

## **R&D Investor Event**

#### Lead with innovation

June 23, 2020



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### **R&D Investor Event | Agenda**

Introduction	Paul Hudson John Reed	Chief Executive Officer Global Head of Research & Development				
<b>Platforms</b> Synthorx	Yong Jun Liu Marcos Milla	Global Head of Research Chief Scientific Officer, Synthorx				
<b>Pathways</b> Venglustat	John Reed Karin Knobe Pablo Sardi	Global Head of Research & Development TA Head, Rare Diseases and Rare Blood Disorders Development TA Head, Rare and Neurologic Diseases Research				
Q&A session 1 20'						
<b>Patients</b> Fitusiran & BIVV001	Vanessa Wolfeler Dietmar Berger	Global Franchise Head, Rare Blood Disorders Global Head of Development, Chief Medical Officer				
Capabilities COVID-19	Dietmar BergerGlobal Head of Development, Chief Medical OfficerJohn ShiverGlobal Head of Research & Development, Sanofi Pasteur					
Conclusion	John Reed	Global Head of Research & Development				
Q&A session 2 40						



## Introduction

Paul Hudson

**Chief Executive Officer** 





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### Continuing to deliver on our priority assets...

#### Asset Key progress in H1 2020

Planned initial submission<sup>(1)</sup>

<b>Pupixent</b> ®(2)	AD U.S. 6-11 years & China Adults approval; EoE pivotal results	Launched
Fitusiran & BIVV001 <sup>(3)</sup>	Fitusiran & BIVV001 Phase 3 enrollment ongoing	2021e/2022e
SERD '859	ASCO 3 posters; 2/3L mBC Phase 3 enrollment ongoing	2021e
Venglustat	ADPKD Part A of Phase 3 fully enrolled (TKV endpoint)	2022e
Nirsevimab <sup>(4)</sup>	Phase 3 ongoing; investor event planned	2023e
BTKi '168 <sup>(5)</sup>	PoC in RMS; pivotal studies started	2024e

Breakthrough designation



PoC: Proof of concept, clinical and commercial evidence to initiate pivotal study; AD: Atopic dermatitis; EoE: Eosinophilic esophagitis; mBC: metastatic Breast cancer; ADPKD: Autosomal dominant polycystic kidney disease; TKV: Total kidney volume; RMS: Relapsing multiple sclerosis

(1) First submission for assets with multiple potential indications (2) Breakthrough designation for AD 6-11 years. Dupixent<sup>®</sup> in collaboration with Regeneron (3) In collaboration with Sobi (4) In collaboration with AstraZeneca (5) In collaboration with Principia

#### ... and our other late-stage molecules

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Asset	Key progress in H1 2020	Planned initial submission(	
Sarclisa <sup>®</sup>	2L RRMM positive pivotal results; 3L RRMM approval U.S. & EU <sup>(3)</sup>		
🚏 Libtayo®(2)	1L NSCLC and 2L BCC positive pivotal results	Launched	
MenQuadfi™	U.S. approval for ≥2 year-old age group	Approved	
Avalgluco- sidase alfa	LOPD positive pivotal trial results	2020e	
🕈 Sutimlimab	Cold Agglutinin Disease Phase 3 priority review	2020e	
Olipudase alfa	ASMD positive pivotal trial results	2021e	
Anti-CEACAM5 '701	Phase 3 lung and Phase 2 in additional settings initiated	2022e	
Breakthrough designatio RRMM:	n Relapsed refractory multiple myeloma; NSCLC: Non-small-cell lung carcinoma; BCC: Basal cell carcinoma; LOPI myelinase deficiency. (1) First submission for products with multiple potential indications. (2) Breakthrough design	2	

Libtayo<sup>®</sup> in collaboration with Regeneron (3) Sarclisa<sup>®</sup> approved for patients with>2 prior therapies, including lenalidomide and a proteasome inhibitor. Approved in the U.S., EU, Canada, Australia and Switzerland, indication in certain non-U.S. countries also includes disease progression on last therapy

<sup>7</sup> 





## Introduction

John Reed

**Global Head of Research & Development** 



### Sanofi R&D is transforming



#### Focus on priorities

- Diabetes & Cardiovascular exit
- Focus on priority assets, within 5 therapeutic areas<sup>(1)</sup>



#### Lead with innovation

 Building industry leading platforms to deliver practicechanging medicines



#### Accelerate efficiency

- Achieving top-tier
  performance
- Digital R&D operations



#### Reinvent how we work

- Faster and more rigorous decision making
- Urgency of execution

## Maximizing the potential of our priority assets



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BC: Breast cancer; PD: Parkinson disease; ADPKD: Autosomal dominant polycystic kidney disease; RSV: Respiratory syncytial virus; MS: Multiple sclerosis (1) In collaboration with Regeneron (2) In collaboration with Sobi (3) In collaboration with AstraZeneca (4) In collaboration with Principia (5) Hemophilia A, B, with and without inhibitors

