pompe Disease**
  - Rare Neurology and Neuromuscular
- **MPS I & II**
  - Rare Pediatric and Metabolic

---

**LSD** = Lysosomal Storage Disorder; **MPS** = Mucopolysaccharidoses
Sanofi Genzyme markets Elaprase® in JaPac (including Japan, South Korea, Taiwan and Australia)
Rare Disease Planned Development and Regulatory Timelines

Expected timeline

**Venglustat**
- ADPKD Accelerated pathway - U.S.
- ADPKD Full approval pathway
- GBA-related Parkinson’s Disease
- Gaucher Disease Type 3

**Patisiran in hATTR Amyloidosis**

**Fitusiran in Hemophilia**

**Avalglucosidase alfa in Pompe Disease**

**Olipudase alfa in ASMD**
- Adult patients
- Pediatric patients

Potential timeline:
- 2017: Phase 2/3
- 2018: Phase 2/3
- 2019: Phase 3
- 2020: Phase 3
- 2021: Phase 3
- 2022+: Submissions in Sanofi territories

Potential U.S. submission | Potential EU submission
Venglustat(1): Oral, Once Daily Inhibitor of GCS with Potential Across Multiple Rare Diseases

Venglustat is an investigational agent and has not been evaluated by any regulatory authority. In preclinical studies, venglustat penetrates the blood-brain barrier.

ERT = Enzyme Replacement Therapies; ADPKD = Autosomal Dominant Polycystic Kidney Disease

(1) Also known as SAR402671
The Glycosphingolipid Pathway is at the Heart of Multiple Rare Diseases

**Gaucher Disease**
- GBA mutations lead to low enzymatic activity
- Low enzymatic activity leads to lysosomal GL1 accumulation
- Gaucher Disease type 3 when CNS involvement

**GBA-Parkinson’s Disease**
- Mutant GBA affects 5-10% of PD patients and is the highest risk factor for PD
- Inhibition of GCS in PD models arrests disease progression

**ADPKD**
- Increased GCS activity leads to GSLs accumulation
- GSL accumulation induce kidney cysts
- Inhibition of GCS in genetic models of ADPKD reduces kidney cyst growth and preserves kidney function

**Fabry Disease**
- α-galactosidase mutations
- Lead to lysosomal GL3 accumulation

---

**Venglustat**
- Glucocerebrosidase (GBA)
- Glucosylceramide Synthase (GCS)
- Glucosylceramide (GlcCer)
- Ceramide
- LacCer
- GL3
- Other glycosphingolipids (GSLs)

---

Venglustat is an investigational agent and has not been evaluated by any regulatory authority.
Venglustat: Autosomal Dominant Polycystic Kidney Disease (ADPKD)

Increased GSL concentrations in kidney

Normal Kidney

Polycystic Kidney Disease

End Stage Kidney Disease

GM3 (AU) in male jck mice

Vehicle

GCSi 0.1%

GCSi 0.2%

120,000 patients

170,000 patients

120,000 patients

170,000 patients

Registrational Phase 2/3 expected to start in 2018, FDA submission targeted for 2021

Venglustat is an investigational agent and has not been evaluated by any regulatory authority

GSL= Glycosphingolipids; GM3= GM3 ganglioside; BUN= Blood Urea Nitrogen; Kidney/BW= Kidney size to body weight ratio


(1) p<0.05, in male mice
Venglustat: Glucocerebrosidase-Related Parkinson’s Disease

GBA-related Parkinson’s Disease

- GBA gene mutations, causative in Gaucher, also associated with Parkinson’s Disease
  - Associated with accelerated clinical progression
  - Estimated prevalence of ~50k-100k patients in the U.S.
- GCS inhibition in relevant mouse models(1):
  - Reduced GL-1
  - Reduced membrane-associated α-synuclein in CNS
  - Improved behavioral and cognitive deficits
- Phase 2 ongoing in ~250 patients

Clinical Impact of GBA Mutation

Proteinase K-resistant α-synuclein immunoreactivity
Patisiran\(^{(1)}\): RNAi Therapeutic for hATTR Amyloidosis

The Multiple Aspects of hATTR Amyloidosis

- **Central Nervous System**
  - Cognitive deficits
  - Headache
  - Ataxia
  - Seizures

- **Kidney**
  - Proteinuria
  - Renal failure

- **Soft Tissue**
  - Carpal tunnel
  - Trigger finger
  - Tongue (rare)

- **Autonomic neuropathy**
  - Orthostatic hypotension
  - Urinary retention
  - Erectile dysfunction
  - Sweating abnormalities

- **Cardiovascular Disease**
  - Conduction disease
  - Cardiomyopathy
  - Arrhythmia
  - Heart failure

- **GI manifestations**
  - Nausea and vomiting
  - Gastroparesis
  - Diarrhea
  - Constipation
  - Weight loss

- **Ocular manifestations**
  - Vitreous opacification
  - Glaucoma
  - Abnormal conjunctival vessels
  - Papillary abnormalities

- **Peripheral neuropathy**
  - Sensorimotor
  - Length dependent
  - Symmetric
  - Small fiber followed by large fiber

**Patisiran APOLO Phase 3 Study**
Primary endpoint change in mNIS+7 from baseline

- **Placebo**
  - 0 months
  - 9 months
  - 18 months

- **Patisiran**
  - Difference: 33.99
  - p=9.26.10\(^{-26}\)

**Estimated 5,000 to 7,000 hATTR patients with polyneuropathy in Sanofi territories**

Patisiran is an investigational agent and has not been evaluated by any regulatory authority. Improvements in exploratory cardiac endpoints also observed. The most commonly reported adverse events (AEs) with patisiran were generally mild to moderate and included peripheral edema and infusion-related reactions (IRRs). The frequency of deaths and serious adverse events (SAEs) was similar in the patisiran and placebo groups. (1) In collaboration with Alnylam; Sanofi has development and commercialization rights in all territories outside the U.S., Canada and Western Europe.
Fitusiran (1): RNAi Therapeutic for Hemophilia Demonstrated Encouraging Efficacy in Phase 1/2 Study

Fitusiran Mechanism of Action

Fitusiran Phase 1/2 Study in Patients with Inhibitors
Primary endpoint Annualized Bleeding Rate (ABR)

<table>
<thead>
<tr>
<th>Pre-Study</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=14</td>
<td>N=14</td>
</tr>
<tr>
<td>38</td>
<td>0</td>
</tr>
</tbody>
</table>

Estimated ~140,000 treated moderate/severe hemophilia patients in Sanofi territories

Fitusiran is an investigational agent and has not been evaluated by any regulatory authority.
Safety/tolerability profile includes increased AST/ALT in HCV Ab positive patients and one case of thrombosis, possibly drug-related.
In collaboration with Alnylam; Sanofi has co-development and co-commercialization rights in the U.S., Canada and Western Europe. Sanofi also has rights for territories outside the U.S., Canada and Western Europe.
(1) Currently on clinical hold pending outcome of FDA discussion – Expected to resume around year-end.
## Fitusiran<sup>(1)</sup>: ATLAS Phase 3 Development Program

### ATLAS-INH
- Adults and adolescents with hemophilia A or B with inhibitors
- On-demand bypassing agents
- N ≈ 50
- **Endpoints:**
  - ABR
  - Spontaneous ABR
  - Joint ABR
  - QOL (Haem-A-QOL)

### ATLAS-A/B
- Adults and adolescents with hemophilia A or B without inhibitors
- On-demand factor replacement
- N ≈ 100
- **Endpoints:**
  - ABR
  - Spontaneous ABR
  - Joint ABR
  - QOL (Haem-A-QOL)

### ATLAS-PPX
- Adults and adolescents with hemophilia A or B with or without inhibitors
- Prophylaxis
- N ≈ 100
- **Endpoints:**
  - ABR
  - Spontaneous ABR
  - Joint ABR
  - QOL (Haem-A-QOL)

<table>
<thead>
<tr>
<th>2:1</th>
<th>9 months fitusiran</th>
<th>OR</th>
<th>9 months OD BPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>2:1</td>
<td>9 months fitusiran</td>
<td>OR</td>
<td>9 months OD Factor</td>
</tr>
<tr>
<td>6 months PPX Factor/BPA</td>
<td>7 months fitusiran</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All completers will be eligible for fitusiran treatment in the Phase 3 Open-Label Extension study.

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<sup>(1)</sup> Preliminary plans subject to further diligence and health authority feedback. Following the completion of the Type A meeting, the FDA will consider removal of the clinical hold upon final review of the amended protocols and other trial materials.

Fitusiran is an investigational agent and has not been evaluated by any regulatory authority.
Avalglucosidase alfa: Developing a Potentially Superior Drug for Pompe Disease

Pompe Disease – A progressive, often fatal myopathy

- Caused by mutations in the GAA gene
- Results in accumulation of glycogen within muscle cells

- rhGAA conjugated with bisM6p residues
  - Engineered to increase cellular uptake
- ~5x more effective than Myozyme® at clearing glycogen (1) from heart, diaphragm, skeletal muscle
- POC data suggest potential for superior efficacy vs. Myozyme®

- In development for LOPD and IOPD
  - Late Onset (LOPD) ~1/37,000
    - Progressive damage to skeletal & respiratory muscle, significant disability, premature death
  - Infantile Onset (IOPD) ~1/138,000
    - Rapidly progressive myopathy, respiratory failure, often fatal in first year of life

(1) based on preclinical data
(2) based on preclinical toxicology studies
Avalglucosidase alfa: U.S. and EU Regulatory Submissions Targeted for Q4 2019

Phase 1/2 Clinical Data

**NEO1 study**

**Late-onset Pompe**

- Phase 3 randomized, double-blind efficacy and safety trial, vs. Myozyme®, in treatment-naïve adults
- Primary endpoint: Change in FVC%
- n=96

**Infantile-onset Pompe**

- Phase 2, open-label, ascending dose, safety/PK/exploratory efficacy trial in patients <18 years of age who progress despite rhGAA treatment
- n=20

Avalglucosidase alfa is an investigational agent and has not been evaluated by any regulatory authority
Avalglucosidase alfa was well-tolerated, with safety profile similar to Myozyme®
(1) Exploratory efficacy of the novel enzyme replacement therapy neoGAA in treatment-naïve and avalglucosidase alfa-treated late-onset Pompe disease patients; Molecular Genetics and Metabolism 117 (2016) S14–S124
(2) COMET Phase 3
(3) Mini-COMET Phase 2
Olipudase alfa: Proof of Concept in ASMD Achieved

**Therapeutic Approach**
Target the underlying metabolic defect by supplementing the deficient enzyme

**Positive Phase 1b Clinical Response**

- 24% pulmonary function
- 23% spleen volume
- 17% liver volume

Well tolerated with no death or adverse events leading to discontinuation over 30 months

**Ongoing ASCEND Clinical Program**

- Phase 1/2 in pediatric patients
- Read-out expected in H2 2019
- Phase 2/3 in adult patients
- Read-out expected in H2 2019
- Designations received to date:
  - Orphan Drug Designation
  - Fast Track
  - Breakthrough Therapy
  - PRIME
  - Sakigake

---

ASMD= Acid Sphingomyelinase Deficiency, also known as Niemann-Pick Disease Type B
Olipudase alfa is an investigational agent and has not been evaluated by any regulatory authority

(1) Phase 1b clinical trial in 5 adults patients with chronic visceral ASMD. Dose escalation study (NCT01722526)
Rare Disease Planned Development and Regulatory Timelines

Expected timeline

**Venglustat**
- ADPKD Accelerated pathway - U.S.
- ADPKD Full approval pathway
- GBA-related Parkinson’s Disease
- Gaucher Disease Type 3

**Patisiran in hATTR Amyloidosis**

**Fitusiran in Hemophilia**

**Avalglucosidase alfa in Pompe Disease**

**Olipudase alfa in ASMD**
- Adult patients
- Pediatric patients

**Potential U.S. submission**

**Potential EU submission**
Jorge Insuasty
Senior Vice President,
Global Head of Development

Building a Competitive Position in Oncology
Leverage Proprietary and Collaborative Platforms to Establish Strong Presence in Oncology

**Capabilities**
- Proprietary and collaborative platforms for creating a pipeline
  - Antibody conjugates
  - Bispecific/multispecific antibodies
  - mRNA
  - Small molecules
- Expertise in translational and precision medicine

**Execution**
- Building a portfolio of internal and partnered assets
- Pipeline in the clinic to test multi-target approach
- Rapidly advancing pre-clinical pipeline

**Ambition to lead**
- Further enhance immune response
- Novel non-IO targeted agents
- Tumor-directed immune activation
- Non-targeted immunomodulators
- Targeted immunomodulators
### Dynamic and Growing Portfolio of Internally Developed and Partnered Assets

**2018 Oncology Development Pipeline**

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Pivotal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SAR439859</strong>&lt;br&gt;SERD Metastatic Breast Cancer</td>
<td><strong>SAR566658</strong>&lt;br&gt;Maytansin-loaded anti-CA6 mAb TNBC</td>
<td><strong>cemiplimab</strong>*&lt;br&gt;Anti-PD-1 mAb Advanced CSCC</td>
</tr>
<tr>
<td><strong>SAR439859</strong>&lt;br&gt;SERD + palbociclib Metastatic Breast Cancer</td>
<td><strong>isatuximab</strong>&lt;br&gt;Anti-CD38 + cemiplimab MM</td>
<td><strong>isatuximab</strong>*&lt;br&gt;Anti-CD38 RRMM (ICARIA)</td>
</tr>
<tr>
<td><strong>SAR439459</strong>&lt;br&gt;Anti-TGFβ mAb Advanced Solid Tumors</td>
<td><strong>REGN3767</strong>*&lt;br&gt;Anti-LAG3 Advanced Cancers</td>
<td><strong>cemiplimab</strong>*&lt;br&gt;Anti-PD-1 mAb 2nd line Cervical Cancer</td>
</tr>
<tr>
<td><strong>SAR439459</strong>&lt;br&gt;Anti-TGFβ + cemiplimab* Solid Tumors</td>
<td><strong>REGN IO mAB</strong>&lt;br&gt;T-Cell Engager Ovarian Cancer</td>
<td><strong>isatuximab</strong>*&lt;br&gt;Anti-CD38 1st line Ti (IMROZ)</td>
</tr>
<tr>
<td><strong>REGN3767</strong>*&lt;br&gt;+ cemiplimab* Anti-LAG3 and anti-PD-1 Malignancies</td>
<td><strong>REGN IO mAB</strong>&lt;br&gt;Checkpoint Inhibitor Solid Tumors</td>
<td><strong>cemiplimab</strong>*&lt;br&gt;Anti-PD-1 mAb Advanced BCC</td>
</tr>
</tbody>
</table>

**New entries**

- **isatuximab***<br>Anti-CD38 1st line Te

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*Partnered with Regeneron **Partnered with BioNTech *** Opt-in rights products for which rights have not been exercised yet,
ADC= Antibody Drug Conjugate; AML= Acute Myeloid Leukemia; BCC= Basal Cell Carcinoma; CSCC= Cutaneous Squamous Cell Carcinoma; GBM= glioblastoma multiforme; MDS= Myelodysplastic Syndrome; MM= Multiple Myeloma; NSCLC= Non-Small Cell Lung Cancer; RCC= Renal Cell Carcinoma; RRMM= Relapsed Refractory Multiple Myeloma; SERD= Selective Estrogen Receptor Degrader; TNBC= Triple Negative Breast Cancer; Te= Transplant eligible; Ti= Transplant ineligible,
Sanofi’s Strong Commitment to Oncology Expected to Begin to Deliver in 2018

6 Pre-clinical programs enter Phase 1

- T-cell engager in AML/MDS (Sanofi)
- Immunostimulatory mRNA (BioNTech)
- T-cell engager$^{(2)}$ in Ovarian Cancer (Regeneron)
- Checkpoint inhibitor (Regeneron)
- cemiplimab + DNA vaccine$^{(2)}$
- cemiplimab + oncolytic$^{(2)}$

14 New proof of concept indications

- Isatuximab + Check-point inhibitor (9)
- Anti-TGFβ monotherapy
- Anti-TGFβ + cemiplimab (2)
- SERD monotherapy
- SERD + palbociclib

4 Potential proof of concept study readouts

- Anti-LAG3 monotherapy and combination with other checkpoint inhibitors in solid tumors/lymphoma (Regeneron)
- SERD in metastatic Breast Cancer
- CEACAM5 ADC in Solid Tumors
- CA6 ADC in metastatic Breast Cancer

9 Pivotal studies ongoing or planned

- Isatuximab: 4 MM
- Cemiplimab*: 3 NSCLC, 1 BCC, 1 Cervical Cancer

3 BLA/MAA submissions

- Cemiplimab* CSCC: U.S., EU
- Isatuximab RRMM: U.S.

1 U.S. launch

- Cemiplimab* CSCC$^{(1)}$

---

SERD= Selective Estrogen Receptor Degrader; NSCLC= Non-Small Cell Lung Cancer; BCC= Basal Cell Carcinoma; CSCC= Cutaneous Squamous Cell Carcinoma; RRMM= Relapsed Refractory Multiple Myeloma; MDS= Myelodysplastic Syndrome; AML= Acute Myeloid Leukemia

*cemiplimab partnered with Regeneron

(1) Subject to U.S. FDA approval
(2) Collaboration with REGN
# Expected First Submission for Cemiplimab\(^{(1)}\) in CSCC, Followed by Other Large or Untapped Opportunities

<table>
<thead>
<tr>
<th>Indication</th>
<th>Pre POC</th>
<th>Pivotal</th>
<th>Submission</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSCC (EMPOWER CSCC 1)</td>
<td>Local advanced or metastatic CSCC</td>
<td></td>
<td>Expected in Q1 2018 in the U.S.</td>
</tr>
<tr>
<td>BCC (EMPOWER BCC 1)</td>
<td>2nd line advanced metastatic BCC</td>
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<tr>
<td>Cervical Cancer (EMPOWER Cervical 1)</td>
<td>Platinum-refractory cervical cancer</td>
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<tr>
<td>NSCLC (EMPOWER Lung 1)</td>
<td>1st line NSCLC PD-L1 ≥ 50% monotherapy</td>
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</tr>
<tr>
<td>NSCLC (EMPOWER Lung 2)</td>
<td>1st line NSCLC PD-L1 ≥ 50% combinations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSCLC (EMPOWER Lung 3)</td>
<td>1st line NSCLC PD-L1 &lt; 50% combinations</td>
<td></td>
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</tr>
</tbody>
</table>

CSCC = Cutaneous Squamous Cell Carcinoma; BCC = Basal Cell Carcinoma; NSCLC = Non-Small Cell Lung Cancer

Cemiplimab is an investigational agent and has not been evaluated by any regulatory authority

\(^{(1)}\) In collaboration with REGN
Cutaneous Squamous Cell Carcinoma (CSCC) is a Disease with Significant Unmet Medical Need

- High patient burden in resectable and unresectable locally advanced and metastatic disease
- Rate of metastasis is 1% to 6%\(^{(1)}\)
- Presence of distal metastasis associated with poor prognosis
  - Median survival <2 years
- Primary management is surgical

\(^{(2)}\) National Cancer Institute
Cemiplimab\(^{(1)}\) Phase 1 Expansion Cohort Results Confirm PD-1 as an Important Therapeutic Target in CSCC

- Positive results from the CSCC expansion cohort of first in human study at ASCO 2017
  - 46.2% ORR and 69.2% DCR
  - Generally well tolerated\(^{(2)}\)

- Deep and durable tumor reductions in target lesions observed

- Breakthrough Therapy Designation granted from the U.S. FDA

Cemiplimab ORR in Phase 1 CSCC\(^{(3)}\)

\(\%\) change in target lesions from baseline

---

Cemiplimab is an investigational agent and has not been evaluated by any regulatory authority

\(^{(1)}\) In collaboration with REGN

CSCC= Cutaneous Squamous Cell Carcinoma; DCR= Disease Control Rate; ORR= Objective Response Rate

\(^{(2)}\) The most common treatment-related adverse event of any grade was fatigue (23.1%).

All grade 3 or higher adverse events occurred once and included arthralgia (3.8%), maculopapular rash (3.8%), asthenia (3.8%), aspartate aminotransferase (AST) elevation (3.8%) and alanine aminotransferase (ALT) elevation (3.8%).