### Progressing on our long-term promises





## Concrete illustrations of Sanofi's approach to R&D

Platforms Expanded tools for drug discovery

Pathways Deep understanding of disease pathways

Patients Relentless patient focus

Capabilities

Leveraging expanding capabilities

#### **Synthorx**

Boosting the impact of cancer immunotherapies by expanding the genetic alphabet

#### Venglustat

Leveraging our knowledge of disease pathways to invent new medicines applicable to multiple disorders

#### Fitusiran & BIVV001<sup>(1)</sup>

Turning cutting-edge protein engineering and new modalities into innovative patient offerings

#### COVID-19

Applying our scale and broad platforms to battle a global health crisis



#### Platforms Synthorx

Yong-Jun Liu Global Head of Research

Marcos Milla Chief Scientific Officer, Synthorx



### Sanofi platforms to expand the druggable universe

85% of the proteome remains undruggable

Multiple platforms required to address difficult targets

Opportunity to create new ("synthetic") biology for tackling disease



# Tri-specific T-cell activation: A novel platform for cancer immunotherapy

**Optimized T-cell activation** by stimulating T-cells through both TCR (CD3) and co-stimulatory receptor (CD28):

- Conventional CD3-based T-cell engagers provide only "signal 1": TCR
- In the absence of "signal 2" from co-stimulatory receptors, this promotes activation-induced T-cell death, limiting anti-tumor response
- CD28 provides "signal 2" to promote survival of activated T-cells and generation of "T-cell memory"

**Improved targeting:** Tri-specific antibody also has the potential to bind 2 targets on tumor cells: the established target CD38 as well as CD28, which is expressed on myeloma and other hematologic cancers



#### Mechanism of action<sup>(1)</sup>

TCR: T-cell receptor



(1) Adapted from Garfall *et al*, Trispecific antibodies offer a third way forward for anticancer immunotherapy, Nature 575, 2019 ©2019, Springer Nature (under permission requested). Article screenshot from Wu *et al*, Trispecific antibodies enhance the therapeutic efficacy of tumor-directed T cells through T cell receptor co-stimulation, Nat Cancer 2020 ©2020, Springer Nature (under permission requested)

# SAR442257: First-in-class next-gen T-cell immunotherapy, now in the clinic

#### Trispecific CD38 antibody

- T-cell engager aiming for enhanced therapeutic efficacy vs conventional T-cell engagers
- Expect CAR-T cell-like efficacy with an antibody

#### Dual function of targeting CD28

- Co-stimulation of T-cells by delivering "signal 2" to promote T-cell survival
- Targeting CD28 (expressed on >95% of MM cells) directs T-cells more efficiently to myeloma cells (even at low levels of CD38 expression)

## Trispecific CD38 antibody showed a 3- to 4-log higher killing potency against human myeloma cell lines vs. daratumumab<sup>(1)</sup>



#### First-in-human study in RRMM and RR-NHL initiated



MM: Multiple myeloma; RRMM: Relapsed refractory multiple myeloma; RR-NHL: Relapsed refractory non-Hodgkin lymphoma (1) Wu, L. *et al* Nature Cancer, 2019: mix peripheral blood mononuclear cells with myeloma cell lines and applied antibodies SAR442257 is an asset under investigation and is not approved by any regulators

## Next-gen T-cell engagers based on Nanobody® platform

#### Advantages inherent to Nanobody® platform

Ability to tune PK profile through clinically validated half-life extension technology reduces dosing frequency

Formatting flexibility

- Multiple options for optimizing
- Multi-valent and multi-specific formats to increase efficacy, selectivity and/or avoid escape
- Engineer high affinity on low-density tumor antigens

Faster production cycle time at lower cost (expressed in yeast) **T-cell** 

Excellent CMC characteristics, robust manufacturing

A leading IP position in the industry



#### Multiple Nanobody<sup>®</sup> candidates entering the clinic next year

# Synthorin platform: Expanding the genetic alphabet to generate more diverse protein drugs



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# Application of the X-Y genetic code for recombinant production of therapeutic proteins: Synthorins

Engineered E. coli to install a novel amino acid (nAA) utilizing X-Y to produce optimized biologics



Production system for Synthorins in E. coli

Translation Machinery decodes X-Y codons introduce nAA into "Synthorin" proteins

#### First application is multi-functional, site-specific pegylation

# IL-2 has dual pharmacology explained by differential engagement of IL-2 receptor subtypes



SANOFI 🕤 Treg: regulatory T cells; Teff: effector T cells; NK: Natural Killer; ILC2: Group 2 Innate Lymphoid Cells

# Site-specific pegylation to turn interleukins into precision drugs for oncology and autoimmune disease indications

#### THOR-707 IL-2 Synthorin for immuno-oncology



#### Unique properties

-"Not-alpha"

- PEG blocks engagement of IL-2R α chain
- Selectively expands antitumor CD8+ T and NK cells
- No expansion of immunesuppressive CD4+ regulatory T cells
- No activation of type 2 innate lymphoid cells and eosinophils responsible for vascular leak syndrome

THOR-809 IL-2 Synthorin for autoimmune diseases



#### **Unique properties**

- PEG blunts engagement of IL-2R β chain, making potency at IL-2R αβγ contingent on α chain binding
- Selectively expands CD4+ regulatory T cells
- No expansion of CD8+ T and NK Cells
- Preclinical therapeutic efficacy in delayed type hypersensitivity

"Reduced beta"

Shared pharmacological properties: pegylation increasing IL-2 half-life and reduced immunogenicity risk

# Single THOR-707 dose induces lymphocyte expansion in non-human primates without increasing eosinophils

Aldesleukin induced both lymphocyte and eosinophil expansion in humans<sup>(1)</sup>

THOR-707 single dose NHP leukocyte Subpopulations: High lymphocytes, no eosinophils



### Compared to aldesleukin, THOR-707 shows a strong preference for expanding tumor-fighting lymphocytes vs. eosinophils which are responsible for VLS



## HAMMER FIH study: Promising early biomarker data

## Pharmacodynamics markers of surrogate anti-tumor activity

Peak peripheral expansion post initial THOR-707 dose<sup>(1)</sup>

## Pharmacodynamics markers of selectivity and surrogate safety

Fold change in cell count<sup>(2)</sup>

Peak peripheral expansion post initial THOR-707 dose<sup>(1)</sup>



Fold change in cell count<sup>(2)</sup>

FIH: First In Human; RP2D: Recommended Phase 2 Dose



(1) Mean across dose cohort of 4 patients, maximum fold expansion following one dose of THOR-707 (2) Normalized to pre-treatment count (3) Surrogate Marker of Potential Tumor-Promoting Immunosuppression (4) Surrogate Marker of Potential Vascular Leak Syndrome (5) Estimated from Melero et al, ESMO 2018, 2-week expansion (6) Estimated from Bentebibel *et al*, Cancer discovery, 2019, mean expansion between day 1 (before treatment) and day 8 (after treatment) THOR-707 is an asset under investigation, not approved by any regulators

# Landscape of IL-2 compounds in development – THOR707 has best-in-class profile

× No 🕢 Yes, limited ✔ Yes	aldesleukin <sup>(1)</sup>	ALKS 4320 <sup>(2)</sup>	NKTR-214 <sup>(3)</sup>	<b>RG7461</b> <sup>(4)</sup>	THOR-707 <sup>(5)</sup>
Description	Native IL2	Fusion protein IL-2 fused to IL-2Rα	Random Lys pegylation with (on avg.) 6 cleavable PEGs	Fusion protein IL-2v fused to FAP-mAb	Site-specific pegylation
Dose (IL-2 equivalent)	37 μg/kg TID x 5 days	6 µg/kg/day	6 µg/kg Q3W	~26 µg/kg QW equivalent	16 μg/kg, dose escalation ongoing
Not Alpha	×	$\checkmark$	×	$\checkmark$	$\checkmark$
Exposure <sup>(6)</sup>	×	×	×	$\bigcirc$	
Q3W dosing	×	×	$\checkmark$	×	$\checkmark$
Expansion of CD8+T-cells Significant fold increase above baseline <sup>(7)</sup>	n.a.		$\bigcirc$	$\checkmark$	
Expansion of NK cells Significant fold increase above baseline <sup>(8)</sup>	n.a.	$\checkmark$	$\checkmark$	$\checkmark$	
No expansion of CD4-Tregs No significant fold increase above baseline <sup>(9)</sup>	n.a.		×	$\checkmark$	
No Vascular Leak Syndrome	×	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
Tolerability	×	$\checkmark$	×	$\checkmark$	$\checkmark$
No anti-drug antibodies	×	?	$\checkmark$	×	