\(^{(3)}\) Data presented at ASCO 2017
Pivotal Results for Cemiplimab\(^{(1)}\) in Advanced CSCC Confirm High Response Rate and Durable Responses

- If approved cemiplimab expected to be the first anti-PD-1 indicated for advanced CSCC
- Results from 82 patients in the pivotal Phase 2 trial
  - 46.3% ORR by independent review
  - 33 of 38 responses ongoing (with at least 6 months of follow up)
  - Safety profile generally consistent with approved anti-PD1 drugs
- FDA and EMA submissions planned in Q1 2018

---

Pivotal Phase 2 Trial

- **Primary Endpoint:** Objective Response Rate
- **Regimen:**
  - Cohort 1\&2: 3mg/kg cemiplimab every 14 days
  - Cohort 3: 350mg flat dose cemiplimab every 3 weeks

---

CSCC = Cutaneous Squamous Cell Carcinoma

\(^{(1)}\) In collaboration with Regeneron

Cemiplimab is an investigational agent and has not been evaluated by any regulatory authority
## Cemiplimab\(^{(1)}\) First-in-Class Opportunity in CSCC, Expansion into Other Untapped Opportunities in IO

### 2\(^{nd}\) Line Advanced Metastatic Basal Cell Carcinoma\(^{(2)}\)
- 28,000 patients diagnosed in U.S. with metastatic BCC
- 3,000 estimated deaths in the U.S. annually

**Study expected to complete H2 2018**

### Platinum-Refractory Cervical Cancer\(^{(3)}\)
- 25,000 patients diagnosed in U.S. and Western EU
- 35% of patients are Stage IV at diagnosis

**Study expected to complete H1 2020**

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\(^{(1)}\) In collaboration with Regeneron  
\(^{(2)}\) Epidemiological data from Mohan et al Curr Derm Rep 2014;3:40-45  
\(^{(3)}\) Epidemiological data from National Cancer Institute  
Cemiplimab is an investigational agent and has not been evaluated by any regulatory authority
First line NSCLC landscape is evolving

- Current standard of care unlikely to remain over the next 5-10 years
- Combination regimens likely to dominate and optimal combinations not clearly identified

Current trials provide foundation for testing new combinations

- Evaluation of monotherapy, IO/IO, and IO/chemo in Phase 3 trials
- Developing multiple novel next generation combinations in preclinical through Phase 2

Supports engagement with healthcare practitioners, investigators and payers

- Most common use for anti-PD-1 antibodies is in NSCLC
Cemiplimab\(^{(1)}\) Strategic Development Program in Non-Small Cell Lung Cancer (NSCLC)

- Large lung cancer indication continues to be an area of major unmet need
- Phase 3 study in front line NSCLC underway
- Phase 3 studies in first line NSCLC using combinations with chemo and ipilimumab in high and low expressers of PD-L1 are planned
- Second line NSCLC study planned

<table>
<thead>
<tr>
<th>Lung 1</th>
<th>Lung 2</th>
<th>Lung 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1L Monotherapy</strong>&lt;br&gt;PDL1 ≥ 50%</td>
<td><strong>1L Combinations</strong>&lt;br&gt;PDL1 ≥ 50%</td>
<td><strong>1L Combinations</strong>&lt;br&gt;PDL1 &lt; 50%</td>
</tr>
<tr>
<td>cemiplimab vs. platinum doublet</td>
<td>cemiplimab combinations vs. pembrolizumab</td>
<td>cemiplimab combinations vs. platinum doublet</td>
</tr>
<tr>
<td>Ongoing P3 N=300</td>
<td>Planned</td>
<td>Initiated</td>
</tr>
</tbody>
</table>

Primary endpoint PFS
Secondary endpoints include OS

\(^{(1)}\) In collaboration with Regeneron
Cemiplimab is an investigational agent and has not been evaluated by any regulatory authority
Significant Opportunity for Isatuximab in Large and Growing Multiple Myeloma Market

- Worldwide Multiple Myeloma market expected to reach $29bn in 2022 driven by:
  - Double/triple branded combination use
  - New options with prolonged PFS benefit
  - Globally ~114k new cases diagnosed annually
- Anti-CD38 class rapidly becoming standard of care
  - Combinability without increased toxicity
  - Unprecedented PFS prolongation

Estimated Worldwide Multiple Myeloma Market\(^{(1)}\)

- 2017
  - Anti-CD38:
  - IMiDs
  - PI’s
  - Other:
  - $14bn
- 2022e
  - $29bn

Isatuximab is an investigational agent and has not been evaluated by any regulatory authority. IMiD = immunomodulatory agent; PI = proteasome inhibitor; PFS = progression free survival

\(^{(1)}\) EvaluatePharma® October 2017
Isatuximab Demonstrated Competitive Profile in Phase 1b

- Targets unique epitope with distinct combination MoA(1)
- Competitive administration profile
  - ~3h for initial infusion
  - 2.5h for subsequent infusions
- Broad development program in Multiple Myeloma with >12 clinical trials ongoing
- Potential benefit in solid tumors being explored

Isatuximab combination with PomDex
Relapse Refractory Multiple Myeloma\(^{(2)}\)

- ORR 61% versus 31% PomDex alone

---

ASCT= Autologous Stem Cell Transplant; CyBorD= cyclophosphamide, bortezomib, and dexamethasone; PomDex= pomalidomide and dexamethasone; ORR= Objective Response Rate

Isatuximab is an investigational agent and has not been evaluated by any regulatory authority

(2) Richardson PG, et al. Poster presented at American Society of Hematology; 2017 Dec 9-12th
Four Large Phase 3 Trials with Isatuximab Address Multiple Myeloma Along the Treatment Continuum

- Two trials in first line setting with “Gold Standard” backbone therapy, VRd
  - GMMG: transplant eligible patients
  - IMROZ: transplant ineligible patients

- IKEMA trial in RRMM patients previously treated with 1-3 lines of therapy

- ICARIA pivotal data to potentially provide entry to market RRMM

- Minimal residual disease (MRD) assessments linked to PFS endpoint

- IMROZ, IKEMA, and ICARIA in progress

PFS= Progression Free Survival; DoT= duration of treatment; SCT= Stem Cell Transplant; MM= Multiple Myeloma; RR= Relapsed Refractory; ND= Newly Diagnosed; VRd= Velcade, Revlimid, dexamethasone; Te= Transplant eligible, GMMG= German Multiple Myeloma Group
Isatuximab is an investigational agent and has not been evaluated by any regulatory authority
Combination indications
• Glioblastoma
• Hepatocellular Cancer
• Ovarian Cancer
• Head & Neck Cancer
• Urothelial Cancer
• Colorectal Cancer
• Multiple Myeloma
• NSCLC
• Prostate Cancer
First Expected FDA Submission for Isatuximab Based on ICARIA Data in 2018, Ahead of Data Readouts in 2L and 1L

Expected timeline

2017  2018  2019  2020  2021  2022+

ICARIA  Phase 3  
IKEMA  Phase 3  
IMROZ  Phase 3  
GMMG  Phase 3  
IO Combos  Phase 2 multiple data readouts  

Potential U.S. submission  Potential EU submission

1L= first line; Te= transplant eligible; GMMG= German Multiple Myeloma Group
Isatuximab is an investigational agent and has not been evaluated by any regulatory authority
Leverage Entry in RRMM to Expand Use of Isatuximab in Earlier Lines of Therapy and Other Cancer Types

Gain Market Entry
Initial submission planned in Relapsed Refractory Multiple Myeloma

Expand in Multiple Myeloma
Utilization in 1L and 2L along treatment continuum of Multiple Myeloma

Combination Use in Solid Tumors
Further enhance response to immuno-oncology agents

Building Hematology Portfolio
3 pre-clinical assets
• Next generation CD38 mAB
• REGN bispecific
• Multispecific T-cell engager

Isatuximab is an investigational agent and has not been evaluated by any regulatory authority
Selective Estrogen Receptor Degrader Demonstrates Strong Tumor Response in Preclinical Models

• Key differentiating factors vs. current treatment option
  • Highly potent against mutant and wild-type ER
  • Activity across all BC cell lines
  • No estrogenic activity on uterine tissue in-vivo
  • Strong anti-tumor activity (regression) in BC models
  • Oral dosing vs infusion

• Trial in ER+ mBC began enrollment November 2017
  • Using FES-PET imaging to demonstrate target engagement
  • Evaluating as monotherapy and in combination with palbociclib

Potential Proof of Concept Study Readout in 2018
Yong-Jun Liu
Senior Vice President
Global Head of Research

Building a Competitive Position in Oncology

Next wave in Oncology
Our Immuno-Oncology Competitive Strategy

**Leverage External Advancement (REGN)**

- **anti-PD-1**
- **anti-PD-1 Combo with Sanofi Assets**

**Probe**

- **Underlying Mechanism of PD-1 Resistance**
  - Innate Resistance (e.g. TGFβ)
  - Acquired Resistance (e.g. CD38)

**Partner**

- **Build on Anti-PD-1 Success**
- **Leverage External Advancement (REGN)**
  - anti-PD-1
  - anti-PD-1 Combo with Sanofi Assets

**Leap**

- **Turn Cold Tumor to Hot Tumor**
  - Immune modulatory multi-specific mAbs mRNA cocktails (BioNTech)
  - Tumor-directed immune activation

**SANOFI Competitive Position**

**Probe Underlying Mechanism of PD-1 Resistance**
Global Immuno-Oncology Collaboration with Regeneron to Develop and Commercialize Antibody Cancer Treatments

**Checkpoint-centric approach with an extension to bispecific antibodies**

<table>
<thead>
<tr>
<th>Checkpoint inhibitors</th>
<th>Combination with checkpoint inhibitors</th>
<th>Bispecific antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-1 (clinic)</td>
<td>PD-1 + LAG-3 (clinical)</td>
<td>Several in pre-clinical development</td>
</tr>
<tr>
<td>LAG3 (clinic)</td>
<td>PD-1 + CD38 (1) (clinical)</td>
<td>REGN IO Ab T-Cell Engager Ovarian Cancer(2)</td>
</tr>
<tr>
<td>Several in pre-clinical development</td>
<td>PD-1 + TGFβ (1) (clinical)</td>
<td>REGN IO Ab Checkpoint inhibitor Solid Tumors(2)</td>
</tr>
</tbody>
</table>

- **REGN IO Ab**
  - Checkpoint inhibitor
  - Solid Tumors

- **REGN3767**
  - Anti-LAG3
  - Advanced Cancers

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>cemiplimab</td>
<td>cemiplimab</td>
<td>cemiplimab</td>
</tr>
<tr>
<td>PD-1 inhibitor</td>
<td>PD-1 inhibitor</td>
<td>PD-1 inhibitor</td>
</tr>
<tr>
<td>Advanced CSCC</td>
<td>Advanced BCC</td>
<td>2nd line Cervical Cancer</td>
</tr>
</tbody>
</table>

- **cemiplimab + DNA vaccine**
  - Anti-PD-1 mAb
  - 1 L GBM(2)

- **cemiplimab + REGN3767**
  - anti PD-1 + LAG3
  - Advanced Cancers

- **cemiplimab + oncolytic virus**
  - Anti-PD-1 mAb
  - Advanced RCC(2)

- **isatuximab + cemiplimab**
  - CD38 and PD-1 inhibitors
  - RRMM

- **cemiplimab + SAR439459**
  - anti- PD-1 + anti-TGFβ
  - Advanced Solid Tumors

Current Status as of December 13 2017. IO Discovery and Development Agreement with Regeneron signed in July 2015; agreement duration 5 years, subject to Tail Period Option

(1) Sanofi only molecule

* Opt-in rights products for which rights have not been exercised yet

| (2) Entering Phase 1 expected in Q1 2018; R- Registration Study | (3) Entering Phase 2 expected in 2018 |
Overcoming anti-PD-1 Resistance by Blocking TGF-β

Genomic Analysis
(Patient Samples)\(^{(1)}\)

Responders vs. Non-responders

Sanofi Internal Results

- TGFβ activation correlates with anti-PD-1 resistance
- TGFβ-mediated immune suppression in melanoma may contribute to anti-PD-1 resistance
- Gateway indication: combination of anti-TGFβ and anti-PD-1 to overcome innate resistance
Overcoming anti-PD-1 Resistance by Blocking TGF-β: \textit{in vivo} Proof of Concept

**Single Agent Control**
SAR439459

**Combination Control**
SAR439459 + Isotype Ctrl + anti-mPD-1

**Combination**
SAR439459 + anti-mPD-1

**Status: Phase 1** Anti-TGF-β + cemiplimab

**Indication: Advanced Solid Tumors**

MC38 syngeneic colon s.c. model in C57BL/6 mice; 8 administrations IP every 3 days beginning <100mm3
Anti-TGF-β, SAR439459 (25 mg/kg), RMP1-14 anti-PD-1 (5 mg/kg)
Anti-PD-1 *in vivo* resistance via CD38 upregulation on tumor cells is reversed by anti-CD38/anti-PD-1 combination\(^1\)

**Status:** Phase 1 expected to start in Solid Tumors in Q1 2018

---

(1) Limo Chen, et al. ASCO-SITC, 2017, MD Anderson Cancer Center (anti-mouse-PD-L1 and CD38 antibodies)
(2) Sanofi internal data (isatuximab + nivolumab)
**Future Pipeline: Turning Cold Tumor to Hot Tumor**

<table>
<thead>
<tr>
<th>mRNA</th>
<th>Antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA Mixture</td>
<td>NK- and T-Cell Engagers</td>
</tr>
<tr>
<td>First Development Candidate <em>in vivo</em> Proof of Concept</td>
<td>Development Candidate <em>in vivo</em> Proof of Concept</td>
</tr>
<tr>
<td>FIH expected in 2018</td>
<td>FIH expected in 2018</td>
</tr>
</tbody>
</table>

PRR= Pattern Recognition Receptor; NK= Natural Killer; M0= Target validation; FIH= First in Human

“Cold” to “Hot”: Anti-PD-1/PD-L1 agents are believed to primarily work on T-cell inflamed tumors. In most patients, their tumors have a non T-cell inflamed microenvironment. In order to drive responsiveness to immune therapy based agents, there is a need to identify and develop agents that can bring T-cells to tumors.
Systemic Anti-Tumor Immunity After mRNA Treatment

Intratumoral injection of immuno mRNA reduces tumors at distant non-injected sites

Status: Phase 1 entry expected in 2018

Immune cells (green) infiltrate melanoma tumors after treatment
Sanofi is Building a Robust IO Discovery Pipeline

- Building a portfolio of internal and partnered assets
- Supported by a talented team with expertise in translational and precision medicine
- 6 pre-clinical programs expected to enter the clinic in 2018

<table>
<thead>
<tr>
<th>Expected FIH Projection</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA (BioNTech)</td>
<td></td>
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<tr>
<td>Immuno mRNA Mix 1</td>
<td></td>
<td>Up to 4 additional Immuno mRNAs</td>
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</tr>
<tr>
<td>CD38</td>
<td></td>
<td>1-2 CD38 mAb 2nd generation</td>
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<tr>
<td>Immune-cell Engagers</td>
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<tr>
<td>T-Cell Engager</td>
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<tr>
<td>Ovarian Cancer</td>
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<tr>
<td>T-Cell Engager</td>
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<tr>
<td>AML/MDS</td>
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<tr>
<td>REGN Bispecific</td>
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<tr>
<td>Multiple Myeloma</td>
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<tr>
<td>NK Cell Engager</td>
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<tr>
<td>Multi-specific Ab</td>
<td></td>
<td>1-2 Multi-Targeting Abs(1)</td>
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<tr>
<td>ADC</td>
<td></td>
<td>1 mAb Toxin</td>
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<tr>
<td>CheckPoint Inhibitors</td>
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</tr>
<tr>
<td>REGN IO Ab</td>
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<tr>
<td>Solid Tumors</td>
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<tr>
<td>cemiplimab + DNA vaccine</td>
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<tr>
<td>1L GBM</td>
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<tr>
<td>cemiplimab + oncolytic virus</td>
<td>Advanced RCC</td>
<td></td>
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</tr>
</tbody>
</table>

FIH= First in Human (1) Collaboration with REGN
Stefan Oelrich
Executive Vice President
Diabetes & Cardiovascular

SANOFI

Sustaining Leadership in DCV
DCV Strategy Will Focus on Innovation While Protecting our Core Business

**Innovation**
- Regain R&D leadership in innovative segments

**Emerging Markets**
- Capitalize on our attractive starting position and momentum in EM

**Mature Markets**
- Optimize value and volume in EU and U.S.

**Integrated Care**
- Create early experience and protect the core while creating long term strategic options

**Cardiovascular**
- Reinforce Praluent® and develop our portfolio with new opportunities
## Broadening our Innovative DCV Portfolio

### 2018 DCV Development Pipeline

<table>
<thead>
<tr>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Registration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SAR441255</strong>&lt;br&gt;GLP-1/GCG/GIP agonist&lt;br&gt;Type 2 Diabetes &amp; Obesity</td>
<td><strong>SAR438335</strong>&lt;br&gt;GLP-1/GIP agonist&lt;br&gt;Type 2 Diabetes</td>
<td><strong>SAR425899</strong>&lt;br&gt;GLP-1/GCG agonist&lt;br&gt;NASH</td>
<td><strong>efpeglenatide</strong>&lt;br&gt;Long acting GLP-1 agonist&lt;br&gt;Type 2 Diabetes</td>
<td><strong>Praluent</strong>&lt;br&gt;Anti-PCSK9 mAb&lt;br&gt;CV events reduction</td>
</tr>
<tr>
<td><strong>SAR440181</strong>&lt;br&gt;Myosin activation&lt;br&gt;Dilated Cardiomyopathy</td>
<td><strong>SAR407899</strong>&lt;br&gt;rho kinase&lt;br&gt;Microvascular Angina</td>
<td><strong>sotagliflozin</strong>&lt;br&gt;Oral SGLT-1&amp;2 inhibitor&lt;br&gt;Type 2 Diabetes</td>
<td><strong>sotagliflozin</strong>&lt;br&gt;Oral SGLT-1&amp;2 inhibitor&lt;br&gt;Type 1 Diabetes</td>
<td></td>
</tr>
<tr>
<td><strong>SAR247799</strong>&lt;br&gt;S1P1 agonist&lt;br&gt;Cardiovascular indication</td>
<td><strong>sotagliflozin</strong>&lt;br&gt;Oral SGLT-1 &amp; 2 inhibitor&lt;br&gt;Worsening HF in Diabetes pts</td>
<td><strong>SAR341402</strong>&lt;br&gt;Rapid acting insulin&lt;br&gt;Type 1/2 Diabetes</td>
<td><strong>mavacamten</strong>&lt;br&gt;Myosin inhibitor&lt;br&gt;Obs. Hypertrophic Cardiomyopathy</td>
<td></td>
</tr>
</tbody>
</table>

HF= Heart Failure; NASH= Nonalcoholic steatohepatitis
(1) Collaboration with Lexicon
(2) Collaboration with Hamni
(3) Collaboration with MyoKardia
(4) Collaboration with Regeneron
(5) 2018 new entries

**Cardiovascular**
**Diabetes & metabolism**
Sanofi Diabetes R&D Strategy Focuses on Type 1 & 2 Diabetes, Obesity and NASH

Several established solutions available

Value Pool

CV= Cardiovascular; DKD= Diabetic Kidney Disease; NASH= Nonalcoholic Steatohepatitis; T1D= Type 1 Diabetes; T2D= Type 2 Diabetes

ILLUSTRATIVE Market Size (Sales)

- 2016
- 2026e

No solutions only symptomatic treatments

T1D

Obesity

NASH

DKD

T2D

CV complications

Several established solutions available

No solutions only symptomatic treatments
Novel Peptide Platform to Potentially Result in Innovative Diabetes, Obesity and NASH Therapies

GLP-1 = Glucagon-Like Peptide-1; GIP = Gastric inhibitory polypeptide; GCG = Glucagon

GLP-1/GCG SAR425899 Phase 2
GLP-1/GIP SAR438335 Phase 1
GLP-1/GCG/GIP SAR441255 Pre-clinical

Dual and Triple Agonist adding Pharmacology of GIP and/or Glucagon
Obesity Is a Medical Challenge and the Source of Substantial Morbidity and Mortality

Obesity: a major driver of subsequent disease
120 million quality adjusted life-years lost to disability/year(1)

Gastric bypass: very effective, but only small fraction of eligible patients do it
Mean BMI Change in T2D from baseline to 5 years(2)

Our development options might bring advantages closer with bypass by inducing 10-15% weight loss

Relative risk reduction(3)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>40%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>92%</td>
</tr>
<tr>
<td>CV disease</td>
<td>49%</td>
</tr>
<tr>
<td>CAD</td>
<td>59%</td>
</tr>
<tr>
<td>Stroke</td>
<td>57%</td>
</tr>
<tr>
<td>Heart failure</td>
<td>41%</td>
</tr>
<tr>
<td>Cancer</td>
<td>60%</td>
</tr>
</tbody>
</table>

Relative risk reduction of common obesity-related diseases 7 years after bariatric surgery(3)

(1) GBD 2015 Obesity Collaborators; NEJM2017; 377:13–27
(2) Schauer et al. NEJM 376:641-51, 2017
(3) Adams et al., 2007 NEJM 357:753-761; Mingrone et al. NEJM 2012; 366:1577-85
Dual Agonist\(^{(1)}\) Shows Significant Body Weight Reduction in Overweight/Obese Diabetic Patients

**Change in Body Weight from Baseline**

**GLP-1/GCG agonist\(^{(1,2)}\)**

- **Change in body weight (kg)**
  - Time (weeks)
  - Placebo
  - Low Dose: 30-60-90 µg
  - High Dose: 60-120-180 µg

**Semaglutide and Liraglutide\(^{(3)}\)**

- **Change in body weight (kg)**
  - Time (weeks)
  - Placebo
  - Low Dose: 0.1 mg
  - Medium Dose: 0.2 mg
  - High Dose: 0.4 mg
  - Highly Dose: 0.8 mg
  - Extremely High Dose: 0.8 mg E
  - Liraglutide
    - 1.2 mg
    - 1.8 mg

---

\(^{(1)}\) SAR425899 is an investigational agent and has not been evaluated by any regulatory authority. Adverse events observed most frequently were related to GI disorders.