TID: three times a day; QD: every day; QW: every week; Q3W: every three weeks; NK: Natural killer; n.a.: non available (1) Lotze M T *et al*, J Immunol 1985; Meyers FJ, *et al* Clin Pharmacol Ther. 1991; Foureau *et al* Cancer Immunol Immunother 2014; Schantz *et al*, Arch Otolaryngol Head Neck Surg 1990 (2) Lopes *et al*, Journal for ImmunoTherapy of Cancer 2020; medication package insert (3) Bentebible *et al*, Cancer discovery, 2019; Charych *et al*, PLOS One 2017 (4) Melero *et al*, ESMO 2018. IL-2 equivalent dose assessed based on recommended dose (20 mg), avg. weight (70 kg) and relative size (RG7461 11x larger than IL-2 as the cytokine is fused to 150,000 daltons IgG) (5) Synthorx data (6) Only THOR-707 has shown sustained exposure: RG7461 exposure is reduced with repeat dosing, all other compounds have low exposure (7) Yes: >2x; Yes, limited: 1.5-2x; No: <1.5x (9) Yes: <2x; No: <2x. For illustrative purposes. Not based on head to head data. Limited conclusions should be derived from this indirect comparison given the variability of study designs. Clinical relevance of these differences is still under investigation

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# Beyond interleukins, the X-Y genetic code technology enables diverse applications using nAA chemistry



### Conclusions

Expanded Genetic Alphabet has the potential to turn interleukins into precision drugs for oncology and autoimmune diseases

THOR-707 and THOR-809 harness dual IL-2 biology:

- "Not-alpha" THOR-707 selectively upregulates CD8+ T and NK cells to eliminate tumors without increasing CD4+ regulatory T cells (Tregs) and eosinophils
- "Decreased beta" THOR-809 selectively upregulates Tregs to suppress autoimmunity without upregulating CD8+ T and NK cells

**Initial biomarker data from human studies** increases our confidence in **THOR-707** potential to become partner of choice for checkpoint inhibitors (no ADA issues; well tolerated; target pathway engagement)

**THOR-707** dose-finding Phase 1b combinations with anti-PD-1 (T-cell) and anti-CD38 (NK cell), final Phase 1 results and RP2D expected in 2021

Wide applicability of Synthorx platform expected to yield multiple clinical candidates in coming years, with further precision interleukins to enter the clinic in 2021-2023



#### Pathways Introduction

John Reed

**Global Head of Research & Development** 



### Two areas where Sanofi science stands out specifically



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 IO: Immuno-oncology; Vx: Vaccines; I&I: Immunology and Inflammation
 (1) Selection of assets (2) Including Hunter disease, Hurler disease, Niemann-Pick Note: Includes Sanofi wholly-owned and assets developed in collaboration

## Human immunology: A view into our immunomodulatory pipeline and products



# Human immunology: A view into our immunomodulatory pipeline and products



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Mf: Macrophages; PC: Plasma cells; TH: T helper cells; TCTL: Cytotoxic T lymphocytes; NK: Natural killer cells; TReg: Regulatory T cells; EOS: Eosinophils; SM: Small molecule; NAb: Nanobody; IO: Immuno-oncology; I&I: Immunology and Inflammation. (1) In collaboration with Regeneron (2) In collaboration with Revolution Medicines (3) In collaboration with BioNTech (4) In collaboration with Principia (5) In collaboration with Denali Therapeutics (6) In collaboration with ImmuNext **31** 

## Sanofi's pioneering history in Monogenic disorders



#### Life-threatening and life-altering indications, still highly under-diagnosed





Karin Knobe

TA Head, Rare Diseases & Rare Blood Disorders Development

Pablo Sardi TA Head, Rare and Neurologic Diseases Research



### Leveraging Sanofi's heritage in LSD and GSL metabolism



Sanofi Genzyme LSD heritage



Making a difference in patients with LSDs

Expanding the reach in more common disorders with large unmet need

## Broad role of glycosphingolipids in cellular functions

- GSLs are components of many cellular membranes
- GSLs can interact with adjacent proteins within the membrane to modulate protein function
- Plasma membrane GSLs provide surface features that provide cell recognition signals
- GSLs modulate many cellular processes required for normal function



## GCS-inhibition as central regulator of GSL metabolism





GSL: Glycosphingolipid; GCS: Glucosylceramide synthase, coded by gene *UGTG*; Gcase: Glucocerebrosidase, coded by gene *GBA*; GlcCer (GL1): Glucosylceramide; LacCer: Lactosylceramide; GL-3: Globotriaosylceramide; ADPKD: Autosomal dominant polycystic kidney disease; PD: Parkinson's disease; GM2 gangliosidoses: rare autosomal recessive genetic disorders including Tay-Sachs and Sandhoff disease; SRT: Substrate-reduction therapy Venglustat is an asset under investigation and is not approved by any regulators
# Treatment dimensions give venglustat potential to be best-in-class oral GCS-inhibitor



GCS: Glucosylceramide synthase; LSD: Lysosomal storage disease; GSL: Glycosphingolipid

(1) Examples include miglustat, eliglustat, lucerastat

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# Venglustat: Leveraging GCS biology in CNS & key organs



### Central Manifestations of LSDs: GD3 & GM2

Brain

U.S. diagnosed GD3 patients: ~75 U.S. diagnosed GM2 patients: ~100 PD with GBA mutations and potentially idiopathic PD with GSL pathologies

U.S. GBA-PD population: ~78,000

Kidney/ heart Potential new treatment option for Fabry patients with lower disease burden (~40% of diagnosed) ADPKD with PKD1 or PKD2 mutations affecting GSL signaling in cilia

U.S. diagnosed Fabry patients: ~3,000

U.S. ADPKD population: ~140,000



GCS: Glucosylceramide synthase; CNS: Central nervous system; LSD: Lysosomal storage disease; GSL: Glycosphingolipid; GD3: Type 3 Gaucher Disease; GM2 gangliosidoses: rare autosomal recessive genetic disorders including Tay-Sachs and Sandhoff disease; PD: Parkinson's disease; ADPKD: Autosomal dominant polycystic kidney disease. Venglustat is an asset under investigation and is not approved by any regulators

## Venglustat's activity validated in GD3 and in Fabry

**Gaucher Type 3** 

Phase 2 data at 1 year

Paired *t*-test between seed-based connectivity maps



Enhanced occipito-parietal connectivity is the most prominent feature

#### Fabry

Phase 2 data at 3 years



#### **Reduction in lysosomal GL3 storage**

# Venglustat: Transformative potential in ADPKD

# GCS inhibition restores differentiation signaling in ADPKD

# Robust preclinical data in validated animal model<sup>(1)</sup>



#### Phase 3 STAGED-PKD: Stage 2 initiated at high dose based on tolerability profile



GCS: Glucosylceramide synthase; ADPKD: Autosomal dominant polycystic kidney disease; GSL: Glycosphingolipid; GlcCer: Glucosylceramide; MRI: Magnetic resonance imaging. (1) Natoli et al, Nat Med. 2010 Venglustat is an asset under investigation and is not approved by any regulators

## Venglustat: Potentially first DMT in GBA-PD

GBA mutations associated with higher PD incidence and greater disease severity

Progression to dementia

Cumulative incidence (%)

Venglustat: potential to be the first disease modifying therapy in PD via GBA-PD

#### MOVES-PD: first industry sponsored clinical trial in a genetic form of PD

Mean % change in CSF GL-1 at week 4 across doses<sup>(1)</sup>



DMT: Disease-modifying therapy; PD: Parkinson's disease; HR: Hazard ratio; GSL: Glycosphingolipid; GCase: Glucocerebrosidase; GCS: Glucosylceramide synthase; CSF: Cerebrospinal fluid; GlcCer (GL1): Glucosylceramide (1) MOVES-PD part 1 data presented at WORLD 2019 for 32 weeks of treatment. pool Japan + Rest of World



### Preclinical evidence for therapeutic benefit of venglustat in sporadic PD population

Loss of GCase activity in sporadic PD and Lewy bodies dementia<sup>(1)</sup>

GCS inhibition reduces toxic  $\alpha$ -Synuclein conversion<sup>(2)</sup>

GCS inhibition improves cognitive function in mouse  $model^{(3,4)}$ 



#### FDA recommendation to include idiopathic PD patients in Phase 3



\*p-value vs. Control <0.05; \*\*p-value vs. Control <0.01 GCase: Glucocerebrosidase; GCS: Glucosylceramide synthase; PD: Parkinson's disease; LD: Low dose, HD: High dose; WT: Wild type (1) Chiasserini *et al*, Mol. NDD 2015 (2) Zunke *et al*, Neuron 2018 (3) Sardi *et al*, PNAS 2017 (4) In A53T-α-synuclein mice carrying wild-type *Gba* allele Venglustat is an asset under investigation and is not approved by any regulators

## Lysosome pathway defects are central to most PD

#### Gene mutations associated to PD affect lysosomal function, GCase activity and GSL flux

- Synuclein overexpression and aggregation reduce GCase activity<sup>(1)</sup>
- SNCA and LRRK2 mutations reduce vesicular trafficking and lysosomal activity<sup>(1,2)</sup>
- LRRK2 and GBA mutations reduce GCase activity and affect GSLs levels<sup>(2,3)</sup>
- Excessive burden of LSD gene variants in PD<sup>(4)</sup>

Modulation of GSLs levels by GCS inhibition improves lysosomal and neuronal function, and reduces alpha-synuclein toxicity