\(^{(2)}\) Phase 1 Results; 4-week study in overweight to obese T2DM, 2-step up-titration after 7 days - Lindauer K et al, Oral presentation #109, European Association for the Study of Diabetes (EASD) 52nd Annual Meeting, September 14, 2016, Munich, Germany; BMI at baseline: 32 kg/m\(^2\)

\(^{(3)}\) Nauck et al. Diabetes Care 2016; BMI at baseline: ~31 kg/m\(^2\)
Dual Agonist\(^{(1)}\) Large Development Program in Obesity and NASH Expected to Start in 2018

PoC= Proof of Concept; CVOT= Cardiovascular Outcome Trial
(1) SAR425899 is an investigational agent and has not been evaluated by any regulatory authority. Adverse events observed most frequently were related to GI disorders
(2) Excluding T2DM
(3) 52 weeks safety extension

SAR425899 is an investigational agent and has not been evaluated by any regulatory authority. Adverse events observed most frequently were related to GI disorders.
Sotagliflozin(1): First Investigational Dual SGLT-1 and SGLT-2 Inhibitor in T1D and T2D(2,3)

Inhibition of SGLT-1 and SGLT-2 Pathways

SGLT-2 inhibition in the kidney(4) increases glucose excretion in the urine
- Reduced levels of blood glucose
- Mechanism is independent of insulin but diminishes in effect with declining renal function

SGLT-1 inhibition in the GI tract(5) reduces post-prandial glucose and elevates GI hormones(6)
- Metabolic benefits
- Mechanism is independent of insulin and is not affected by declining renal function

(1) Sotagliflozin is an investigational agent and has not been evaluated by any regulatory authority. The full risk/benefit assessment with regulators is pending. Sotagliflozin was generally well tolerated.
(6) GLP-1 and PYY
Sotagliflozin is Potentially Differentiated vs. SGLT-2 Inhibitors in Type 2 Diabetes

Sotagliflozin is an investigational agent and has not been evaluated by any regulatory authority. The full risk/benefit assessment with regulators is pending. Sotagliflozin was generally well tolerated.

(2) Change in Urinary Glucose Excretion measured at week 12

Additional HbA$_1$c lowering without further increase in urinary glucose excretion

Change in HbA$_1$c (%)$^{(1)}$

Urinary Glucose Excretion (g/day)$^{(1,2)}$
Sotagliflozin: Impact on Post Prandial Glucose (PPG) in Type 2 Diabetes

Sotagliflozin 400mg
n=16(1)

Placebo
n=15

Glucose (mg/dl)

Data from Study 107 in Type 2 Diabetes patients with Chronic Kidney Disease

(1) Sotagliflozin is an investigational agent and has not been evaluated by any regulatory authority. The full risk/benefit assessment with regulators is pending. Sotagliflozin was generally well tolerated.

(2) Phase 2 study 107 T2DM with CKD
Plasma glucose after standard meal p=0.003, sotagliflozin vs. placebo
Sotagliflozin\(^{(1)}\) Demonstrated Significant HbA1c Reduction when Added to Insulin in Type 1 Diabetes Patients

**Phase 3 Clinical Trials in Type 1 Diabetes Patients**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Treatment Group</th>
<th>HbA1c Reduction (%)</th>
<th>Study Population</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>inTandem1</strong></td>
<td>400mg</td>
<td>-0.49%</td>
<td>(n=793)</td>
</tr>
<tr>
<td></td>
<td>200mg</td>
<td>-0.43%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>placebo</td>
<td>-0.08%</td>
<td></td>
</tr>
<tr>
<td><strong>inTandem2</strong></td>
<td>400mg</td>
<td>-0.37%</td>
<td>(n=782)</td>
</tr>
<tr>
<td></td>
<td>200mg</td>
<td>-0.39%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>placebo</td>
<td>-0.03%</td>
<td></td>
</tr>
<tr>
<td><strong>inTandem3</strong></td>
<td>400mg</td>
<td>-0.79%</td>
<td>(n=1,402)</td>
</tr>
<tr>
<td></td>
<td>placebo</td>
<td>-0.33%</td>
<td></td>
</tr>
</tbody>
</table>

(1) Sotagliflozin is an investigational agent and has not been evaluated by any regulatory authority. The full risk/benefit assessment with regulators is pending. Sotagliflozin was generally well tolerated.

(2) Buse J et al, Presentation 69-OR at American Diabetes Association 77th Scientific Sessions (ADA 2017), San Diego, CA, US.

(3) Danne T et al, Presentation 146-LB at ADA 2017, San Diego, CA, US.

(4) Garg S et al, New England Journal of Medicine, Sept 2017b
Sotagliflozin(1): A Potentially Differentiated Value Proposition in Type 1 and Type 2 Diabetes

**Potential in Type 1 Diabetes**
- HbA$_1^C$ control as an adjunct to insulin
- Potent effect on PPG
- Weight reduction

**Potential in Type 2 Diabetes**
- Efficacy through HbA$_1^C$
- Efficacy in patients with renal impairment
- Weight reduction comparable to class
- CV outcomes data in renal and Heart Failure population
- Low risk of hypoglycemia

---

(1) Sotagliflozin is an investigational agent and has not been evaluated by any regulatory authority. The full risk/benefit assessment with regulators is pending. Sotagliflozin was generally well tolerated.
Broad Phase 3 Program Underway in Type 2 Diabetes for Sotagliflozin\(^{(1)}\), Including CKD Focus

- **Type 1 Diabetes**
- **Type 2 Diabetes**

**Expected timeline**

- **2017**
  - Monotherapy
  - Combo studies
  - CKD

- **2018**
  - Cardiovascular Safety Trial

- **2019**
  - Worsening HF in Diabetes patients

- **2020**

- **2021**

- **2022**

---

CKD= Chronic Kidney Disease; HF= Heart Failure

\(^{(1)}\) Sotagliflozin is investigational. The full risk/benefit assessment with regulators is pending. Sotagliflozin was generally well tolerated.
Efpeglenatide\(^{(1,2)}\): A New Weekly GLP-1 Agonist

Once weekly GLP-1R agonist based on Hanmi Pharmaceuticals strong proprietary technology

- Therapeutic agent (CA-Exendin-4)
- Flexible linker
- Non-glycosylated Fc

Phase 3 in Type 2 Diabetes started in Q4 2017 to confirm expected target profile:

- Significant HbA\(_{1c}\) lowering
- Weight loss and favorable GI tolerability
- Convenient device platform

GI=Gastro-Intestinal

(1) Collaboration with Hanmi, efpeglenatide is an investigational agent and has not been evaluated by any regulatory authority.
(2) The efficacy and safety of efpeglenatide will be investigated in a Phase 3 program.
Efpeglenatide\(^{(1)}\) Data and Modelling Suggest Strong HbA1c Reduction Potential

---

**Phase 2 Dose-Finding Study\(^{(2)}\)**

<table>
<thead>
<tr>
<th>Week</th>
<th>Placebo</th>
<th>2mg/week</th>
<th>3mg/week</th>
<th>4mg/week</th>
<th>Liraglutide 1.8mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.3</td>
<td>6.5</td>
<td>6.6</td>
<td>6.6</td>
<td>6.4</td>
</tr>
<tr>
<td>2-13</td>
<td>7.6</td>
<td>7.6</td>
<td>7.6</td>
<td>7.5</td>
<td>7.0</td>
</tr>
</tbody>
</table>

---

**Modeling & Simulation HbA\(_{1c}\)**

<table>
<thead>
<tr>
<th>Probability</th>
<th>HbA(_{1c}) Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-2.0</td>
</tr>
<tr>
<td>1</td>
<td>-1.5</td>
</tr>
<tr>
<td>2</td>
<td>-1.0</td>
</tr>
<tr>
<td>3</td>
<td>-0.5</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

---

(1) Efpeglenatide is an investigational agent and has not been evaluated by any regulatory authority. The efficacy and safety of efpeglenatide will be investigated in a Phase 3 program.

Efpeglenatide is an investigational agent and has not been evaluated by any regulatory authority. The efficacy and safety of efpeglenatide will be investigated in a Phase 3 program CVOT= Cardiovascular Outcome Trial.
ODYSSEY Outcomes Study Topline Results Expected in Q1 2018

- All patients enrolled following an Acute Coronary Syndrome
  - Recent ACS: prior coronary event 1-12 months before randomization
- Praluent® added to standard of care maximum tolerated dose of high potency statin
- Average duration of treatment
  - Median exposure - 33 months
  - Some patients treated for up to 5 years

(1) Powered to detect 15% difference in MACE defined as: CHD death, any non-fatal MI, fatal and non-fatal ischemic stroke, unstable angina requiring hospitalization
MyoKardia’s Collaboration Represents One of the Largest R&D Commitments to Genetic Forms of Cardiomyopathy

HCM is the leading cause of sudden cardiac death in young adults

DCM is the leading genetic illness requiring heart transplantation

**Phase 1**

**MYK-491/SAR440181**
- Increased cardiac contractility in a DCM heart
- Topline data expected by early 2018
- Initiation of single ascending dose trial in symptomatic DCM patients expected before end of 2017

**Phase 2**

**Mavacamten (1)**
- Reduced hypercontractility in a HCM heart

---

**Pre-clinical**

**HCM-2**

- **HCM Sarcomere**
  - Too many engaged cross-bridges
- **DCM Sarcomere**
  - Too few engaged cross-bridges

---

**Normal Sarcomere**
- Actin thin filament
- Actin-myosin cross-bridge
- Myosin thick filament
- Force-producing myosin head

---

**MYK-461**
- Increased cardiac contractility in a DCM heart
- Topline data expected by early 2018
- Initiation of single ascending dose trial in symptomatic DCM patients expected before end of 2017

---

**DCM-1**
- Reduced hypercontractility in a HCM heart

---

HCM= Hypertrophic cardiomyopathy; DCM: Dilated Cardiomyopathy

(1) MYK-461/SAR439152
Mavacamten: Positive Results from Phase 2a PIONEER Cohort A\(^{(1)}\) Study in Symptomatic oHCM

<table>
<thead>
<tr>
<th>PIONEER-HCM Study in Symptomatic oHCM</th>
<th>Baseline, mean (SD) n=11</th>
<th>Week 12, mean (SD) n=10</th>
<th>Change from Baseline to week 12, mean (SD) n=10</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-exercise peak LVOT gradient, mmHg</td>
<td>125 (60.0)</td>
<td>19 (12.9)</td>
<td>-112 (63.8)</td>
<td>0.002</td>
</tr>
<tr>
<td>Peak VO(_2), mL/kg/min</td>
<td>20.7 ±7.4</td>
<td>24.6 ±8.8</td>
<td>+3.5 (3.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>Change in NT-proBNP pg/mL</td>
<td>929 (647)</td>
<td>454 (551)</td>
<td>-459 (722)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

- **Primary endpoint met**
  - Post-exercise peak LVOT gradient, mmHg

- **Key secondary endpoints met, incl. peak VO\(_2\)**
  - Peak VO\(_2\), mL/kg/min

- **Change in NT-proBNP**
  - Change in NT-proBNP pg/mL

- **PIONEER-HCM study in symptomatic oHCM**
  - Generally well tolerated (one patient experienced a serious adverse event due to a recurrence of atrial fibrillation)
  - Orphan Drug designation granted for symptomatic oHCM in 2016

- **Second low-dose cohort in PIONEER-HCM ongoing**

- **Expected transition to Phase 2b/3 in 2018**

---

LVOT = Left ventricular outflow tract; oHCM = obstructive Hypertrophic Cardiomyopathy
NT-proBNP: N-terminal pro-brain natriuretic peptide

\(^{(1)}\) [https://clinicaltrials.gov/ct2/show/NCT02842242](https://clinicaltrials.gov/ct2/show/NCT02842242)
David Loew
Executive Vice President,
Sanofi Pasteur

SANOFI
Sustaining Leadership in Vaccines
Vaccines: An Attractive Business with Major Opportunities

- Long cycle times, no real patent cliff mostly due to manufacturing complexity
- Some significant diseases left to be tackled
- Life cycle activities can generate strong value
- Capacity and territory expansion on new vaccines
Vaccines R&D Strategy: Aim to Deliver High Value Products

Focus on high value markets / medical needs

- MenQuadTT
- Influenza
- RSV infants & elderly

Leverage key collaborations & in-licensing

- Flublok® / Protein Sciences
- RSV mAb / MedImmune
- RSV infant Vaccine / NIH

Pursue transformative technologies to remain in industry forefront

- Broadly Protective Flu
- Adjuvants
**Influenza**

Influenza segment supported by differentiation, ageing & urbanization

- Differentiation: Fluzone® High-Dose, Flublok®
- Vaccine Coverage Rate increase ex-U.S.

**Meningitis**

Meningitis segment to be driven by fully liquid formulation, broader age indication and geography

- MenQuadTT Phase 3 ongoing

**RSV**

Entering RSV segment with two complementary approaches

- Monoclonal antibody – Phase 2
- RSV vaccine – Phase 1
John Shiver
Senior Vice President,
Vaccines R&D

SANOFI
Sustaining Leadership in Vaccines
Burden of Influenza is Underestimated, Resulting in Suboptimal Vaccine Coverage Rates

Flu burden is greater than every other vaccine preventable disease

U.S. Annual costs of four major vaccine-preventable diseases in 50+

- Influenza: $16.0Bn (60%)
- Pneumococcal: $5.0Bn (19%)
- Herpes Zoster: $5.0Bn (19%)
- Pertussis: $0.4Bn (2%)

But too often considered as a mild illness

- Heart attack
- Stroke
- Pneumonia
- Aggravation of underlying chronic illnesses
- Diabetes, Asthma, COPD… Death

Sanofi Pasteur Focuses Where the Disease Burden Is the Highest

Cumulative Flu Related Hospitalization Rate\(^{(1)}\)

Rates per 100,000 population

Traditional influenza vaccine response declines with age

---

Protein Sciences Broadens Our Leading Flu Vaccines Portfolio With Flublok®(1)

Flublok® differentiated with greater efficacy in adults 50 years and older

Growth driven by product differentiation

Cumulative confirmed Flu cases(2,3)

Traditional QIV vaccines

Flublok® Influenza vaccine
FDA approved for 18 and older

-43%

65y old
Fluzone® HD TIV
Fluzone® HD QIV

50y old
Flublok®

6m old
Fluzone® TIV
Fluzone® QIV
VaxiGrip® TIV
VaxiGrip® QIV

Differentiate with better efficacy

Change standard of care

HD = High-Dose
(1) The Only FDA approved recombinant protein-based influenza vaccine approved for all adults 18 and older
(2) Source: Full prescribing information
Meningococcal Disease Has a Low Incidence Rate with High Fatality and Devastating Consequences

- Unpredictable and affects previously healthy individuals
- Difficult to diagnose early and rapidly progressive
- Potentially fatal, with devastating consequences in 20% of survivors

Impact and Incidence of Vaccine-Preventable Diseases

Vaccination essential

Source: J Travel Med 2005 Intl Soc of Travel Med
Sanofi Pasteur is the leader with 63% MS(1) in Quad ACWY Meninge Vaccines Market thanks to Menactra®

Global Meningococcal Market Sales in 2016(1/2)

- Men B: 30%
- Rest: 20%
- Approximately €1.9bn

Quadrivalent Conjugate

Meninge ACWY Conjugate Market Sales in 2016

- Sanofi Pasteur: 63%
- Pfizer: 29%
- GSK: 7%
- Others: 1%

Approximately €1bn

Only fully liquid presentation

GSK Menveo®: Lyophilized MenA + liquid Men CWY

Sources (1) 2016 Actual Sales Pfizer and GSK – based on company reported sales
Moving From Menactra® to MenQuadTT

Expected timeline

- **2017**
  - Infants Toddlers
  - Teens Adults
  - >55 years incl. elderly

- **2020**
  - 9m – 55y Menactra®
  - 9m – 55y Menactra®
  - 10y+ U.S., 10y+ International, 12m+ EU

- **2023+**
  - 6wks+ MenQuadTT
  - Fully liquid formulation

Tender Markets
MenQuadTT: Phase 3 Program in All Age Groups Ongoing

Potential First Submissions

- Q2 2019: 10y+ U.S. submission
- Q3 2019: 12m+ EU submission
- Q4 2019: 10y+ International submission
- Q1 2020: 10y+ International submission

Expected Benefits

- Unique fully liquid formulation vs. competition
- Broad age indication from infants\(^{(1)}\) to elderly
- Geographic expansion especially in Europe
- Co-administration possible with multiple routine pediatric vaccines
- Potential Quadrivalent backbone for Pentavalent Meningitis vaccine

\(^{(1)}\) 6 weeks
RSV: The Most Common Cause of LRTI in Infants Worldwide

<table>
<thead>
<tr>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circulates seasonally like influenza virus</td>
</tr>
<tr>
<td>Around 30 million children affected per year</td>
</tr>
<tr>
<td>Infants and young children most at risk</td>
</tr>
<tr>
<td>Primary infection tends to cause the most severe respiratory infections</td>
</tr>
<tr>
<td>No vaccine nor broadly effective antiviral drug or prophylactic drug available for all infants</td>
</tr>
</tbody>
</table>
2.1 million children require medical care annually in the U.S.\(^1\)

1.7 million GP visits in the U.S.\(^1\)

$1.15\text{ bn of annual medical cost}\(^1\)

400k visits in Emergency Room\(^2\)

\(0\) \(1\) \(2\) \(3\) \(4\) \(5\) \(6\) \(7\) \(8\) \(9\) \(10\) \(11\) \(12\) \(13\) \(14\) \(15\)

\(0\) \(50\) \(100\) \(150\) \(200\) \(250\) \(300\)

**RSV hospitalizations & outpatient visits (/1,000)**

- RSV outpatient visits per age (Hall, 2009)
- RSV hospitalizations per age (Stockman, 2012)

**Most hospitalizations occur during the infant’s first RSV season**

\(^1\) Regnier, Vaccine. 2013 Sep 13;31(40):4347-54.