### GSLs regulate cellular processes driving Parkinson's disease progression<sup>(5)</sup>

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GCase: Glucocerebrosidase; GCS: Glucosylceramide synthase; PD: Parkinson's disease; GSL: Glycosphingolipid; LSD: Lysosomal storage disease (1) Mazzulli *et al*, Cell 2011 (2) Ysselstein *et al*, Nature Comm 2019 (3) Gegg *et al*, Ann Neurol 2012 (4) Robak *et al*, Brain 2017 (5) Sardi *et al*, PNAS 2017; Zunke *et al*, Neuron 2018

# PD-FIDI: Potentially first validated digital endpoint in PD

	ePRO & App		Wrist-worn device _ assessments
Part I Motor impacts	Part II Dyskinesia impacts <sup>(1)</sup>	Part III Functional motor impacts	Part IV Continuously monitored functional impacts
13 items adapted from MDS-UPDRS Part II	<ul> <li>2 items adapted from MDS-UDyRS Part lb</li> </ul>	<ul> <li>Gait and balance including stride length</li> <li>Postural tremor of hands</li> <li>Pronation/supination of hands</li> <li>Finger tapping</li> </ul>	<ul> <li>Gait and balance</li> <li>Physical activity and general mobility</li> <li>Measured passively and continuously</li> </ul>
Exploratory Sleep Assessments	<ul><li>4 original ePRO items assessing</li><li>Sleep duration and quality actigrate</li></ul>	sleep duration and quality aphy measures (measured passive	ly and continuously)

#### Additional data could mean lower variability, so fewer subjects needed to achieve statistical power



PD: Parkinson's disease; FIDI: Functional impacts digital instrument; MDS-UPDRS: Movement Disorder Society Unified Parkinson's Disease Rating Scale; MDS-UDyRS: Movement Disorder Society Unified Dyskinesia Rating Scale; PRO: Patient reported outcomes (1) Only included for patients taking PD medications

# Venglustat: Leveraging GCS biology in CNS & key organs



#### GD3: LEAP Phase 2/3 ongoing<sup>(1)</sup>

Submission expected by H1 2023

### Brain

#### GM2: Phase 3 started

Submission expected by H2 2023

### Parkinson (MOVES-PD)

- Phase 2 PoC expected by H1 2021
- Submission expected by 2025

#### Fabry: Phase 3 in preparation

• Submission expected by H2 2023

### ADPKD (STAGED-PKD)

- Part A fully enrolled (TKV)
- Part A (TKV) pivotal results expected by Q4 2021
- Submission expected by 2022

Kidney/ heart

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GCS: Glucosylceramide synthase; CNS: Central nervous system; LSD: Lysosomal storage disease; PoC: Proof of concept, clinical and commercial evidence to initiate pivotal study; ADPKD: Autosomal dominant polycystic kidney disease; GD3: Type 3 Gaucher Disease; GM2 gangliosidoses: rare autosomal recessive genetic disorders including Tay-Sachs and Sandhoff disease; TKV: Total Kidney Volume; GFR: Glomerular Filtration Rate. Venglustat is an asset under investigation and is not approved by any regulators (1) Current LEAP Phase 2 study to be expanded to Phase 3 by end of year

### **Q&A** session 1



Paul Hudson Chief Executive Officer



John Reed Global Head of R&D



**Jean-Baptiste de Chatillon** Chief Financial Officer



**Bill Sibold** Global Head of Sanofi Genzyme



**Yong-Jun Liu** Global Head of Research



**Dietmar Berger** Global Head of Development



Marcos Milla Chief Scientific Officer, Synthorx



Karin Knobe TA Head, RD and RBD Development



Pablo Sardi TA Head, RND Research



Shannon Resetich Global Franchise Head, RD



### Patients Fitusiran & BIVV001<sup>(1)</sup>

Vanessa Wolfeler Global Franchise Head, Rare Blood Disorders

Dietmar Berger Global Head of Development, Chief Medical Officer



# Limitations of current Hemophilia treatments



#### Future treatments aim to minimize treatment burden and remove activity restrictions



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# Patients' daily activities are defined by protection levels



# Current treatments require trade-off between treatment burden and protection levels



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#### **Factors**

High protection, high dose frequency

- Short-period: 2-3 infusions per week required
- Patients at risk when at trough
- Patients at risk when missing infusion

#### Non-Factor (emicizumab)

Reduced dose frequency, lower protection

- ~9% FVIII equivalent level<sup>(4)</sup>
- 90% patients experiencing acute bleeds require additional Factor<sup>(5)</sup>
- 7% patients on monthly regimen<sup>(6)</sup>

Patients achieve protection permitting strenuous activity <50% of their time

(1) Illustration of Factor VIII levels of Hemophilia A patients, or equivalent for non-Factor (2) Advate 50 IU/Kg (Phase 3) (3) Eloctate<sup>®</sup> 50 IU/Kg (Phase 3). Source: Mahlangu, J., *et al*, Blood (4) Equivalent FVIII level, based on Lenting P *et al*, ISTH 2019, Lenting P *et al*, Blood Adv. 2020 (5) Consumer Awareness, Trial, and Usage study among patients conducted over 359 Adult patients and caregivers surveyed online in April 2019, of which 131 were Adult Hemophilia A patients and 78 were Hemophilia A caregivers. Patients who switched to emicizumab answered questions specific to their treatment experience (6) 2019 Specialty Pharmacy data obtained through Specialty Pharmacy Distributors, Hemophilia Alliance HTCs and Direct HTCs. No head-to-head studies comparing the above products have been conducted

# Our ambition: Pushing patients protection beyond current limitations



### **BIVV001** target profile

Higher for longer

- One week of protection, including ~3.5 days at normal activity level and ~6 days at strenuous activity level
- Increased joint protection

#### Fitusiran target profile

High-efficacy monthly therapy

- Aiming for 15-20% FVIII equivalent level<sup>(4)</sup>, allowing strenuous activity level
- First real once-monthly Hemophilia treatment

Aiming to get more patients above strenuous level for >80% of their time<sup>(6)</sup>



(1) Illustration of Factor VIII levels of Hemophilia A patients, or equivalent for non-Factor (2) Advate 50 IU/Kg (Phase 3) (3) Eloctate<sup>®</sup> 50 IU/Kg (Phase 3). Source: Mahlangu, J., *et al*, Blood (4) Equivalent FVIII level, based on Lenting P *et al*, ISTH 2019, Lenting P *et al*, Blood Adv. 2020 (5) BIVV001 50 IU/Kg (Phase 1) – Day 22 (6) Assuming FVIII level >15% all the time for fitusiran and 6 days a week for BIVV001. Fitusiran and BIVV001 are assets under investigation and are not approved by any regulators – BIVV001 in collaboration with Sobi. No head-to-head studies comparing the above products have been conducted

### BIVV001: New class of factor therapy engineered to achieve higher factor levels, for longer



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Scissors represent thrombin activity. rFVIIIFc: recombinant factor VIII Fc fusion protein; VWF: von Willebrand factor. aXTEN® is a registered trademark of Amunix Pharmaceuticals, Inc. (1) Julie Rayes et al, A molecular jewel for hemophilia A treatment, Blood, 2020 ©2020, Blood Journal (under permission requested); Ekta Seth Chhabra et al, BIVV001, a new class of factor VIII replacement for hemophilia A that is independent of von Willebrand factor in primates and mice, Blood, 2020 ©2020, Blood Journal (under permission requested) (2) Konkle BA et al. Haemophilia, 2019 (3) Podust VN. et al. J Control Release, 2016 (4) Roopenian DC, Akilesh S, Nat Rev Immunol, 2007 (5) Shapiro A. Expert Opin Biol Ther. 2013. BIVV001 is an asset under investigation and is not approved by any regulators - in collaboration with Sobi

# No bleed events in BIVV001 Phase 1 repeat dose study



#### No bleeds reported during treatment period and for at least 10 days after last dose of BIVV001



(1) Pre-study treatment regimen: 21 patients treated with on-demand regimen and 3 with prophylactic regimen (2) Once-weekly BIVV001 dose of 50 IU/kg (n=10) or 65 IU/kg (n=14). Source: World Federation of Hemophilia Virtual Summit (June 2020). Exploratory results, BIVV001 is an asset under investigation and is not approved by any regulators – in collaboration with Sobi

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# Fitusiran: Aiming to be the only therapy designed to bring high protection in a subcutaneous monthly therapy

Unique approach to rebalance the deficient coagulation cascade by reducing antithrombin



Hemophilia A and B are caused by an **imbalance in hemostasis** due to Factor deficiency, resulting in insufficient thrombin generation

Fitusiran is designed to **improve thrombin generation** by lowering antithrombin

**250+ patients enrolled in clinical trials**, with 4+ years of clinical data

# Fitusiran target profile confirmed in Phase 2 OLE trial

Efficacy: median ABR



OLE: Open-label extension: ABR: Annualized bleed rate

Safety and tolerability (n=34)

No thrombotic events in any subjects who remained compliant with the bleed management guidelines since their implementation in December 2017

No cases of anti-drug antibody formation

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#### 0.84 overall median ABR during observation period & median 2.6 yrs of fitusiran dosing (max. 4.7 yrs)