RSV mAb\(^{(1)}\) Provides Best Approach for Young Infants

**Phase 1b/2a Results**

- Subjects were followed 1 year for safety
- Half-life (~70 days) supporting single dose administration for full RSV respiratory season
- Ph1b/2a data (including safety) supported advancing to Phase 2b

---

(1) Collaboration with Medimmune
Phase 1b/2a First-Time-in-Infant Study in Healthy Preterm Infants

**MEDI8897\(^{(1)}\) Serum Concentrations (µg/mL) (Mean ± SD)**

- **MEDI8897 50 mg IM**
- **MEDI8897 25 mg IM**
- **MEDI8897 10 mg IM**

**Graph Details:**
- LLOQ (<0.5 µg/mL)
- 6.8 µg/mL

**Timeline:**
- **Day -30 to Day 1**
  - N=1,000
  - MEDI8897: Single 50 mg IM dose
- **Day 30 to Day 1**
  - N=500
  - Placebo: Single IM dose

**Endpoints:**
- Monitor for LRTI endpoint
- Subject randomization (2:1) and dosing
- Post dose follow-up visits

\(^{(1)}\) Collaboration with Medimmune
RSV mAb(1) is a Unique Opportunity for All Infants Entering their First RSV Season

- Solid preliminary Phase 1b/2a Results
- First mAb to market for all infants
- Targeted population: Infants entering their first RSV season

- Phase 2b started in Q4 2016
  - Results expected in H2 2018
- FDA fast track designation granted in 2015

(1) Collaboration with Medimmune
### Phase 1 (Total: 15)

<table>
<thead>
<tr>
<th><strong>Code</strong></th>
<th><strong>Name</strong></th>
<th><strong>Disease</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>SAR440340(™)</td>
<td>Anti IL-23 mAb</td>
<td>Asthma</td>
</tr>
<tr>
<td>SARC39794</td>
<td>TLR4 agonist</td>
<td>Peanut Allergy</td>
</tr>
<tr>
<td>SAR408701</td>
<td>Maytansin-loaded anti-CEACAM5 mAb</td>
<td>Solid Tumors</td>
</tr>
<tr>
<td>SAR439459</td>
<td>anti-TGFβ mAb</td>
<td>Advanced Solid Tumors</td>
</tr>
<tr>
<td>REGN3767™</td>
<td>Anti LAG-3 mAb</td>
<td>Advanced Cancers</td>
</tr>
<tr>
<td>SAR439859</td>
<td>SERD</td>
<td>Metastatic Breast Cancer</td>
</tr>
<tr>
<td>ALN-TTRsc02(™)</td>
<td>sub-cutaneous siRNA inhibitor targeting TTR</td>
<td>Hereditary ATTR Amyloidosis</td>
</tr>
<tr>
<td>ALN-GO1(™)</td>
<td>investigational RNAi therapeutic</td>
<td>Primary Hyperoxaluria Type 1 (PH1)</td>
</tr>
</tbody>
</table>

### Phase 2 (Total: 15)

<table>
<thead>
<tr>
<th><strong>Code</strong></th>
<th><strong>Name</strong></th>
<th><strong>Disease</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>UshStat™</td>
<td>Myosin 7A gene therapy</td>
<td>Usher Syndrome 1B</td>
</tr>
<tr>
<td>SAR156597</td>
<td>IL-4R/IL-13 b-specific mAb</td>
<td>Systemic Sclerosis</td>
</tr>
<tr>
<td>GZ39988</td>
<td>TRKA antagonist</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>SAR428810</td>
<td>Anti protocollar AB mAb</td>
<td>Alzheimer’s Disease</td>
</tr>
<tr>
<td>SAR438335</td>
<td>GLP-1/GIP dual agonist</td>
<td>Type 2 Diabetes</td>
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<tr>
<td>SAR418011(™)</td>
<td>Myosin activation</td>
<td>Dilated Cardiomyopathy</td>
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<tr>
<td>SAR247799</td>
<td>STP1 agonist</td>
<td>Cardiovacular indication</td>
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<tr>
<td>SAR39375™(™)</td>
<td>miRNA-21</td>
<td>Alport Syndrome</td>
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<tr>
<td>SAR242549</td>
<td>ABCL4 gene therapy</td>
<td>Stargardt Disease</td>
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### Phase 3 (Total: 7)

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<tr>
<th><strong>Code</strong></th>
<th><strong>Name</strong></th>
<th><strong>Disease</strong></th>
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<tbody>
<tr>
<td>SAR425899</td>
<td>GLP-1/GCG dual agonist</td>
<td>Obesity/Overweight in T2D</td>
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<tr>
<td>MAVACAMER™(™)</td>
<td>Myosin inhibitor</td>
<td>Obstructive Hypertrophic Cardiomyopathy</td>
</tr>
<tr>
<td>SAR407899</td>
<td>rho kinase</td>
<td>Microvascular Angina</td>
</tr>
<tr>
<td>SAR439965</td>
<td>Maytansin-loaded anti-CA6 mAb</td>
<td>Triple Negative Breast Cancer</td>
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<tr>
<td>SAR66558</td>
<td>Acid Sphingomyelinase Deficiency(™)</td>
<td>Sphingomyelinase Deficiency</td>
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<tr>
<td>SP0232(™)</td>
<td>mAb(™)</td>
<td>Respiratory syncytial virus Monoclonal Antibody</td>
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### Registration

<table>
<thead>
<tr>
<th><strong>Code</strong></th>
<th><strong>Name</strong></th>
<th><strong>Disease</strong></th>
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<tbody>
<tr>
<td>REGN3767™</td>
<td>Anti LAG-3 mAb</td>
<td>Advanced Cancers</td>
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<tr>
<td>SAR41402</td>
<td>Rapid acting insulin</td>
<td>Type 1/2 Diabetes</td>
</tr>
<tr>
<td>efpeglenatide(™)</td>
<td>Long-acting GLP-1 agonist</td>
<td>Type 2 Diabetes</td>
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</table>

### Opt-in rights products for which rights have not been exercised yet

- **Immuno-inflammation**
  - Diabetes Solutions
  - Cardiovascular & metabolism
- **Oncology**
- **Rare Disease**
- **Infectious Diseases**
- **MS, Neuro, Gene therapy**
- **Vaccines**
## Additional Indications(*)

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<tr>
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<tr>
<td><strong>isatuximab + cemiplimab(1)(2)</strong></td>
<td><strong>dupilumab(3)</strong> Anti-IL4Rα mAb Eosinophilic Esophagitis</td>
<td><strong>sotagliflozin(4)</strong> Anti-IL4Rα mAb SGLT 1 &amp; 2 inhibitor – WHF in Diabetes</td>
<td><strong>isatuximab</strong> Anti-CD38 1st line Ti (IMROZI)</td>
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<tr>
<td><strong>isatuximab</strong> Anti-CD38 mAb + CyBord®</td>
<td><strong>sarilumab(3)</strong> Anti-IL6R mAb Polyarticular Juvenile Idiopathic Arthritis</td>
<td><strong>mavacamten(5)</strong> Anti-IL4Rα mAb Myosin inhibitor Non-Obstructive Hypertrophic Cardiomyopathy</td>
<td><strong>isatuximab</strong> Anti-CD38 Relapsing Refractory Multiple Myeloma (IKEMA)</td>
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<tr>
<td><strong>SAR439459 + cemiplimab(2)(6)</strong> Anti-TGFβ mAb + PD1 inhibitor mAb Advanced Solid Tumors</td>
<td><strong>sarilumab(3)</strong> Anti-IL6R mAb Systemic Juvenile Arthritis</td>
<td><strong>dupilumab(3)</strong> Anti-IL4Rα mAb Asthma 6-11 years old</td>
<td><strong>Aubagio® teriflunomide Relapsing Multiple Sclerosis - Pediatrics</strong></td>
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<tr>
<td><strong>SAR439859 SERD + Pabocilb Metastatic Breast Cancer</strong></td>
<td><strong>cemiplimab(6)</strong> PD-1 inhibitor mAb Advanced Basal Cell Carcinoma</td>
<td><strong>cimelumab(7)</strong> PD-1 inhibitor mAb Atopic Dermatitis 12 – 17 years old</td>
<td><strong>sotagliflozin</strong> Oral SGLT-1/2 inhibitor Type 2 Diabetes</td>
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<tr>
<td><strong>cemiplimab(7)(8)</strong> cimelumab® PD-1 inhibitor mAb + anti-LAG-3 mAb Advanced Cancers</td>
<td><strong>velaglumab(9)</strong> Oral GCS inhibitor Gaucher Disease Type 3</td>
<td><strong>Shan 6</strong> DTP-HepB-Polio-Hib Pediatric hexavalent vaccine</td>
<td><strong>Praluent®</strong> Anti-PCSK9 mAb CV events reduction</td>
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<tr>
<td><strong>velaglumab(9)</strong> Oral GCS inhibitor Fabry Disease</td>
<td><strong>Adacel+</strong> Tdap booster</td>
<td><strong>Dupixent (</strong>) Anti-IL4Rα mAb Atopic Dermatitis 6 – 11 years old</td>
<td><strong>Fluzone® QIV HD Quadrivalent inactivated Influenza vaccine - High dose</strong></td>
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<tr>
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<td></td>
<td><strong>Dupixent (</strong>) Anti-IL4Rα mAb Atopic Dermatitis 6 months - 5 years old</td>
<td><strong>Men Quad TT</strong> Advanced generation meningococcal ACTYW conjugate vaccine</td>
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<td><strong>cemiplimab(10)</strong> PD-1 inhibitor mAb 2nd line Cervical Cancer</td>
<td><strong>Pediatric pentavalent vaccine</strong> DTP-Polio-Hib Japan</td>
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<td><strong>cemiplimab(10)</strong> PD-1 inhibitor mAb 3rd line NSCLC</td>
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</tr>
</tbody>
</table>

(1) Also known as SAR439684 and REGN2810
(2) Cyclophosphamide + bortezomib (Velcade) + dexamethasone
(3) Regeneron product for which Sanofi has opt-in right
(4) Also known as SAR439152 and as MYK-461
(5) Data related to all studies published in clinicaltrials.gov

(*) Partnered and/or in collaboration - Sanofi may have limited or shared rights on some of these products.

**Registration Study**
Opt-in rights products for which rights have not been exercised yet

- Diabetes Solutions
- Immuno-inflammation
- Cardiovascular & metabolism
- Oncology
- Rare Disease
- Infectious Diseases
- MS, Neuro, Gene therapy
- Vaccines
## Expected Submission Timeline (1)

### Immunology
- **2017**
  - Dupilumab (2, 7)
  - Proluent (5, 7)
- **2018**
  - Dupilumab (2, 7)
  - Dupixent (4, 7)
  - Praluent (5, 7)
  - Cemiplimab (4, 7)
- **2019**
  - Dupilumab (2, 7)
  - Dupixent (4, 7)
  - Cemiplimab (4, 7)
- **2020**
  - Dupilumab (2, 7)
  - Dupixent (4, 7)
  - Cemiplimab (4, 7)
- **2021 and beyond**
  - Isatuximab (3)
  - Venglustat (3)
  - Sarilumab (3)
  - Dupilumab (2, 7)

### Oncology
- **2019**
  - Sarilumab (3)
  - Cemiplimab (4, 7)
- **2020**
  - Sarilumab (3)
  - Cemiplimab (4, 7)
- **2021 and beyond**
  - Venglustat (3)
  - Sarilumab (3)
  - Dupilumab (2, 7)

### Rare Disease
- **2020**
  - Cemiplimab (4, 7)
  - Sarilumab (3)

### Cardiovascular & Metabolism
- **2018**
  - Dupilumab (2, 7)
  - Cemiplimab (4, 7)
- **2021 and beyond**
  - Sarilumab (3)

### Infectious Diseases
- **2017**
  - VaxiGrip® QIV IM
- **2018**
  - Dupilumab (2, 7)
  - Cemiplimab (4, 7)
  - Sarilumab (3)
- **2019**
  - Dupilumab (2, 7)
  - Cemiplimab (4, 7)
  - Sarilumab (3)
- **2020**
  - Dupilumab (2, 7)
  - Cemiplimab (4, 7)
- **2021 and beyond**
  - Venglustat (3)

### Vaccines
- **2017**
  - VaxiGrip® QIV IM
- **2021 and beyond**
  - Venglustat (3)

---

(1) Excluding Phase I - Data related to all studies published in clinicaltrials.gov
(2) Also known as SAR43884 and RG62008
(3) Also known as SAR43564 and REGN2810
(4) Also known as SAR43564 and REGN2810
(5) Submission strategy for the US under evaluation.
(6) Currently on clinical hold pending outcome of FDA discussion – Expected to resume around year-end
(7) Also known as SAR43564 and REGN2810
(8) Also known as SAR43564 and REGN2810
(9) Also known as SAR43564 and REGN2810
(10) Discussion about development plan is ongoing with Health Authorities
(11) Also known as SAR43564 and REGN2810
(12) Also known as SAR43564 and REGN2810
(13) Filled jointly and/or in collaboration – Sanofi may have limited or shared rights on some of these products
## Pipeline Movements Since Q3 2017

### Additions to the pipeline

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### Removals from the pipeline

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<td>IL4/IL13 bi-specific mAb</td>
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### R&D Pipeline Summary – Total Projects

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Includes 4 Phase I products and 1 Phase 2 product for which Sanofi has Opt-in rights but has not yet exercised these rights.
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<td>Dose-Limiting Toxicity</td>
</tr>
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<td>Duration Of Disease</td>
</tr>
<tr>
<td>DOR</td>
<td>Duration Of Response</td>
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<td>Incidence of Adverse Events</td>
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<tr>
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<td>Infusion Associated Reaction</td>
</tr>
<tr>
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### Dupilumab (anti-IL4Rα mAb) Asthma 1/3

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| LIBERTY        | Phase 2/3 Open label extension study long-term safety & tolerability evaluation in patients with asthma who participated in previous studies | 2,287    | • For patients coming from DRI12544, PDY14192, EFC13579, EFC13691 studies: dupilumab loading dose sc on Day 1, followed by 1x dose Q2W added to current controller medications  
• Open-label, max. 3 weeks screening and 108 weeks Tx                                                                                                     | • Primary: N and % of patients experiencing any TEAE  
• Secondary: Safety                                                                                                                                       | SSD: Jul. 2014  
DE: 2019                                          |
| ASTHMA TRAVERSE|                                                                               |          |                                                                                                                                                                                                                                                                     |                                                                           |                      |
| LTS12551       |                                                                               |          |                                                                                                                                                                                                                                                                     |                                                                           |                      |
| NCT02134028    |                                                                               |          |                                                                                                                                                                                                                                                                     |                                                                           |                      |
## Dupilumab (anti-IL4Rα mAb)
### Asthma 2/3

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<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
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</table>
| EXPEDITION ASTHMA   | Phase 2a Evaluation of dupilumab's effects on airway inflammation in patients with asthma | 42       | • Randomized, double-blind, parallel, placebo-controlled Study, 5 to 6 weeks screening, 12 weeks Tx, 12 weeks post Tx | • Primary: Change from baseline in N of inflammatory cells and in mucin-stained area in the bronchial submucosa per mm²  
• Secondary: Safety, Tolerability, Immunogenicity of dupilumab compared to placebo | • SSD: Jan. 2016  
• DE: 2018 |
| PDY14192 NCT02573233 |                                                                              |          |                                                                       |                                                                           |                             |
## Dupilumab (anti-IL4Rα mAb)
### Asthma 3/3

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<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
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| CHILDREN ASTHMA VOYAGE | Evaluation of dupilumab in children (6 to <12 years) with uncontrolled asthma | 294 | • In children 6 to <12 years of age with uncontrolled persistent asthma  
• Randomized, Double-blind, Placebo-controlled, parallel group 52 weeks Tx, 12 weeks post Tx | • Primary: Annualized rate of severe exacerbation events during Tx period  
• Secondary: Safety and tolerability, PROs, Systemic exposure and incidence of anti-drug antibodies, Association between dupilumab Tx and pediatric immune responses to vaccines | SSD: Jun. 2017  
DE: 2021 |

| | | | | | |
| | | | | | |
## Dupilumab (anti-IL4Rα mAb)
### Atopic Dermatitis (AD)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
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<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OLE Pediatrics AD</strong>&lt;br&gt;R668-AD-Reg 1434&lt;br&gt;NCT02612454</td>
<td>Phase 3&lt;br&gt;A study to assess the long-term safety of dupilumab administered in patients 6 to &lt;18 years of age with AD</td>
<td>765 expected</td>
<td>• For patients having participated in a prior dupilumab study in pediatrics with AD&lt;br&gt;• Non-Randomized, Parallel Assignment, Open label extension study</td>
<td>• Primary: Incidence and rate of TEAEs&lt;br&gt;• Secondary: SAEs and AEs of special interest, % of patients who achieve and maintain remission, EASI-75: % of patients achieving and maintaining at least 75% reduction in EASI score over time, EASI-50: % of patients achieving and maintaining at least 50% reduction in EASI scores over time</td>
<td>• SSD: Oct. 2015&lt;br&gt;• DE: 2018</td>
</tr>
<tr>
<td><strong>Pediatrics (12 to 17 years) AD</strong>&lt;br&gt;R668-AD-Reg 1526&lt;br&gt;NCT03054428</td>
<td>Phase 3&lt;br&gt;A study to investigate the efficacy and safety of dupilumab monotherapy in patients 12 to 17 years of age, with moderate-to-severe AD</td>
<td>240</td>
<td>• Pediatric patients (12 to 17 years old) with moderate-to-severe AD&lt;br&gt;• A randomized, double-blind, placebo-controlled, 3-arm: dupilumab dose 1, dupilumab dose 2, placebo</td>
<td>• Primary: % of patients with IGA 0 to 1 (on a 5-point scale), % of patients with EASI-75&lt;br&gt;• Secondary: % change in EASI score</td>
<td>• SSD: Apr. 2017&lt;br&gt;• DE: 2018</td>
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</table>
**Dupilumab (anti-IL4Rα mAb)**  
**Atopic Dermatitis (AD)**

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</thead>
</table>
| LIBERTY AD PRESCHOOL  
NTC03346434 | Phase 2/3  
Safety, Pharmacokinetics and Efficacy of Dupilumab in Patients ≥6 Months to <6 Years With Severe Atopic Dermatitis | 280 | • Part A: Open-label, single-ascending dose, sequential cohort phase 2 study  
• Part B: Randomized, double-blind, parallel-group, placebo-controlled phase 3 study | • Primary: PK, TEAEs, SAEs  
• Secondary: SEAs, TEAEs, % chanhe in EASI score, Change in children’s Dermatology Quality of Life Index | • SSD: Dec. 2017  
• DE: 2022 |
| AD in 6 - 11 Years Old  
NCT03345914 | Phase 3  
Efficacy and safety of Dupilumab administered with Topical Corticosteroids in participants ≥6 to <12 years with Severe Atopic Dermatitis | 240 | • Randomized, Double-blind, Placebo-controlled Study | • Primary: Proportion of patients with Investigator's Global Assessment "0" or "1" (on a 5-point scale) at week 16  
• Secondary: Change from baseline to week 16 in Children's Dermatology Life Quality Index, Percent change in EASI score from baseline to week 16, Incidence of serious TEAEs through week 16 | • SSD: Dec. 2017  
• DE: 2019 |
# Dupilumab (anti-IL4Rα mAb)
## Nasal Polyposis (NP)

<table>
<thead>
<tr>
<th>Study</th>
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<th>Patients</th>
<th>Design</th>
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</thead>
</table>
| NP SINUS-24 | Phase 3 Evaluation of dupilumab in patients with bilateral NP on a background of mometasone furoate nasal spray | 276 finally included | ● Patients with bilateral sinonasal polyposis that despite prior Tx with systemic corticosteroids have an endoscopic bilateral NPS with a score at least of 5 over 8  
● Randomized, double-blind, placebo-controlled study, 4 weeks run-in, 24 weeks Tx, 24 weeks post-Tx |
| EFC14146    |                                                                             |          | ● Primary: NC symptom severity score based on the patient daily morning assessment & by endoscopy, Sinus opacifications as assessed by CT  
● Secondary: TSS, Loss of smell, Sinus opacification |
| NCT02912468 |                                                                             |          | • SSD: Dec. 2016  
• DE: 2018 |
| LIBERTY     | Phase 3 Evaluation of dupilumab in patients with bilateral NP on a background of mometasone furoate nasal spray | 448 finally included | ● Patients with bilateral sinonasal polyposis that despite prior Tx with systemic corticosteroids have an endoscopic bilateral NPS with a score at least of 5 over 8  
● Randomized, double-blind, placebo-controlled study, 4 weeks run-in, 52 weeks Tx, 12 weeks post-Tx, 3-arm, dupilumab dose regimen 1, dupilumab dose regimen 2, placebo |
| NP SINUS-52 |                                                                             |          | ● Primary: NC symptom severity score based on the patient daily morning assessment & by endoscopy, Sinus opacifications as assessed by CT  
● Secondary: TSS, Loss of smell, Sinus opacification |
| EFC14280    |                                                                             |          | • SSD: Dec. 2016  
• DE: 2018 |
### Sarilumab (anti-IL6 mAb)
#### Rheumatoid Arthritis (RA)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
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<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARIL-RA-EXTEND</td>
<td>Long-term evaluation of sarilumab in RA patients</td>
<td>2000</td>
<td>• In patients with RA having participated to previous trials</td>
<td>• Primary: N of patients with AE</td>
<td>SSD: Jun. 2010</td>
</tr>
<tr>
<td>LTS11210</td>
<td></td>
<td></td>
<td>• Multi-center, uncontrolled extension, open-label; up to 1 week screening, at least 264 weeks of Tx to 516 weeks max., 6 weeks post-Tx</td>
<td>• Secondary: Long term efficacy of sarilumab in patients with RA (ACR20, DAS28, EULAR response)</td>
<td>DE: 2020</td>
</tr>
<tr>
<td>NCT01146652</td>
<td></td>
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</tbody>
</table>
## Sarilumab (anti-IL6 mAb) Juvenile Idiopathic Arthritis (JIA)

<table>
<thead>
<tr>
<th>Study</th>
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<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| Polyarticular JIA Children & Adolescents | Dose-finding study of sarilumab in children and adolescents with Polyarticular-course Juvenile Idiopathic Arthritis (pcJIA) | 36       | • In children and adolescents, Aged 2 to 17 years, with pcJIA  
• Open-label, sequential, ascending, repeated dose-finding Study; 4-week screening, 12-week core Tx, 92-week extension, 6-week post-Tx | • Primary: PK parameters (Up to week 12)  
| Systemic JIA Children & Adolescents | Dose-finding study of sarilumab in children and adolescents with Systemic Juvenile Idiopathic Arthritis (sJIA) | 36       | • In children and adolescents, aged 1 to 17 years, with sJIA  
• Open-label, sequential, ascending, repeated dose finding study, 4-week screening, 12-week Tx, 92-week extension, 6-week post-Tx | • Primary: PK parameters (Up to week 12)  
# SAR156597 (anti-IL13/IL4 mAb)  
**Scleroderma**

<table>
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<tr>
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</tr>
</thead>
</table>
| POC in Scleroderma  
ACT14604  
NCT02921971 | Phase 2a  
Efficacy and safety of SAR156597 in the Tx of Diffuse Cutaneous Systemic Sclerosis (dcSSc) | 94 | • Randomized, double-blind, Parallel Assignment, placebo-controlled, 4-week screening, 24-week Tx period, 11-week follow-up | • Primary: Change from baseline in mRSS  
• Secondary: Change from baseline in Health Assessment Questionnaire Disability Index (HAQ-DI), assessed with SHAQ. Change from baseline in respiratory function as measured by observed Forced Vital Capacity Change from baseline in observed Carbon Monoxide Diffusing Lung Capacity (DLco [corrected for hemoglobin]) | • SSD: Dec. 2016  
• DE (1st part) (1): 2018 |
### SAR440340 (Anti-IL33 mAb)

#### Asthma

<table>
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<tr>
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</tr>
</thead>
</table>
| Asthma | Phase 1 Assess the safety and tolerability of multiple ascending subcutaneous doses of REGN3500 in adult patients with Moderate Asthma | 24       | • Randomized, double-blind, Placebo-controlled, Multiple ascending dose study of the safety | • Primary: Incidence of TEAEs after repeat subcutaneous administration, severity of TEAEs  
• Secondary: Concentration-time profile of REGN3500 after repeat subcutaneous administration, Immunogenicity, % change in total from baseline forced expiratory volume | • SSD: Jan. 2017  
• DE: Nov. 2018 |

**NCT02999711**
# Isatuximab (anti-CD38 mAb)

## Hematological Malignancies (HM)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
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<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| CD38+HM     | Phase 1/2 Dose escalation and efficacy study of isatuximab in patients with selected CD38+ HM | 346      | • Phase 1: MTD  
• Phase 2: Stage 1: isatuximab activity at different doses/schedules and to select dose and regimen as single agent or in combination with dexamethasone  
Stage 2: activity at the selected dose/schedule from stage 1, as single agent (ISA arm) and in combination with dexamethasone (ISAdex arm)  
• Randomized, Open-label, Parallel assignment | • Primary: DLT, ORR  
• Secondary: DOR, PFS, OS, Immune Response | SSD: Jun. 2010  
DE: 2019 |
| TED10893    | NCT01084252                                                                 |          |                                                                                                                                       |                                                                           |                             |

| Oncology    |                               |          |                                                                           |                                                                           |                             |
| Cardiovascular |                             |          |                                                                           |                                                                           |                             |
| Rare Diseases |                             |          |                                                                           |                                                                           |                             |
| Infectious disease |                        |          |                                                                           |                                                                           |                             |
| MS, Neuro, Gene therapy |                      |          |                                                                           |                                                                           |                             |
| Vaccines     |                               |          |                                                                           |                                                                           |                             |
# Isatuximab (anti-CD38 mAb) Multiple Myeloma (MM)

<table>
<thead>
<tr>
<th>Study</th>
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</tr>
</thead>
</table>
| Lenalidomide Combination RRMM | Phase 1b Isatuximab, in Combination With lenalidomide and dexamethasone for the Tx of Relapsed or Refractory MM | 60 | • Patients with diagnosis of MM and documentation of at least 2 prior therapies (induction therapy, autologous stem cell transplant, consolidation and maintenance therapy is considered one prior therapy)  
• Open-label, Parallel assignment  
• Isatuximab (escalating doses) + lenalidomide + dexamethasone  
• Total duration for one patient: up to 21 days screening, at least 4 weeks Tx, up to 60 days follow-up | • Primary: N of patients with AE  
DE: 2019 |

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<thead>
<tr>
<th>TCD11833 NCT01749969</th>
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</thead>
</table>

**Notes:**
- SSD: Study Start Date
- DE: Date of Enrollment
**Isatuximab (anti-CD38 mAb) Multiple Myeloma (MM)**

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<tr>
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</thead>
</table>
| Pomalidomide Combination RRMM | Phase 1b Isatuximab, in combination with pomalidomide and dexamethasone for the Tx of Relapsed/Refractory MM | 45 | • Patients previously diagnosed with MM based on standard criteria and currently require Tx because MM has relapsed following a response  
• Open-label, Parallel assignment  
• Isatuximab (escalating doses) + pomalidomide + dexamethasone  
• Total duration for one patient: up to 21 days screening, Tx period up to disease progression or AEs, 60-day follow-up | • Primary: DLTs, N of patients with AE  
• Secondary: ORR, PK, Immunogenicity, DOR, CB | • SSD: May 2015  
• DE: 2018 |
# Isatuximab (anti-CD38 mAb) Multiple Myeloma (MM)

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</tr>
</thead>
</table>
| **Bortezomib Combination RRMM**  
TCD13983  
NCT02513186 | Phase 1  
Isatuximab in combination with bortezomib - based regimens in adult patients with newly diagnosed MM non eligible for transplantation | 44 | • Patients with a diagnosis of MM with evidence of measurable disease, having received prior Tx with an IMiD and with at least 3 prior lines of therapy  
• Open-label, Single Group assignment  
• Isatuximab (escalating dose) + bortezomib + cyclophosphamide + dexamethasone: VCDI cohort (3-week screening, 50-week duration for induction and then up to disease progression, or unacceptable AEs + follow-up)  
• Isatuximab + bortezomib + dexamethasone + lenalidomide: VRDI cohort to begin after VCDI completion (4-week screening, 24-week duration for induction and then up to disease progression, or unacceptable AEs, + follow-up) | • Primary: DLTs/VCDI  
For both VCDI & VRDI: ORR, CR  
• Secondary: N of patients with AE, and significant changes in lab tests, PK, DOR | • SSD: Sep. 2015  
• DE: 2024 |
<table>
<thead>
<tr>
<th>Study</th>
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<th>Design</th>
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</tr>
</thead>
</table>
| RRMM          | Phase 1 Safety, PK and Efficacy of isatuximab in patients with Relapsed/Refractory MM | 64       | - Patients with a diagnosis of MM with evidence of measurable disease and with evidence of disease progression  
- Open-label, Single Group assignment, isatuximab (escalating doses)  
- Total duration for one patient: up to 21 days screening, Tx period up to disease progression or AEs , 60- day follow-up at least | - Primary: Part A: DLTs, N of patients with AE; Part B: ORR  
- Secondary: PK, N of patients with AEs, DOR, CB, PFS, Immunogenicity | SSD: Sep. 2015  
DE: 2019          |
# Isatuximab (anti-CD38 mAb) Multiple Myeloma (MM)

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<tr>
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<th>Patients</th>
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<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISLANDS (Japanese Patients) RRMM</td>
<td>Phase 1 Phase 2</td>
<td>42</td>
<td>Patients with a diagnosis of symptomatic MM, having received at least 3 prior lines of therapy OR whose disease is double refractory to an IMiD and a PI • Open-label, Single Group assignment, isatuximab monotherapy • Total duration for one patient: up to 21-day screening, Tx period up to disease progression or unacceptable AEs, post-Tx follow-up</td>
<td>Primary: Phase 1: DLTs Phase 2: ORR Secondary: N of patients with AE, CB, OS, PFS, DOR, TTR, PK, PD, Immunogenicity</td>
<td>SSD: Sep. 2016 DE: 2018</td>
</tr>
<tr>
<td>TED14095 NCT02812706</td>
<td>Isatuximab single-agent in Japanese patients with Relapsed and Refractory MM</td>
<td></td>
<td></td>
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</tbody>
</table>

**Endpoints**
- **Primary**: Phase 1: DLTs Phase 2: ORR
- **Secondary**: N of patients with AE, CB, OS, PFS, DOR, TTR, PK, PD, Immunogenicity

**Status**
- DE: 2018
# Isatuximab (anti-CD38 mAb) Multiple Myeloma (MM)

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<tr>
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</thead>
<tbody>
<tr>
<td>Cemiplimab Combination RRMM</td>
<td>Phase 1 Phase 2 Safety, PK and Efficacy of isatuximab in combination with cemiplimab in patients with Relapsed/Refractory MM</td>
<td>54</td>
<td>• Patients with a diagnosis MM with evidence of measurable disease, having received prior Tx with an IMiD and with at least 3 prior lines of therapy • Open-label, Single Group assignment • Isatuximab + cemiplimab • Total duration for one patient: up to 21-day screening, Tx period up to disease progression or unacceptable AEs, 3-month post-Tx follow-up</td>
<td>• Primary: DLTs, N of patients with AE, ORR • Secondary: CB, DOR, TTR, PFS, OS, PK, Immunogenicity (isatuximab and cemiplimab)</td>
<td>• Not yet recruiting</td>
</tr>
</tbody>
</table>
# Isatuximab (anti-CD38 mAb)
## Multiple Myeloma (MM)

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</thead>
<tbody>
<tr>
<td>ICARIA-MM RRMM</td>
<td>Phase 3&lt;br&gt;Isatuximab, pomalidomide, and dexamethasone to pomalidomide and dexamethasone in Refractory or Relapsed and RRMM</td>
<td>300</td>
<td>• Isatuximab in combination with pomalidomide and low-dose dexamethasone, compared to pomalidomide and low-dose dexamethasone in patients with RRMM&lt;br&gt;• Randomized, Open-label, Parallel assignment</td>
<td>• Primary: PFS&lt;br&gt;• Secondary: ORR, OS, TTP, PFS, DOR</td>
<td>• SSD: Jan. 2017&lt;br&gt;• DE (1st Part): 2018</td>
</tr>
<tr>
<td>EFC14335 NCT02990338</td>
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(1) Final Data Collection date for primary outcome measure
# Isatuximab (anti-CD38 mAb) Multiple Myeloma (MM)

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</thead>
</table>
| IKEMA RRMM EFC15246 NCT03275285 | Phase 3 Isatuximab combined with carfilzomib and dexamethasone vs. carfilzomib with dexamethasone in patients With Relapse and/or Refractory MM previously treated with 1 to 3 prior lines | 300 | - Patients with MM previously treated with prior 1 to 3 lines and with measurable serum M-protein (≥ 0.5 g/dL) and/or urine M-protein (≥ 200 mg/24 hours)  
- Randomized, Open-label, Parallel assignment, 2-arm: (a) isatuximab +carfilzomib+dexamethasone, (b) carfilzomib+dexamethasone | - Primary: PFS  
DE (1st Part): 2020 |

(1) Final Data Collection date for primary outcome measure
## Isatuximab (anti-CD38 mAb) Multiple Myeloma (MM)

### Study Description

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<th>Status</th>
</tr>
</thead>
</table>
| IMROZ NDMM     | Isatuximab in combination with bortezomib (Velcade®), lenalidomide (Revlimid®) and dexamethasone vs. bortezomib, lenalidomide and dexamethasone in patients with newly diagnosed MM not eligible for transplant | 440      |        | • Primary: PFS  
• Secondary: ORR, % of patients with CR, and VGPR, OS, TTP, DOR, PFS on next line of therapy (PFS2), AE, PK, Immunogenicity, QOL | SSD: 2017  
DE (1st Part): 2022 |
| EFC12522 NCT03319667 |                                                                 |          |        | • Newly diagnosed MM not eligible for transplant due to age (≥ 65 years) or patients < 65 years with comorbidities impacting possibility of transplant or patient's refusal of transplant  
• Randomized, Open-label, Parallel assignment  
• IVRd arm (Isatuximab/bortezomib/lenalidomide/dexamethasone)  
• VRd arm (Bortezomib/lenalidomide/dexamethasone)  
• Ird crossover arm (Isatuximab/lenalidomide/dexamethasone)  
• Total duration for each patient: screening period up to 4 weeks, induction period of 24 weeks, continuous Tx period and crossover when applicable |          |        | | |

(1) Final Data Collection date for primary outcome measure
# Cemiplimab (PD-1 inhibitor)
## Advanced Malignancies (AM)

<table>
<thead>
<tr>
<th>Study</th>
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<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| AM    | Phase 1     | 1,167    | • Non-Randomized, Open-label, Parallel assignment, ascending-dose  
• Monotherapy, cemiplimab alone  
• Dual combination: cemiplimab in combination with hypofractionated radiotherapy or with cyclophosphamide or with docetaxel  
• Triple combination: cemiplimab with hypofractionated radiotherapy plus cyclophosphamide, or hypofractionated radiotherapy plus GM-CSF or carboplatin plus paclitaxel or carboplatin plus pemetrexed or carboplatin plus docetaxel  
• Quadruple combination: cemiplimab with hypofractionated radiotherapy plus GM-CSF plus cyclophosphamide | • Primary: TEAE, Incidence of abnormal laboratory findings, N of participants with DLT  
• Secondary, RECIST as measured by CT or MRI, Immune-Related Response | • SSD: Jan. 2015  
• DE: 2020 |
| R2810-ONC-1423 NCT02383212 | A first-in-human study of repeat dosing with cemiplimab, as single therapy and in combination with other Anti-Cancer therapies in patients with AM |
# Cemiplimab (PD-1 inhibitor) Advanced Malignancies (AM)

<table>
<thead>
<tr>
<th>Study</th>
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<th>Patients</th>
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<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>PK in Japanese patients AM</td>
<td>Phase 1 To investigate the safety and PKs of cemiplimab in Japanese patients with AM</td>
<td>6</td>
<td>• Histologically or cytologically confirmed diagnosis of malignancy with no alternative standard-of-care therapeutic option • Single Group assignment, Open-label</td>
<td>• Primary: TEAEs cemiplimab PK parameters • Secondary: Immunogenicity against cemiplimab</td>
<td>SSD: Sep. 2017 • DE: 2019</td>
</tr>
<tr>
<td>R2810-ONC-1622 NCT03233139</td>
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**Study**

<table>
<thead>
<tr>
<th>Immuno-inflammation</th>
<th>Diabetes</th>
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</thead>
<tbody>
<tr>
<td>Oncology</td>
<td>Cardiovascular</td>
</tr>
<tr>
<td>Rare Diseases</td>
<td>Infectious disease</td>
</tr>
<tr>
<td>MS, Neuro, Gene therapy</td>
<td>Vaccines</td>
</tr>
</tbody>
</table>
# Cemiplimab (PD-1 inhibitor) Melanoma

<table>
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<tr>
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</tr>
</thead>
</table>
| Biomarkers Melanoma        | Phase 1 Exploratory Tumor Biopsy-driven study to understand the relationship between biomarkers and clinical response in Melanoma patients receiving cemiplimab | 30       | • For Histologically confirmed diagnosis of stage III (unresectable) or stage IV melanoma with at least 1 lesion that is measurable by RECIST 1.1 criteria and accessible for biopsies        | • Primary: Correlation between changes in the tumor microenvironment and the change in tumor volume following cemiplimab Tx  
   • Secondary: Correlation between baseline tumor characteristics and the change in tumor volume following Tx, cemiplimab serum concentrations, antibodies levels, PFS, ORR | SSD: Apr. 2017, DE (1st Part) (2018) |

(1) Final Data Collection date for primary outcome measure
Cemiplimab (PD-1 inhibitor)  
Cutaneous Squamous Cell Carcinoma (CSCC)

<table>
<thead>
<tr>
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<th>Endpoints</th>
<th>Status</th>
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</thead>
<tbody>
<tr>
<td>Advanced CSCC</td>
<td>Phase 2 Cemiplimab monotherapy for patients with metastatic (nodal or distant) CSCC (Groups 1 and 3) or with unresectable locally advanced CSCC (Group 2)</td>
<td>150</td>
<td>• Non-Randomized, Open-label, Parallel assignment</td>
<td>• Primary: ORR (96 weeks), Groups 1 and 3: RECIST version 1.1 will be used to determine ORR, Group 2: Clinical response criteria will be used to determine ORR</td>
<td>• SSD: May 2016</td>
</tr>
<tr>
<td>R2810-ONC-1540</td>
<td></td>
<td></td>
<td>• Group 1: Patients with metastatic CSCC: to distant sites or lymph nodes cemiplimab administered intravenously every 2 weeks</td>
<td>• Secondary: Investigator Assessments of ORR, DOR, DOD, PFS, OS, CRR</td>
<td>• DE: 2019</td>
</tr>
<tr>
<td>NCT02760498</td>
<td></td>
<td></td>
<td>• Group 2: Patients with unresectable locally advanced CSCC. cemiplimab administered intravenously every 2 weeks</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>• Group 3: Patients with metastatic CSCC: to distant sites or lymph nodes, cemiplimab administered intravenously every 3 weeks</td>
<td></td>
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</tr>
</tbody>
</table>
# Cemiplimab (PD-1 inhibitor)
## Basal Cell Carcinoma (BCC)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCC</td>
<td>Phase 2&lt;br&gt; Cemiplimab in patients with Advanced BCC who experienced progression of disease on Hedgehog Pathway Inhibitor Therapy, or were intolerant of Prior Hedgehog Pathway Inhibitor Therapy</td>
<td>147</td>
<td>• Patients with confirmed diagnosis of invasive BCC&lt;br&gt; • Non-Randomized, Open-label, Parallel assignment&lt;br&gt; • Group 1: Patients with metastatic BCC&lt;br&gt; • Group 2: Patients with unresectable locally advanced BCC</td>
<td>• Primary: ORR for mBCC measured by RECIST version 1.1 ORR for unresectable locally advanced BCC measured by Composite Response Criteria&lt;br&gt; • Secondary: DOR, CR, PFS, OS</td>
<td>• SSD: July 2017&lt;br&gt; • DE (1st Part) (1): 2018</td>
</tr>
<tr>
<td>R2810-ONC-1620</td>
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<tr>
<td>NCT03132636</td>
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</tbody>
</table>
## Cemiplimab (PD-1 inhibitor)
### Non-Small Cell Lung Cancer (NSCLC)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| mNSCLC | Phase 3 First-line Tx in patients with advanced or metastatic NSCLC whose tumors express PD-L1, vs. Platinum Based Chemotherapy | 300 | • For histologically or cytologically documented squamous or non squamous NSCLC with stage IIIB or stage IV disease who received no prior systemic Tx for recurrent or metastatic NSCLC  
• Randomized, Open-label, Cross-over assignment  
• Active Comparator: Standard-of-care chemotherapy: paclitaxel + cisplatin OR paclitaxel + carboplatin OR gemcitabine + cisplatin or gemcitabine + carboplatin OR Pemetrexed + cisplatin followed by optional pemetrexed maintenance OR pemetrexed + carboplatin followed by optional pemetrexed maintenance | • Primary: PFS as assessed by a blinded Independent review committee using RECIST 1.1  
• Secondary: OS, Objective response rates, BOR, DOR | • SSD: May 2017  
• DE: 2021 |
## Cemiplimab (PD-1 inhibitor)
### Cervical cancer (CC)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC</td>
<td>Phase 3 Cemiplimab vs. therapy of IC chemotherapy in Recurrent or Metastatic Platinum-Refractory CC</td>
<td>800</td>
<td>• Patients with recurrent or metastatic platinum-refractory CC treated with either REGN2810 or IC chemotherapy • Randomized, Open-label, Parallel assignment, Tx cycle 6 weeks, Planned Tx for up to 96 weeks</td>
<td>• Primary: OS • Secondary: PFS, ORR, DOR, QOL</td>
<td>• SSD: Oct. 2017 • DE (1st Part): 2020</td>
</tr>
</tbody>
</table>

(1) Final Data Collection date for primary outcome measure
SAR566658 (maytansin loaded anti-CA6 mAb)
Triple Negative Breast Cancer (TNBC)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>mTNBC</td>
<td>Phase 2b Efficacy and safety of SAR566658 Tx in patients with CA6 Positive Metastatic TNBC</td>
<td>62</td>
<td>• Patients with Measurable Metastatic TNBC, with CA6-positive disease  • Randomized, Open-label, Parallel assignment; Tx cycle 3 weeks  • Part 1: SAR566658 will be given as Dose 1 (cohort 1) and Dose 2 (cohort 2) at Day 1 and Day 8 every 3 weeks intravenously (dose selection)  • Part 2: SAR566658 will be given as Dose 1 or Dose 2 (depending on dose level selected from part 1) at Day 1 and Day 8 every 3 weeks intravenously (efficacy of the selected dose)</td>
<td>• Primary: ORR  • Secondary: DCR, DOR, PFS, TTP, Impact of ocular primary prophylaxis on the incidence of keratopathies, Potential immunogenicity of SAR566658</td>
<td>• SSD: Mar. 2017  • DE: 2019</td>
</tr>
</tbody>
</table>

ACT14884 NCT02984683

- **Status**: SSD: Mar. 2017  DE: 2019
# SAR439459 (TGFβ inhibitor mAb)
## Advanced Solid Tumors (AST)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| AST Monotherapy and combination with cemiplimab | Phase 1/1b PK, PD and Anti-tumor activity of SAR439459 Monotherapy and in combination with cemiplimab in adult patients with AST | 130 expected | • Patients with histologically confirmed, advanced unresectable or metastatic solid tumor  
• Randomized, Open-label, Parallel assignment  
• Part 1A: SAR439459 monotherapy escalating doses/14-day cycle  
• Part 2A: SAR439459 monotherapy/14-day cycle with the previously recommended dose  
• Part 1B: SAR439459 escalating dose + cemiplimab standard dose /14-day cycle  
• Part 2B: SAR439459 at previously recommended dose + cemiplimab standard dose / 14-day  
• Escalation periods non randomized followed par expansion periods randomized | • Primary: DLTs (Part 1), ORR (Part 2)  
• Secondary: Safety, Immunogenicity, PFS, TTP, PK | SSD: Jun. 2017  
DE: 2020 |

TCD14678 NCT03192345
## SAR408701 (maytansin loaded anti-CEACAM5 mAb)
### Advanced Solid Tumors (AST) 1/2

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-in-Human</td>
<td>Phase 1</td>
<td>152</td>
<td>• Patients with locally advanced or metastatic solid malignant tumor</td>
<td>• Primary: MTD, Anti-tumor response RECIST</td>
<td>SSD: Sep. 2014</td>
</tr>
<tr>
<td></td>
<td>Phase 2</td>
<td></td>
<td>• Non-Randomized, Open-label, Parallel assignment</td>
<td>• Secondary: Safety, Immunogenicity, PK</td>
<td>DE: 2019</td>
</tr>
<tr>
<td></td>
<td>PK and antitumor activity of SAR408701 in patients with AST</td>
<td></td>
<td>• Arm 1: SAR408701 monotherapy escalating cohorts</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Arm 2: SAR408701 expansion cohort in CRC with MTD previously defined</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Arm 3: SAR408701 expansion cohort lung adenocarcinoma at MTD</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Arm 4: SAR408701 expansion cohort gastric adenocarcinoma at MTD</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Arm 5: SAR408701 loading dose at first cycle followed by MTD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Study Identifiers:**
- TED13751
- NCT02187848
# SAR408701 (maytansin loaded anti-CEACAM5 mAb) Advanced Solid Tumors (AST) 2/2

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| Japanese patients Monotherapy and Combination | Phase 1 Safety and PK of SAR408701 Monotherapy and in combination with other anti-tumor drug in Japanese patients with Advanced Malignant Solid Tumors | 27 | • Patients with malignant solid tumor  
  • Non-Randomized, Open-label, Sequential assignment  
  • Phase 1: SAR408701 monotherapy escalating doses/ 4 weeks  
  • Phase 1B: SAR408701 at MTD in combinations with other anti-tumor drugs, 4 weeks | • Primary: DLTs, Phase 1 and 1B  
  • Secondary: Safety, Immunogenicity, PK, Plasma CEACAM5 levels, Anti-tumor response RECIST | • SSD: Oct. 2017  
  • DE: 2019 |

TCD15054 NCT03324113
# GZ402666 (avalglucosidase alfa)
## Pompe disease (PD) 1/3

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| COMET          | Phase 3                                                                    | 96       | Repeated Biweekly Infusions of avalglucosidase alfa (GZ402666) and alglucosidase alfa in patients with late-onset PD age 3 years and older  
Randomized, Double-Blind, Parallel Assignment  
Total study duration for one patient: 3 years [14-day screening, 49-week blinded Tx period, 96-week open-label Tx and 4-week post-Tx observation period | Primary: Change from baseline in percent predicted forced vital capacity (%FVC) in upright position  
Secondary: Change from baseline in six-minute walk test scores, maximal inspiratory / expiratory pressure in upright position, hand-held dynamometry measurement of lower extremity muscle strength in Quick Motor Function Test scores, 12- Item Short-form health survey scores | SSD: Nov. 2016  
DE (1st Part)\(^{(1)}\): 2019 |
| Late Onset     |                                                                             |          |                                                                                           |                                                                                             |                                             |
| EFC14028       | To compare efficacy and safety of Enzyme Replacement therapies avalglucosidase alfa and alglucosidase alfa in patients with Late-onset PD who have not been previously treated for PD |          |                                                                                           |                                                                                             |                                             |
| NCT02782741    |                                                                             |          |                                                                                           |                                                                                             |                                             |

\(^{(1)}\) Final Data Collection date for primary outcome measure
# GZ402666 (avalglucosidase alfa)
## Pompe disease (PD) 2/3

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
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<th>Status</th>
</tr>
</thead>
</table>
| Mini-COMET             | Phase 2 To assess safety and efficacy of avalglucosidase alfa in Pediatric  | 20       | • In Patients with Infantile-onset PD treated with alglucosidase alfa  | • Primary: N of participants with AE  
• Secondary: PK parameters, Change from baseline in Gross Motor Function (GMF) Measure-88 Test, Change from baseline revised GMF Classification System score, Pompe specific Pediatric Evaluation of Disability Inventory, Functional Skills Scale, Mobility Domain Test score and Quick Motor Function Test scores, Left Ventricular Mass Index, Eyelid position measurements, Creatine kinase value | • SSD: Oct. 2017  
• DE (1st Part)(1): 2019 |
| Infantile Onset        | patients with infantile-onset PD previously treated With alglucosidase alfa |          | • Randomized, Open-label, Ascending dose, Parallel assignment          |                                                                                                      |                                                                      |
| ACT14132               |                                                                             |          | • Total study duration for one patient: 3 years [14-day screening, 25-week Tx period, a 120-week extension period and 4-week post-Tx observation period |                                                                                                      |                                                                      |
| NCT03019406            |                                                                             |          |                                                                        |                                                                                                      |                                                                      |

(1) Final Data Collection date for primary outcome measure
# GZ402666 (avalglucosidase alfa) Pompe disease (PD) 3/3

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
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<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEO-EXT</td>
<td>Phase 2&lt;br&gt;Phase 3&lt;br&gt;Long-term safety and PK of repeated biweekly infusions of avalglucosidase alfa in patients with PD</td>
<td>24</td>
<td>In patients with PD who previously completed a avalglucosidase alfa study [adult, senior]&lt;br&gt;Non-randomized, Open-label, Parallel assignment&lt;br&gt;Total study duration for one patient: 6 years [until the patient withdraws, the Investigator withdraws the patient, or the Sponsor terminates the study]</td>
<td>Primary: AEs and TEAEs, including IARs &amp; deaths, Hematology, biochemistry and urinalysis, vital signs&lt;br&gt;Secondary: ECG, PK parameters, anti-avalglucosidase alfa immunoglobulin G (IgG) antibodies, and neutralizing antibody formation in IgG seropositive patients, anti-avalglucosidase alfa IgG antibodies, Skeletal muscle glycogen content, Qualitative and quantitative muscle degenerative assessments MRI, Urinary Hex4, plasma analyses of circulating mRNA and micro RNA, Serum analyses of skeletal muscle RNA expression</td>
<td>• SSD: Feb. 2014&lt;br&gt;• DE: 2020</td>
</tr>
<tr>
<td>LTS13769</td>
<td>NCT02032524&lt;br&gt;Phase 2&lt;br&gt;Phase 3&lt;br&gt;Long-term safety and PK of repeated biweekly infusions of avalglucosidase alfa in patients with PD</td>
<td>24</td>
<td>In patients with PD who previously completed a avalglucosidase alfa study [adult, senior]&lt;br&gt;Non-randomized, Open-label, Parallel assignment&lt;br&gt;Total study duration for one patient: 6 years [until the patient withdraws, the Investigator withdraws the patient, or the Sponsor terminates the study]</td>
<td>Primary: AEs and TEAEs, including IARs &amp; deaths, Hematology, biochemistry and urinalysis, vital signs&lt;br&gt;Secondary: ECG, PK parameters, anti-avalglucosidase alfa immunoglobulin G (IgG) antibodies, and neutralizing antibody formation in IgG seropositive patients, anti-avalglucosidase alfa IgG antibodies, Skeletal muscle glycogen content, Qualitative and quantitative muscle degenerative assessments MRI, Urinary Hex4, plasma analyses of circulating mRNA and micro RNA, Serum analyses of skeletal muscle RNA expression</td>
<td>• SSD: Feb. 2014&lt;br&gt;• DE: 2020</td>
</tr>
</tbody>
</table>
# Patisiran (siRNA targeting TTR) Hereditary ATTR (hATTR) Amyloidosis

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>APOLLO Global OLE FAP</td>
<td>Phase 3</td>
<td>228</td>
<td>• For patients having completed a previous patisiran efficacy study&lt;br&gt;• Safety and tolerability of long-term dosing of patisiran&lt;br&gt;• Single Group assignment, Open-label</td>
<td>• Primary: Safety and tolerability of long-term dosing of patisiran as measured by the proportion of subjects with AE leading to discontinuation of study drug&lt;br&gt;• Secondary: Changes from baseline in neurologic impairment assessed using the Neuropathy Impairment Score (NIS), the Modified NIS (mNIS +7) composite score, the NIS+7 QOL [(QOL-DN) and EuroQOL (EQ-5D)], autonomic and motor function, disability, nutritional status, serum TTR lowering</td>
<td>• SSD: Jul. 2015&lt;br&gt;• DE: 2019</td>
</tr>
</tbody>
</table>
# Fitusiran (siRNA targeting Antithrombin/AT3)\(^{(1)}\)

## Hemophilia A & B

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| Hemophilia A or B | Phase 1/2 Hemophilia A and Hemophilia B 
Fitusiran in patients with moderate or severe hemophilia A or B | 34 | • For patients having participated in a previous fitusiran study 
• Single Group assignment, Open-label | • Primary: % of patients experiencing AEs, SAEs, and AEs leading to study drug discontinuation 
• Secondary: Changes in the N of Bleeding Event, the Amount of Factor VIII or Factor IX administered for the Tx of bleeding episodes, health-related QOL plasma levels of antithrombin and thrombin generation | • SSD: Sep. 2015 
• DE: 2019 |

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\(^{(1)}\) Currently on clinical hold pending outcome of FDA discussion – Expected to resume around year-end
## Olipudase Alfa (rhASM ERT) 1/3
### Acid Sphingomyelinase Deficiency (ASMD)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCEND</td>
<td>Phase 2&lt;br&gt;Phase 3&lt;br&gt;Efficacy, Safety, PD, and PK study of olipudase alfa in patients with ASD</td>
<td>36</td>
<td>• Randomized, Double-blinded, Placebo-controlled, Parallel assignment&lt;br&gt;• Total study duration for one patient at least 3 years up to 5 years and 3 months (2-month screening, 52-week double-blind Tx period, 4-year and 1 month open label extension period with olipudase)</td>
<td>• Primary: % change in spleen volume, % change in diffusing capacity of the lung for carbon monoxide&lt;br&gt;• Secondary: Change in splenomegaly-related symptom score (except US, where it is part of the primary &quot;combination spleen endpoint&quot;), % change in liver volume, % change in platelet count, Change in fatigue severity as measured by item 3 of the Brief Fatigue Inventory scale, Change in pain severity as measured by item 3 of the Brief Pain Inventory scale, Change in dyspnea severity as measured by the Functional Assessment of Chronic Illness Therapy dyspnea tool</td>
<td>• SSD: Jun. 2016&lt;br&gt;• DE (1st Part)(^2): 2019</td>
</tr>
<tr>
<td>Niemann-Pick disease type B(^1)</td>
<td>DF112712&lt;br&gt;NCT02004691</td>
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</tbody>
</table>

\(^1\) Non-neurological manifestations of ASMD
\(^2\) Final Data Collection date for primary outcome measure
## Olipudase Alfa (rhASM ERT) 2/3
### Acid Sphingomyelinase Deficiency (ASMD)

<table>
<thead>
<tr>
<th>Study</th>
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<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCEND Peds</td>
<td>Phase 1&lt;br&gt;Phase 2&lt;br&gt;Safety, Tolerability, PK, and efficacy evaluation of olipudase alfa in pediatric patients &lt;18 years of age with ASMD</td>
<td>20</td>
<td>• Open-label, ascending dose, Single group assignment &lt;br&gt; • Total study duration for one patient approximately 18 months [up to 60-day screening, 64-week Tx period, 37-day post Tx period except if patient enrolled in a long-term extension study]</td>
<td>• Primary: N of AE, Clinically significant changes in laboratory parameters, Clinically significant changes in physical examinations &lt;br&gt; • Secondary: PK parameters, Change in sphingomyelin levels and sphingomyelin metabolite levels</td>
<td>SSD: Jun. 2015&lt;br&gt;DE: 2019</td>
</tr>
<tr>
<td>DF113803 NCT02292654</td>
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</table>

### Relevant Fields
- Immuno-inflammation
- Diabetes
- Oncology
- Cardiovascular
- Rare Diseases
- Infectious disease
- MS, Neuro, Gene therapy
- Vaccines
## Olipudase Alfa (rhASM ERT) 3/3 Acid Sphingomyelinase Deficiency (ASMD)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
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<th>Status</th>
</tr>
</thead>
</table>
| Long-Term      | Phase 2 Long-term study of olipudase alfa in patients with ASDM | 25       | • For patients who have completed a previous study with olipudase alfa (DFI13803 for pediatric patients, and DFI13412 for adult patients)  
• Open-label, Single group assignment  
• Total study duration for one patient: 5 years | • Primary: N of patients experiencing AE, Physical examinations including neurologic examinations, Clinical laboratory tests, Safety biomarkers, IR assessments, Vital signs, echocardiogram and electrocardiogram, Liver biopsy and Liver ultrasound/Doppler for patients previously enrolled in DFI13412  
• Secondary: Spleen and Liver Volumes, Pulmonary imaging and function tests, Hematology and Lipid profiles, Health Outcomes Questionnaires  
For pediatrics patients: Hand X-ray for bone age and bone maturation, Tanner Staging and Linear patient growth by height Z-score | • SSD: Dec. 2013  
• DE: 2021 |
| LTS13632       | NCT02004704                                      |          |                                                                       |                                                                                            |                 |
|                |                                                  | 25       |                                                                       |                                                                                            |                 |
|                |                                                  |          |                                                                       |                                                                                            |                 |
|                |                                                  |          |                                                                       |                                                                                            |                 |
Venglustat (GCS inhibitor)
Fabry disease (FD)

<table>
<thead>
<tr>
<th>Study</th>
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<th>Patients</th>
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<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>FABRY LONG-TERM LTS14116</td>
<td>Phase 2 Long-term safety, PD, and exploratory efficacy of venglustat in Tx-naïve adult male patients with FD</td>
<td>8</td>
<td>• Male patients with FD who previously completed study ACT13739</td>
<td>• Primary: Safety profile, Clinically significant changes in laboratory parameter, and physical examinations</td>
<td>SSD: Jul. 2015/ DE: 2018</td>
</tr>
<tr>
<td>NCT02489344</td>
<td></td>
<td></td>
<td>• Open-label, Single group Assignment</td>
<td>• Secondary: Change from baseline in plasma globotriaosylceramide (GL-3), plasma lyso GL-3, Change from baseline in plasma glucosylceramide (GL 1), Urine GL-3</td>
<td></td>
</tr>
</tbody>
</table>
# Venglustat (GCS inhibitor)
**Gaucher disease (GD) Type 3**

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| LEAP GD Type 3      | Phase 2 Tolerability, PK, PD, and exploratory efficacy of venglustat in combination with cerezyme in adult patients with GD Type 3       | 10       | • 52-week Two-part, Open-label, Single group Assignment  
  • Part 1: Evaluate CNS biomarkers in adult GD type 3 patients that distinguish GD3 from GD type 1, Screen adult GD3 patients who qualify for Tx with venglustat in Part 2, Total duration 45 days  
  • Part 2: Safety and tolerability in GD3 patients, Total duration up to 61 weeks including 52 weeks of treatment | • Primary: N of patients with AE, Change from baseline in biomarker levels (CSF and Plasma)  
  • Secondary: PK parameters (CSF and Plasma)                                                                                                      | • SSD: Mar. 2017  
  • DE (1st Part)(1): 2021                                                                                                                      |
| PDY13949 NCT02843035 |                                                                                                                                             |          |                                                                                                                                                                           |                                                                                                                                                           |                                                                                              |

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(1) Final Data Collection date for primary outcome measure
## Teriflunomide Multiple Sclerosis (MS)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| TERIKIDS RMS     | Phase 3 Efficacy, Safety and PK of teriflunomide in Pediatric Patients With Relapsing Forms of MS | 165      | • Patients with RMS meeting the criteria of MS based on McDonald criteria 2010 and International Pediatric MS Study Group criteria for pediatric MS  
• With at least one relapse (or attack) in the 12 months preceding randomization or at least two relapses (or attack) in the 24 months preceding randomization  
• Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Tx 96 weeks followed by Open-label extension (96 weeks up to a max of 192 weeks after randomization), follow-up 4 weeks after Tx discontinuation | • Primary: Time to first clinical relapse after randomization  
• Secondary: % of relapse free patients, N of new/newly enlarged T2 lesions, N of T1 Gd-enhancing T1 lesions, Change in volume of T2 lesions, of T1 hypointense lesions, brain atrophy, % of patients free of new or enlarged MRI T2-lesions, Change in performance on SDMT and Cognitive Battery Test, Safety, PK | • SSD: Jul. 2014  
• DE: 2019                        |
# SAR422459 (ABCA4 gene therapy) Stargardt Disease

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stargardt's Macular Degeneration</td>
<td>Phase 1</td>
<td>46</td>
<td>Patients with a diagnosis of Stargardt's Macular Degeneration, with at least one pathogenic mutant ABCA4 allele on each chromosome&lt;br&gt;Non-randomized, Single Group assignment, Open-label, ascending doses</td>
<td>Primary: IAE, Change from baseline in ocular safety assessments&lt;br&gt;Secondary: Delay in retinal degeneration</td>
<td>SSD: Jun. 2011&lt;br&gt;DE: 2020</td>
</tr>
<tr>
<td>TDU13583 NCT01367444</td>
<td>Phase 2a</td>
<td></td>
<td>Safety and tolerability of ascending doses of SAR422459 in patients with Stargardt's Macular Degeneration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stargardt's Macular Degeneration</td>
<td>Phase 2b</td>
<td>28</td>
<td>Long term safety, tolerability and Biological activity of an experimental gene transfer agent, SAR422459, designed to treat patients With Stargardt Macular Degeneration</td>
<td>Primary: IAE&lt;br&gt;Secondary: Delay in retinal degeneration</td>
<td>SSD: 2012&lt;br&gt;DE: 2036</td>
</tr>
<tr>
<td>LTS13588 SG1/002/11 NCT01736592</td>
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</tbody>
</table>
## SAR421869 (Myosin 7A gene therapy)
**Usher 1B Syndrome**

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UshStat®</strong>&lt;br&gt;<strong>Usher Syndrome Type 1B</strong>&lt;br&gt;TDU13600&lt;br&gt;NCT01505062</td>
<td>Phase 1&lt;br&gt;Phase 2a&lt;br&gt;Safety and tolerability of ascending doses of subretinal injections of UshStat® in patients with Retinitis Pigmentosa associated with Usher syndrome Type 1B</td>
<td>18</td>
<td>• Patients with clinical and molecular diagnosis of Retinitis Pigmentosa associated with Usher Syndrome type 1B. With at least one pathogenic mutation in the MYO7A gene on each chromosome&lt;br&gt;• Non-randomized, Single Group assignment, Open-label, ascending doses</td>
<td>• Primary: IAE&lt;br&gt;• Secondary: Delay in retinal degeneration</td>
<td>SSD: Apr. 2012&lt;br&gt;DE: 2020</td>
</tr>
<tr>
<td><strong>UshStat®</strong>&lt;br&gt;<strong>Usher Syndrome Type 1B</strong>&lt;br&gt;LTS13619&lt;br&gt;NCT02065011</td>
<td>Phase 2b&lt;br&gt;Long-Term Safety, Tolerability and Biological Activity of UshStat® in Patients With Usher Syndrome Type 1B</td>
<td>28</td>
<td>• Long-term follow up of patients who received UshStat® in a previous study (TDU13600)&lt;br&gt;• Single Group assignment, Open-label</td>
<td>• Primary: IAE&lt;br&gt;• Secondary: Change from baseline in ocular safety assessments, Delay in retinal degeneration</td>
<td>SSD: Dec. 2012&lt;br&gt;DE: 2035</td>
</tr>
</tbody>
</table>
### GZ402668 (Anti-CD52 mAb) Relapsing Multiple Sclerosis (RMS)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| Long Term Follow-Up MS | Phase 2b, Open-label, Long-term follow-up study of MS patients who participated in previous Genzyme-sponsored studies of GZ402668 | 72       | • Long Term safety follow up of patients who received GZ402668 in a previous study (TDU13475 or TDU14981)  
• No administration of GZ402668 in the LTS14120 study, Patients who already received investigational medicinal product (GZ402668 or placebo) in TDU13475 or TDU14981 will be followed up to 47 months in the LTS14120 | • Primary: N of patients with AE, Safety, as assessed by clinical (physical examination), laboratory (hematology, creatinine, and urinalysis with microscopy), ECG, vital sign events, Clinically significant changes in thyroid function tests from baseline  
• Secondary: Time to lymphocyte repopulation, Number of patients with anti-drug antibodies | SSD: Jan. 2015  
DE: 2022         |
# Venglustat (GCS inhibitor) GBA-PD

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| MOVES-PD    | Phase 2 Drug Dynamics, Efficacy, Safety of venglustat in Parkinson's Disease (PD) patients carrying a Glucocerebrosidase (GBA) Gene Mutation       | 15       | • Male and female adults with a diagnosis of PD and who are heterozygous carriers of a GBA mutation associated with PD  
• Randomized, Double-blind, Placebo Controlled, Parallel Assignment  
• Part 1: Increasing dose of venglustat administered once per day. Duration: up to 48 weeks outside Japan, and up to 64 weeks in Japan  
• Part 2: venglustat dose determined in Part 1 administered once a day. Duration: 5,6-week screening, 52-week Tx period, 104-week follow-up period and 6-week post Tx observation | • Primary: Change from baseline in Movement Disorder Society Unified PD Rating Scale Part II and III score  
• Secondary: Change from baseline in PD Cognitive Rating Scale, Movement Disorder Society Unified PD Rating Scale Part I, II, and III score, Hoehn and Yahr score | • SSD: Jan. 2017  
• DE: 2021 |
## Insulin glargine / lixisenatide
### Type 2 Diabetes Mellitus (T2DM)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIXILAN-G</td>
<td>Phase 3 Efficacy and safety of lixilan vs. GLP-1 receptor agonist in patients with type 2 Diabetes not controlled on GLP-1 RAs + OADs, with an extension period</td>
<td>500</td>
<td>Patients with T2DM • Randomized, Open-label, Active Controlled, Parallel-group • Active comparator: Liraglutide/Exenatide/Exenatide ER/Albiglutide/Dulaglutide, Metformin, pioglitazone and SGLT2 inhibitor if taken prior to the study continued • 1st period: up to 2 weeks screening, 26-week Tx period and 3 to 9 days follow-up post Tx • Extension period 26-week extension after the 26-week Tx for the lixiLan arm only, 3-day follow-up post extension</td>
<td>Primary: Change from baseline in HbA1c • Secondary: % of participants reaching HbA1c targets, Change from baseline in FPG, in 7-point SMPG, in 2-hour PPG during standardized meal test, in blood glucose excursion during standardized meal test, in body weight, Symptomatic hypoglycemia, Safety, % of patients requiring rescue therapy</td>
<td>SSD: Jul. 2016 DE: 2018</td>
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<tr>
<td>EFC13794</td>
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<tr>
<td>NCT02787551</td>
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</tbody>
</table>
## Insulin glargine / lixisenatide
### Type 2 Diabetes Mellitus (T2DM) - Japan

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIXILAN JP-O1</td>
<td>Efficacy and safety of lixilan compared to lixisenatide on top of OADs in Japanese patients with T2DM with an extension period</td>
<td>318</td>
<td>• Japanese Patients with T2DM</td>
<td>• Primary: Change from baseline in HbA1c</td>
<td>• SSD: May 2016</td>
</tr>
<tr>
<td>EFC14112</td>
<td></td>
<td></td>
<td>• Randomized, Open-label, Active Controlled, Parallel-group, 2- Tx arm</td>
<td>• Secondary: % of patients reaching HbA1c &lt;7% or ≤6.5%, Change from baseline in FPG, in 7 point SMPG, % of patients reaching HbA1c &lt;7% with no body weight gain, Change in daily dose of lixilan for the combination group, N of hypoglycemic events, N of AE, Measurement from baseline of anti-lixisenatide antibodies and of anti-insulin antibodies</td>
<td>• DE: 2018</td>
</tr>
<tr>
<td>NCT02749890</td>
<td></td>
<td></td>
<td>• Active comparator: lixisenatide</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>• Background therapy with OADs (except dipeptidyl-peptidase-4 inhibitor)</td>
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<tr>
<td></td>
<td></td>
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<td>should be continued during the Tx period</td>
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<td></td>
<td>• Study duration: approximately 55 weeks: up to 2-week screening, 26-week</td>
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<td></td>
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<td></td>
<td>Tx period, 26-week safety extension Tx period and 3-day post Tx follow-up</td>
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</tr>
</tbody>
</table>

**Endpoints**
- Primary: Change from baseline in HbA1c
- Secondary: % of patients reaching HbA1c <7% or ≤6.5%, Change from baseline in FPG, in 7 point SMPG, % of patients reaching HbA1c <7% with no body weight gain, Change in daily dose of lixilan for the combination group, N of hypoglycemic events, N of AE, Measurement from baseline of anti-lixisenatide antibodies and of anti-insulin antibodies

**Status**
- SSD: May 2016
- DE: 2018
### Insulin glargine / lixisenatide
#### Type 2 Diabetes Mellitus (T2DM) - Japan

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<tr>
<th>Study</th>
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<th>Endpoints</th>
<th>Status</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Randomized, Open-label, Active Controlled, Parallel-group, 2 Tx arm</td>
<td>Secondary: % of patients reaching HbA1c &lt;7% or ≤6.5%, Change from baseline, in 2-hour PPG, in blood glucose excursion during standardized meal test, in 7-point SMPG profiles (each time point and average daily value), in body weight, in FPG, in daily dose of insulin glargine, % of patients reaching HbA1c &lt;7% with no body weight gain/no documented symptomatic hypoglycemia, % of patients requiring a rescue therapy, hypoglycemic events, AE, Measurement from baseline of anti-lixisenatide antibodies and of anti-insulin antibodies from baseline</td>
<td>DE: 2018</td>
</tr>
<tr>
<td>EFC14113 NCT02752412</td>
<td></td>
<td></td>
<td>Active comparator: insulin glargine</td>
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<td></td>
<td></td>
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<td>Background therapy: Metformin will be continued</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Study duration: approximately 41 weeks: up to 2-week screening, 12-week run-in, 26-week randomized Tx period and 3-day post Tx follow-up</td>
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</tbody>
</table>

**MN:** LIXILAN JP-L
**NCT:** NCT02752412

**Vaccines**

**Diabetes**

**Oncology**

**Cardiovascular**

**Rare Diseases**

**Infectious disease**

**MS, Neuro, Gene therapy**

**Vaccines**
### Insulin glargine / lixisenatide

**Type 2 Diabetes Mellitus (T2DM) - Japan**

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| LIXILAN JP-O2 | Efficacy and safety of lixisenatide compared to Insulin Glargine on top of OADs in Japanese patients with T2DM | 534 | • Japanese Patients with T2DM  
• Randomized, Open-label, Active Controlled, Parallel-group, 2-Tx arm  
• Active comparator: insulin glargine  
• Background therapy with OADs (except dipeptidyl-peptidase-4 inhibitor) should be continued during the Tx period  
• Study duration: approximately 29 weeks: up to 2-week screening, 26-week randomized open-label Tx period and 3-day post Tx follow-up | • Primary: Change from baseline in HbA1c  
• Secondary: % of patients reaching HbA1c <7% or ≤6.5%, Change from baseline, in 2-hour PPG, in 7 point SMPG profiles during standardized meal test, in body weight % of patients reaching HbA1c <7% with no body weight gain/no documented symptomatic hypoglycemia, % of patients requiring a rescue therapy, N of AE, N of hypoglycemic events, Measurement from baseline of anti-lixisenatide antibodies and of anti-insulin antibodies from baseline | • SSD: Jun. 2016  
• DE: 2018 |
### Lantus – Toujeo U300 Type 1 Diabetes Mellitus (T1DM) - Children

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| EDITION JUNIOR | Efficacy and safety of a new formulation of insulin glargine (U300) and Lantus® injected once daily in children and adolescents Age 6 - 17 years with T1DM with a 6-month safety extension period | 450      | • Children: 6 to 17 years old with T1DM  
  • Randomized, Open-label, Parallel-group, 2- Tx arm  
  • Active comparator: insulin glargine  
  • Study duration: approximately 58 weeks: up to 2-week screening, 6-month comparative Tx period, 6-month comparative extension period and 4-week post Tx follow-up | • Primary: Change from baseline in Hba1c  
  • Secondary: % of patients with Hba1c values of <7.5% and % of patients with FPG of ≤130 mg/dL (7.2 mmol/L) without any episode of severe and/or documented (SMPG <54 mg/dL; 3.0 mmol/L) symptomatic hypoglycemia during the last 3 months of the main 6-month randomized period, Change from baseline in FPG, Change from baseline in 24-hour mean plasma glucose and in variability of 24-hour mean plasma glucose based on 8-point SMPG profiles, % of patients with hypoglycemia, % of patients with hyperglycemia with ketosis, % of patients with AE | • SSD: April 2016  
  • DE: 2018                                      |
## Sotagliflozin (SGLT 1/2 inhibitor)
### Type 2 Diabetes Mellitus (T2DM)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| SOTA-MONO   | Efficacy and safety of sotagliflozin vs. placebo in patients with T2DM not currently treated with antidiabetic therapy  | 400      | • Patients (male and female) with T2D, who are treated with diet and exercise only during the 12 weeks prior to screening  
• Randomized, Double-blind, Placebo-controlled, Parallel-group, 3-Tx arm, sota dose 1/200mg, sota dose 2/400mg, placebo  
• Study duration: up to 34-week: up to 2-week screening period, 2-week single-blind placebo run-in, 26-week double-blind Tx period and 4-week post Tx follow-up | • Primary: Change from Baseline in HbA1c in comparison of sotagliflozin dose 1 vs. placebo  
• Secondary: Change from baseline in 2-hour PPG following a mixed meal in comparison of sotagliflozin doses 1/2 vs. placebo, FPG in comparison of sotagliflozin dose 1 vs. placebo, Body weight in comparison of sotagliflozin doses 1/2 versus placebo, % of patients with HbA1c <6.5% in comparison of sotagliflozin dose 1 vs. placebo, % of patients with HbA1c <7.0% in comparison of sotagliflozin dose 1 vs. placebo, Change from Baseline in HbA1c in comparison of sotagliflozin dose 2 vs. placebo, Change from baseline in SBP for patients with baseline SBP ≥130 mmHg in comparison of sotagliflozin dose 1 vs. placebo and SBP for all patients in comparison of sotagliflozin doses 1/2 vs. placebo | • SSD: Dec. 2016  
• DE: 2019 |
| T2DM        |                                                                                                 |          |                                                                                           |                                                                                                     |                                  |
| EFC14833    |                                                                                                 |          |                                                                                           |                                                                                                     |                                  |
| NCT02926937 |                                                                                                 |          |                                                                                           |                                                                                                     |                                  |
Sotagliflozin (SGLT 1/2 inhibitor)  
Type 2 Diabetes Mellitus (T2DM)

<table>
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<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| SOTA-MET (302) | Phase 3 Efficacy and safety of sotagliflozin added to metformin in patients with T2DM who have inadequate glycemic control on metformin | 500      | • Patients with T2DM currently treated with diet and exercise and on metformin at a stable dose ≥1500 mg/day for at least 12 weeks  
  • Randomized, Double-blind, Placebo-controlled, Parallel-group, 2-Tx arm (placebo – sota 400mg), On top of metformin  
  • Study duration: up to 87-week: up to 2-week screening period, 2-week single-blind placebo run-in, 26-week double-blind core Tx period, 53-week double-blind extension period and 4-week post Tx follow-up | • Primary: Change from Baseline in HbA1c  
  • Secondary: Change from Baseline I in 2-hour PPG following a mixed meal, in FPG, in body weight % of patients with HbA1c <6.5% - % patients with HbA1c <7.0%  
  • Change from Baseline I in systolic blood pressure (SBP) for patients with baseline SBP ≥130 mmHg in SBP for all patients. | • SSD: Dec. 2016  
  • DE: 2019 |
<p>| EFC14834       |                                                                               |          |                                                                                             |                                                                                                                                                                                                       |              |
| NCT02926950    |                                                                               |          |                                                                                             |                                                                                                                                                                                                       |              |</p>
<table>
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<tr>
<th>Study</th>
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<th>Patients</th>
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<th>Endpoints</th>
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</thead>
</table>
| SOTA-SU (307)       | Phase 3 Efficacy and safety of sotagliflozin added to a sulfonylurea alone or in combination with metformin in patients with Type 2 Diabetes who have inadequate glycemic control on a sulfonylurea alone or with metformin | 500      | • Patients with T2DM treated with a sulfonylurea (≥half the maximum recommended dose as per local label or MTD as monotherapy or in combination with metformin (≥1500 mg per day or MTD) each at a stable dose for at least 12 weeks  
  • Randomized, Double-blind, Placebo-controlled, Parallel-group, 2-Tx arm (placebo – sota 400mg)  
  • On top of sulfonylurea alone or in combination with metformin  
  • Study duration: up to 85-week: up to 2-week screening period, 2-week single-blind run-in, 26-week double-blind core Tx period, 53-week double-blind extension period and 2-week post Tx follow-up | • Primary: Change from Baseline in HbA1c  
  • Secondary: Change from baseline in FPG, in body weight, in Systolic Blood Pressure (SBP) for patients with baseline SBP ≥130 mmHg, in SBP for all patients, % of patients with HbA1c <6.5%, % of patients with HbA1c <7.0% | • SSD: Mar. 2017  
  • DE: 2019 |
| EFC14835 NCT03066830 |                                                                                                                                             |          |                                                                                                                                            |                                                                                                                                              |                 |
Sotagliflozin (SGLT 1/2 inhibitor)  
Type 2 Diabetes Mellitus (T2DM)

<table>
<thead>
<tr>
<th>Study</th>
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<th>Design</th>
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<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOTA-CKD3</td>
<td>Phase 3 Evaluate the efficacy and safety of sotagliflozin in patients with</td>
<td>780</td>
<td>Patients with T2DM (drug-naïve or on antidiabetic therapy) and documented moderate renal insufficiency defined by an estimated glomerular filtration rate (based on the 4 variable Modification of Diet in Renal Disease equation) of ≥30 and &lt;60 mL/min/1.73 m2 (CKD 3A, 3B) Randomized, Double-blind, Placebo-controlled, Parallel-group, 3-Tx arm (placebo – sota 200mg - sota 400mg) Study duration: up to 60-week: up to 2-week screening period, 2-week single-blind run-in, 52-week randomized Tx period and 4-week post Tx follow-up</td>
<td>Primary: Change in HbA1c for sota dose 1 and sota dose 2 Secondary: Change from Baseline in FPG (doses 1/2) in SBP for patients with baseline SBP ≥130 mmHg (doses 1/2), in SBP for all patients (doses 1/2) and in body weight (doses 1/2), % change in UACR for patients with UACR &gt; 30 mg/g (doses 1/2), % of patients with HbA1c less than 6.5% (doses 1/2), % of patients with HbA1c less than 7.0% (doses 1/2), % of patients with AE (doses 1/2)</td>
<td>SSD: Sept. 2017 DE: 2019</td>
</tr>
<tr>
<td>(306) T2DM</td>
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<tr>
<td>EFC14837</td>
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<tr>
<td>NCT03242252</td>
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</table>
# Sotagliflozin (SGLT 1/2 inhibitor)

## Type 2 Diabetes Mellitus (T2DM)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| SOTA-CKD4 (306) T2DM | Evaluate the efficacy and safety of sotagliflozin in patients with T2DM and severe renal impairment who have inadequate glycemic control | 276      | Patients with T2DM (drug-naïve or on antidiabetic therapy) and documented severe renal insufficiency - CKD4 - defined by an estimated glomerular filtration rate equation (based on the 4 variable modification of diet in renal disease equation) of ≥15 and <30 mL/min/1.73 m²  
  • Randomized, Double-blind, Placebo-controlled, Parallel-group, 3-Tx arm (placebo – sota 200mg - sota 400mg)  
  • Study duration: up to 60-week: up to 2-week screening period, 2-week single-blind run-in, 52-week randomized Tx period and 4-week post Tx follow-up |  
  • Primary: Change from Baseline in HbA1c comparing sotagliflozin dose 1 vs. placebo in CKD4 patients  
  • Secondary: Change from baseline in HbA1c comparing sotagliflozin dose 2 vs. placebo, in FPG (doses 1/2), in SBP at for patients with SBP greater than or equal to 130 mmHg (doses 1/2), in SBP in all patients (doses 1/2), in body weight (doses 1/2), % change in the UACR for patients with a UACR > 30 mg/g at baseline (doses 1/2), % of patients with HbA1c less than 6.5% (doses 1 and 2), % of patients with HbA1c less than 7.0% (doses 1 and 2), N of patients with AE (doses 1/2) | SSD: Sept. 2017  
  DE: 2019 |
# Sotagliflozin (SGLT 1/2 inhibitor)
## Type 2 Diabetes Mellitus (T2DM)

<table>
<thead>
<tr>
<th>Study</th>
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<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| SOTA-INS (312) T2DM | Efficacy and safety of sotagliflozin in patients with T2DM who have inadequate glycemic control on Basal Insulin alone or in addition to Oral Antidiabetes Drugs (OADs) | 560      | • Patients with T2DM using any types of basal insulin alone or in combination with up to 2 OADs  
  • Randomized, Double-blind, Placebo-controlled, Parallel-group, 3-Tx arm (placebo – sota 200mg - sota 400mg)  
  • Background therapy with insulin glargine (Lantus®) (with or without OADs) throughout the study  
  • Study duration: up to 60-week: up to 2-week screening period, 4-week Lantus® titration single-blind placebo run-in period, 52-week double-blind Tx period and 2-week post Tx follow-up | • Primary: Absolute change in hemoglobin A1c (HbA1c) (for sotagliflozin dose 1)  
• Secondary: Change in FPG (for sotagliflozin doses 1/2), in Body Weight (for sotagliflozin doses 1/2), in HbA1c (for sotagliflozin dose 2), in SBP for patients with baseline SBP ≥130 mmHg (for sotagliflozin doses 1/2), in SBP for all patients (for sotagliflozin dose 1), % of patients with Hemoglobin A1c (HbA1c) <7.0% (for sotagliflozin doses 1/2), % of patients with Hemoglobin A1c (HbA1c) <6.5% (for sotagliflozin doses 1/2), % of patients with AE | • SDD: Oct. 2017  
• DE: 2019 |
# Sotagliflozin (SGLT 1/2 inhibitor)
## Type 2 Diabetes Mellitus (T2DM)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| SCORED (303) T2DM | Effects of sotagliflozin on CV and renal events in patients with T2DM, CV risk factors and moderately impaired renal function | 10 500   | • Patients : T2DM with glycosylated hemoglobin (HbA1c) ≥ 7%, Estimated glomerular filtration rate (eGFR) ≥ 25 and ≤ 60 mL/min/1.73 m2, Age 18 years or older with at least one major CV risk factor or age 55 years or older with at least two minor CV risk factors  
  • Randomized, Double-blind, Placebo-controlled, Parallel-group, 2-Tx arm (placebo - sota 400mg)  
  • Total Study duration: approximately 27 to 51 months, 24-month recruitment and 27-month of follow-up after the last patient randomized | • Primary: Baseline to approx. 51 months, Time to the first occurrence of any of the following clinical events: CV death, Non-fatal myocardial infarction, Non-fatal stroke, Time to the first occurrence of any of the following clinical events: CV death; Hospitalization for heart failure  
  • Secondary: Baseline to approx. 51 months, Time to first composite renal event, Time to first composite renal event in subgroup of patients with macroalbuminuria, Total N of heart failure events, CV death , All cause mortality | • SSD: Nov. 2017  
  • DE: 2022 |

| EFC14875 NCT03315143 |                                                                                                         |          |                                                                                           |                                                                                                                     |                        |

---
# Sotagliflozin (SGLT 1/2 inhibitor)
**Type 2 Diabetes Mellitus (T2DM)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| GLIM        | Phase 3 Efficacy and safety of sotagliflozin vs. glimepiride and placebo in patients with T2DM that are taking metformin monotherapy | 930      | • Patients: Patients with T2DM treated with metformin at a stable dose ≥1500 mg/day or MTD (documented) for at least 12 weeks prior to screening visit  
  • Randomized, Double-blind, Double-dummy, Active and Placebo-controlled, Parallel-group, 4-Tx arm (placebo – glimepiride, sota dose 1, sota dose 2)  
  • Total Study duration: up to 58 weeks including 2-week screening phase, 2-week single-blind placebo run-in, 52-week double-blind Tx period and 2-week post Tx follow-up | • Primary: Absolute change in hemoglobin A1c (HbA1c) (for sotagliflozin dose 1)  
  • Secondary: Change in Body Weight (for sotagliflozin dose), in HbA1c (for sotagliflozin dose 2), in SBP for patients with baseline SBP ≥130 mmHg (for sotagliflozin dose 1), in SBP for all patients (for sotagliflozin dose 1), % of patients with at least one hypoglycemic event (for sotagliflozin dose 1), % of patients with AE | • SSD: Nov. 2017  
  • DE: 2019 |
| (304) T2DM  |                                                                               |          |                                                                                                             |                                                                                               |                           |
| EFC14838    |                                                                               |          |                                                                                                             |                                                                                               |                           |
| NCT03332771 |                                                                               |          |                                                                                                             |                                                                                               |                           |
# SAR341402 (Rapid Acting Insulin)  
**T1 & T2 DM**

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
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<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| GEMELLI 1 | Phase 3  
Comparison of SAR341402 to NovoLog®/NovoRapid® in adult patients with Diabetes also using Insulin Glargine, with a 6-month safety extension period | 500      | • Patients with T1DM or T2DM diagnosed for at least 12 months, who have been treated with a multiple daily injection regimen with NovoLog®/NovoRapid® OR insulin lispro (100 U/mL) in the last 6 months prior to screening visit AND insulin glargine (100 U/mL) in the last 6 months prior to screening visit OR insulin detemir (Levemir®) in the last 12 months prior to screening visit  
• Randomized, Open-label, Parallel-group  
• Active comparator: NovoLog®/NovoRapid®  
• Study duration: 54-week per patient: 2-week screening period, 26-week Tx period, 26-week comparative safety extension, 1-day follow-up period | • Primary: Change in HbA1c (%) from baseline to Week 26  
• Secondary: Change in HbA1c, Patients with HbA1c <7%, Change in FPG, Change in mean 24-hour plasma glucose concentration, Change in PPG, Change in 7-point SMPG, Hypoglycemic patients, Hypoglycemic events, Anti-SAR341402/NovoLog/NovoRapid antibody status, Tx-induced, Tx-boosted and Tx-emergent anti-insulin antibodies | • SSD: Aug. 2017  
• DE: 2019 |
| EFC15081  
NCT03211858 |                                                                 |          |                                                                                          |                                                                                               |                            |
### SAR425899 (GLP-1R/GCGR) Type 2 Diabetes Mellitus (T2DM)

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
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<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| SAR425899 T2DM | Safety and efficacy of SAR425899 in overweight to obese patients with T2DM | 270      | • Overweight and obese patients with T2DM for at least 3 months before the screening visit. On diet/exercise and/or Tx with metformin (stable dose of ≥1500 mg/day or maximal tolerated dose) for at least 3 months prior to screening  
• Randomized, Double-blind, Placebo-controlled, Dose-ranging (SAR425899 3 doses, placebo)  
• Active comparator: liraglutide  
• Study duration: approximately 30-week: 3-week screening period at site, 26-week Tx period, 3-day follow-up period | • Primary: Change in HbA1c (%)  
• Secondary: Change in body weight, % of patients achieving predefined HbA1c targets of <7%, % of patients achieving predefined HbA1c targets of <6.5%, % of patients achieving ≥5% body weight loss, % of patients achieving ≥10% body weight loss, PK parameters | SSD: Dec. 2016  
DE: 2018 |
| EFC13940 NCT02973321 |                                                                                |          |                                                                                                                       |                                                                          |              |
# Alirocumab (anti-PCSK-9 mAb)
## CV Events Reduction

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>ODYSSEY Outcomes</td>
<td>Phase 3 Evaluate the effect of alirocumab on the occurrence of CV Events in patients who have recently experienced an Acute Coronary Syndrome (ACS)</td>
<td>18,600</td>
<td>• Patients recently (&lt; 52 weeks) hospitalized for ACS&lt;br&gt;• Randomized, Double-Blind, Placebo-Controlled, Parallel-Group&lt;br&gt;• Study duration: max 64 months: up to 4 months run-in period, 60 months randomized Tx period</td>
<td>• Primary: Time from randomization to first occurrence of one of the following clinical events: CHD death, any non-fatal MI, fatal and non-fatal ischemic stroke, unstable angina requiring hospitalization&lt;br&gt;• Secondary: Time to the first occurrence of any CHD event, major CHD event, any CV event, composite of all cause mortality/non-fatal MI/non-fatal ischemic stroke, all cause mortality, Change from baseline in blood lipids and LP levels</td>
<td>• SSD: Nov. 2012&lt;br&gt;• DE: 2018</td>
</tr>
<tr>
<td>EFC11570 NCT01663402</td>
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</tbody>
</table>
Alirocumab (anti-PCSK-9 mAb)  
Heterozygous Familial Hypercholesterolemia (HeFH)

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<tr>
<th>Study</th>
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<th>Status</th>
</tr>
</thead>
</table>
| ODYSSEY KIDs    | Phase 2 Efficacy and safety of alirocumab in children and adolescents with heFH followed by an extension phase | 30       | • Patients with diagnosis of heFH through genotyping or clinical criteria, 8 to 17 years old, treated with optimal dose of statin +/- other LMT(s) or non-statin LMT(s) if statin intolerant at stable dose for at least 4 weeks prior to screening lipid sampling  
• Open-Label, Sequential, Repeated Dose-Finding Study (6 doses tested)  
• Background therapies: optimal dose of statin with or without other LMT or non-statin LMT if statin intolerant at stable dose  
• Study duration: approximately 16-23 weeks: up to 6 (+1) weeks screening period, 8 weeks open-label Tx period, 6 to 8 weeks follow-up period | • Primary: % change in calculated LDL-C  
• Secondary: Absolute change in calculated LDL-C, % change in APO B (Apo B), % change in non-high density LP cholesterol (non HDL-C), % change in Total-C, in LP, in TG, in HDL-C, in Apo A-1, Absolute change in Apo B, in non-HDL-C, in Total C, in Lp(a), in TG, in HDL-C, in Apo A-1, in ratio apo B/Apo A-1, % of participants achieving a calculated LDL-C level lower than 130 mg/dL (3.37 mmol/L), % of participants achieving a calculated LDL-C level lower than 110 mg/dL (2.84 mmol/L) | • SSD: Sep. 2016  
• DE: 2018 |
| DFI14223        |                                                                                       |          |                                                                                          |                                                                           |                   |
| NCT02890992     |                                                                                       |          |                                                                                          |                                                                           |                   |
**Alirocumab (anti-PCSK-9 mAb) HeFH & non-FH Japan**

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<tr>
<th>Study</th>
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</tr>
</thead>
</table>
| ODYSSEY NIPPON | Phase 3 Efficacy and safety of alirocumab in patients with Hypercholesterolemia not adequately controlled with non-statin lipid modifying therapy or the lowest strength of statin | 159      | • Japanese Patients with hypercholesterolemia HeFH or non-familial hypercholesterolemia receiving non statin LP modifying therapies (LMTs) or the lowest strength of statin  
• Randomized, Double-blind, Placebo-controlled, Parallel Group, 3-arm (alirocumab dose 1, alirocumab dose 2, placebo)  
• Background therapies: stable and lowest-dose statin therapy or stable non-statin LMTs (e.g., atorvastatin, fenofibrate, bezafibrate, ezetimibe) including diet therapy  
• Study duration: approximately 71 weeks: 4-week run-in period, 3-week screening period, 12-week double-blind Tx period, 52-week open-label Tx period | • Primary: % change in calculated LDL-C using all LDL-C values regardless of adherence to Tx  
• Secondary: % change in calculated LDL-C values during the efficacy Tx period, % change in calculated LDL-C, % change in Apo-B, non-HDL-C, in TC, % of patients reaching LDL-C goal, % change in Lp(a), HDL-C, fasting TG, Apo A-1 | • SSD: Sep. 2016  
• DE: 2018 |
| EFC14305      | NCT02584504                                                                 |          |                                                                        |                                                                            |              |
# Alirocumab (anti-PCSK-9 mAb) LDL Lowering China

## Study Description

<table>
<thead>
<tr>
<th>Study</th>
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</tr>
</thead>
</table>
| ODYSSEY EAST  | Efficacy and safety of alirocumab vs. ezetimibe in Asia in High CV risk patients with Hypercholesterolemia not adequately controlled with their statin therapy | 600      | - Patients with hypercholesterolemia and established coronary heart disease (CHD) or CHD risk equivalents who are not adequately controlled with a maximally tolerated daily dose of statin at a stable dose for at least 4 weeks prior to the screening visit (Week -3)  
- Randomized, Double-blind, Parallel Group, 2-Arm  
- Active comparator: ezetimibe  
- Background therapies: atorvastatin, rosuvastatin, or simvastatin continued during the course of the trial  
- Study duration: max 35 weeks: 3-week screening period, 24-week randomized Tx period, 8-week follow-up period | - Primary: % change in calculated LDL-C in the intent-to-treat (ITT) population  
- Secondary: % change in calculated LDL-C in the modified ITT (mITT) population, % change in calculated LDL-C, % change in Apo B, in non-HDL-C, in TC, in Lp(a), in HDL-C, in fasting TG, in Apo A-1, % of patients reaching calculated LDL-C <70 mg/dL (1.81 mmol/L) | SSD: Aug. 2016  
DE: 2018 |
| EFC13889     | NCT02715726                                                                 |          |                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                     |                   |

### Endpoints
- Primary: % change in calculated LDL-C in the intent-to-treat (ITT) population
- Secondary: % change in calculated LDL-C in the modified ITT (mITT) population, % change in calculated LDL-C, % change in Apo B, in non-HDL-C, in TC, in Lp(a), in HDL-C, in fasting TG, in Apo A-1, % of patients reaching calculated LDL-C <70 mg/dL (1.81 mmol/L)
### Alirocumab (anti-PCSK-9 mAb)
**Homozygous Familial Hypercholesterolemia (HoFH)**

<table>
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<tr>
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</tr>
</thead>
</table>
| HoFH  | Evaluate the efficacy and safety of alirocumab in patients with HoFH | 54 | • Diagnosis of HoFH by specific genotype or clinical criteria (all patients on LDL apheresis must be diagnosed based on genotype)  
• Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, 2-Arm (alirocumab Q2W, placebo)  
• Study duration: 12-week double-blind Tx period followed by 10-week alirocumab open-label Tx period | • Primary: % change in LDL-C ITT population  
• Secondary: % change in Apo B, % change in non-HDL-C, % change in TC, % change in LP(a), % change in HDL-C, % change in fasting TG, % change in Apo A-1, % change in LDL-C, % change in LDL-C, ApoB, non-HDL-C, TC, Lp(a), HDL-C, fasting TG, Apo A-1 / (m)ITT population, Absolute change in the ratio of Apo B/Apo A-1 (ITT), % of patients with ≥15% reduction in LDL-C, % of patients with ≥30% reduction in LDL-C, % of patients with ≥50% reduction in LDL-C, % of patients with ≥15% reduction, ≥30% reduction, and ≥50% reduction in LDL-C | SSD: Oct. 2017  
DE: 2019 |
### PIONEER-HCM

**MyoKardia collaboration**

**MYK-461-004**

**NCT02842242**

<table>
<thead>
<tr>
<th>Study</th>
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<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| PIONEER-HCM    | Phase 2                                                                     | 21       | • Patients with HCM (hypertrophied and non-dilated left ventricle in absence of systemic or other known cause), with LV wall thickness ≥ 15 mm at time of initial diagnosis or ≥ 13 mm with a positive family history of HCM  
• Open-label, Pilot, Single Group Assignment | • Primary: Change in post-exercise peak LVOT gradient from baseline to Week 12  
DE: 2018          |
**SAR407899 (Rho.kinase inhibitor)  
Microvascular Angina (MA)**

<table>
<thead>
<tr>
<th>Study</th>
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<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| Rho-Kinase  | Phase 2a Effects of SAR407899 in patients with MA and/or Persistent Stable Angina despite angiographically successful elective Percutaneous Coronary Intervention | 78       | • Patients with Symptomatic stable angina pectoris (typical or atypical symptoms with at least once weekly episodes); ECG evidence of ischemia with ST-segment depression during a symptom limited exercise test or non-invasive evidence of ischemia  
• Randomized, Double-blind, Placebo-controlled Parallel Arm Dose Titration over 4-week administration | • Primary: Assess effects of SAR407899 on coronary vasomotor function using coronary flow reserve assessed by 13N-ammonia or 82rubidium PET scan  
• Secondary: Assess effects of SAR407899 on QOL using Seattle Angina Questionnaire physical limitation domain (SAQ-PL) safety with a focus on hypotension and orthostatic hypotension plasma concentrations | • SSD: Oct. 2017  
• DE: 2018 |
| ACT14656    | NCT03236311                                                                  |          |                                                                                                                     |                                                                                                                                                                                                          |                               |
| NCT03236311 |                                                                                                                                 |          |                                                                                                                     |                                                                                                                                                                                                          |                               |
## Alirocumab (anti-PCSK-9 mAb) Neurocognitive Evaluation

### Study \n**Neurocognitive Evaluation Regeneron**  
**R727-CL-1532 NCT02957682**

<table>
<thead>
<tr>
<th>Study Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| Phase 3 Evaluate the effect of alirocumab on Neurocognitive function in patients with HeFH and non-HeFH at high and very high cardiovascular risk | 2100 | - Patients with hypercholesterolemia and established coronary heart disease (CHD) or CHD risk equivalents who are not adequately controlled with a maximally tolerated daily dose of statin at a stable dose for at least 4 weeks prior to the screening visit  
- Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, 2-Arm (alirocumab Q2W, placebo, 1:1)  
- Study duration: 3 weeks screening, 96-weeks double-blind Tx period | - Primary: Change in Cambridge Neuropsychological Test Automated Battery (CANTAB) cognitive domain Spatial Working Memory (SWM) strategy score from baseline to week 96.  
- Secondary (safety) at week 96 in the CANTAB domains and compared to baseline raw scores: Paired Associates Learning, Reaction Time, SWM, global composite  
- Secondary (efficacy): % change in calculated LDL-C, % change in Apo B, in non-HDL-C, in TC, in Lp(a), in HDL-C, in fasting TG, in Apo A-1, % of patients reaching calculated LDL-C <70 mg/dL (1.81 mmol/L) and LDL-C < 50mg/dL(1.29 mmol/L). | · SSD: Nov 2016  
· DE: 2020 |
# Ferroquine – Artefenomel / OZ439 Malaria

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>FALCI</td>
<td>Phase 2 Efficacy, Safety, Tolerability and PK of a single dose regimen of ferroquine with artefenomel (OZ439) in adults and children with Uncomplicated Plasmodium Falciparum Malaria</td>
<td>662</td>
<td>Patients from 6 months to 70 years suffering from mono-infection by P. falciparum, Randomized, Double-blind, Parallel Assignment, 4 doses of ferroquine associated to 1 dose of artefenomel according to age and body weight, Study duration: up to 67 days for each patient</td>
<td>Primary: % of patients with Polymerase Reaction Chain (PCR)-adjusted Adequate Clinical and Parasitological Response (ACPR), Secondary: Time to re-emergence, Time to recrudescence, Parasite clearance time, % of patients with PCR - crude ACPR, SAE, AESI, TEAE, % of patients with PCR - adjusted ACPR</td>
<td>SSD: Jul. 2015, DE: 2019</td>
</tr>
<tr>
<td>DRI12805</td>
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<tr>
<td>NCT02497612</td>
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</tbody>
</table>

**Ferroquine** – Artefenomel / OZ439 Malaria

**Study**

- **FALCI**
- **DRI12805**
- **NCT02497612**

**Description**

- Phase 2

**Patients**

- 662

**Design**

- Patients from 6 months to 70 years suffering from mono-infection by P. falciparum
- Randomized, Double-blind, Parallel Assignment
- 4 doses of ferroquine associated to 1 dose of artefenomel according to age and body weight
- Study duration: up to 67 days for each patient

**Endpoints**

- Primary: % of patients with Polymerase Reaction Chain (PCR)-adjusted Adequate Clinical and Parasitological Response (ACPR)
- Secondary: Time to re-emergence, Time to recrudescence, Parasite clearance time, % of patients with PCR - crude ACPR, SAE, AESI, TEAE, % of patients with PCR - adjusted ACPR

**Status**

- SSD: Jul. 2015
- DE: 2019
Dengue Vaccine
Co-administration w/ Tdap booster

<table>
<thead>
<tr>
<th>Study</th>
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</tr>
</thead>
</table>
| NCT02992418 | Phase 3 Study of a Tetravalent Dengue Vaccine Administered Concomitantly or Sequentially With Adace® in Healthy Subjects | 688      | • Randomized, multicenter, open-label study in 688 subjects aged from 9 to 60 years | • Immunogenicity and safety of CYD dengue vaccine and Tdap vaccine when both vaccines are administered concomitantly or sequentially | • SSD: Dec. 2016
|          |                                                                              |          |                                                                        |                                                                           | • DE: 2019                  |
### Dengue Vaccine

#### Different schedules

<table>
<thead>
<tr>
<th>Study</th>
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</tr>
</thead>
</table>
| NCT02628444 | Phase 2a Immunogenicity and Safety of 3-Dose and Booster Dose of Tetravalent Dengue Vaccine in Healthy Subjects 9 to 50 Years of Age | 1050     | Two-stage, multi-national, multi-center, observer-blind, randomized, placebo-controlled Phase II immunogenicity and safety study of tetravalent dengue vaccine | Immunogenicity and safety of 3-dose primary series and booster dose | SSD: May. 2016  
DE: 2020 |
## Dengue Vaccine Booster dose

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
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<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| NCT02623725 | Study of a Booster Dose of a Tetravalent Dengue Vaccine in Subjects Who Previously Completed the 3-dose Schedule | 252      | • Multi-center, observer-blind, randomized, placebo-controlled, Phase II trial | • Immunogenicity and safety of a booster dose                              | • SSD: Apr. 2016
<p>|         |                                                                              |          |                                                                        |                                                                           | • DE: 2019                      |</p>
<table>
<thead>
<tr>
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<th>Design</th>
<th>Endpoints</th>
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</tr>
</thead>
</table>
| NCT01622062 | Phase 3 Immunogenicity and Safety of Verorab® in a "One-week" Intradermal Post-exposure Prophylaxis Regimen | 600      | • Open-label, randomized, controlled, multi-center, multi-country trial | • Immunogenicity and safety of Verorab® in a "One-week" intradermal post-exposure prophylaxis regimen | • SSD: Jun. 2012  
• DE: 2019 |
# Flu Vaccine

## Fluzone HD-QIV HV

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT03282240</td>
<td>Phase 3 Safety and Immunogenicity of High-Dose Quadrivalent Influenza Vaccine in Participants ≥65 Years in the US</td>
<td>2616</td>
<td>• Ph3 randomized, modified double blind, active controlled, multi center</td>
<td>• Safety, immunogenicity, consistency</td>
<td>• SSD: Sep. 2017</td>
</tr>
</tbody>
</table>
## Flu Vaccine
### Fluzone HD-QIV HV (Japan)

<table>
<thead>
<tr>
<th>Study</th>
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<th>Endpoints</th>
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</tr>
</thead>
<tbody>
<tr>
<td>NCT03233217</td>
<td>Safety and Immunogenicity of High-Dose Quadrivalent Influenza Vaccine in Patients ≥65 Years</td>
<td>175</td>
<td>- Ph1/2 randomized, modified double blind, multi center</td>
<td>- Safety and immunogenicity</td>
<td>- SSD: Sep. 2017</td>
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<td>- DE: 2018</td>
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</tbody>
</table>

**Endpoints:**
- Safety and immunogenicity

**Status:**
- SSD: Sep. 2017
- DE: 2018
# Meninge Vaccine
## MenQuadTT

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>Design</th>
<th>Endpoints</th>
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</tr>
</thead>
</table>
| NCT03205371 | Phase 3 Immunogenicity and Safety of a Meningococcal Conjugate Vaccine Given Concomitantly With Other Vaccines in Toddlers | 1200     | • Open-label (immunology laboratory technicians will be blinded to group assignment), randomized, parallel-group, active-controlled, multi-center study | • Immunogenicity and safety | • SSD: Nov. 2016  
• DE: 2020 |
## Dengue Vaccine Booster

<table>
<thead>
<tr>
<th>Study</th>
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<th>Patients</th>
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<th>Endpoints</th>
<th>Status</th>
</tr>
</thead>
</table>
| NCT02824198 | Immunogenicity and Safety of a Tetravalent Dengue Vaccine Booster Injection in Subjects Who Previously Completed a 3-dose Schedule | 260      | • Multi-center, observer-blind, randomized, placebo-controlled, Phase II non-inferiority trial | • Immunogenicity and safety of a booster dose                              | • SSD: Jul. 2016  
• DE: 2019 |

**Tags:** Immuno-inflammation, Cardiovascular, Rare Diseases, Infectious disease, MS, Neuro, Gene therapy, Vaccines
# Rabies Vaccine

## Purified Vero Rabies

<table>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>NCT03145766</td>
<td>Phase 2 Immunogenicity and Safety of a Purified Vero Rabies Vaccine</td>
<td>320</td>
<td>• Multicenter, observer-blind, controlled, randomized, Phase II study</td>
<td>• Immunogenicity and safety</td>
<td>• SSD: Apr. 2017</td>
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<td>• DE: 2018</td>
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</tbody>
</table>
# Dengue Vaccine Co-administration w/ HPV

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<tr>
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| NCT02979535 | Phase 3b Immunogenicity and Safety of a Tetravalent Dengue Vaccine Administered Concomitantly or Sequentially With Cervarix® | 480      | • Randomized, open-label, multicenter study  | • Immunogenicity and safety of a Tetravalent Dengue Vaccine administered concomitantly or sequentially with Cervarix® | • SSD: Nov. 2016  
|             |                                                                              |          |                                             |                                                                            | • DE: 2019                    |
# Dengue Vaccine Co-administration w/ HPV

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