Data cutoff: March 10, 2020. ABR and duration represent pooled data from Phase 1 and Phase 2 OLE studies. Phase 1 data are included if gap between studies was <56 days. Only subjects with 28 days of follow-up during the observation period are included in this analysis. Clinical hold period (last dose before hold + 29 days, first dose after hold + 28 days) is excluded. Source: Fitusiran Phase 2 OLE Interim Results, WFH (June 2020). Fitusiran is an asset under investigation and is not approved by any regulators

# Fitusiran: Potential best-in-class non-Factor therapy for all Hemophilia patients

	Fitusiran (target profile)Emicizumab(2)		Ib <sup>(2)</sup>
ABR <1 for Hem A & B (monthly dose)	<b>S</b>	×	ABR >2 for $Q4W^{(2)}$ for Hem A
First SQ for all Hem B	<b></b>	×	
1 prefilled syringe <sup>(1)</sup>	Ø	×	Up to 4 injections <sup>(3)</sup>
Low-volume fixed dose	Ø	×	Weight-based dose; up to $4 \text{ mL}^{(3)}$
Room temperature stable	Ø	×	Refrigeration & cold chain storage required
Reversal agent available	Ø	×	



ABR: annual bleed rate; Hem: Hemophilia; Q4W: once every four weeks; SQ: subcutaneous (1) Fitusiran prefilled syringe, room temperature stable: planned for launch (2) Hemlibra<sup>®</sup> U.S. Prescribing Information (3) Hemlibra<sup>®</sup> U.S. Prescribing Information, assuming some patients may be over 75kg. Fitusiran is an asset under investigation and is not approved by any regulators

### Wrap-up: Sanofi portfolio addresses white space of current patients needs



### **Expected submissions**

#### H2 2021<sup>(8)</sup> – Fitusiran

- Three ATLAS studies (>12 years old)
- Two of three Phase 3 studies fully enrolled; near completion of 3<sup>rd</sup>
- Pediatric Phase 3 study enrolling

#### H1 2022<sup>(8)</sup> – BIVV001

- Phase 3 study in previously treated patients initiated (>12 years), n=150
- Study initiated in Q4 2019
- Endpoints to capture impact on restrictions in daily activities

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Q4W: once every four weeks; Q2W: once every two weeks; Q1W: once per week; ABR: annualized bleed rate

(1) emicizumab: 2.1 ABR with Q4W; 1.6 ABR with Q2W; 0.6 ABR with Q1W (U.S. prescribing information; median ABR (HAVEN-3 for Q1W & Q2W, HAVEN-4 for Q4W) (2) Based on Evaluate Pharma 2020, U.S. patients (3) 7% of remicizumab patients on monthly dosing – 2019 Specialty Pharmacy data obtained through Specialty Pharmacy Distributors, Hemophilia Alliance HTCs & Direct HTCs (4) fitusiran: 0.84 ABR with Q4W (Phase 2 OLE Interim Results) (5) BIVV001: Target Product Profile aiming for weekly dose, no bleed reported in Phase 1 repeat dose study (6) Individualized prophylaxis varies from daily to every 4 days and between <1 and >1 ABR (7) No head-to-head studies comparing the efficacy of emicizumab and fitusiran or BIVV001 have been conducted (8) Expected submission in the U.S. Fitusiran and BIVV001 are assets under investigation and are not approved by any regulators – BIVV001 in collaboration with Sobi



# Aiming for first "true" cure in Hemophilia with LVV GT



### AAV limitations for Hemophilia patients

- DNA insert size limitations: challenging to package BDD Factor VIII cDNA into AAV
- Limitations on target population
  - 21-74% of patients have pre-existing antibodies to AAV<sup>(1)</sup>
  - Episomal AAV cargo gets diluted when liver grows – expression lost if treated too early, cannot treat pediatric patients
- FVIII levels continuously declining over time (long-term Hemophilia A data)



### LVV target profile for Hemophilia patients

- Larger DNA insert size permits BDD Factor VIII cDNA and additional control elements
- Aiming to address all patients
  - No pre-existing antibodies to VSVG pseudotyped LVV
  - Treat in pediatrics: LVV cargo integrates into the host genome, growing with the patient
- **Expected to be durable** (integrative nature), as demonstrated in preclinical models

#### Sanofi/SR-TIGET to develop first-ever in vivo lenti application – expected to enter clinic by 2022



LVV: Lentiviral vector; GT: Gene Therapy; AAV: Adeno-associated virus; BDD: B-domain deleted; cDNA: complementary DNA; VSVG: Vesicular stomatitis virus glycoprotein; SR-TIGET: San Raffaele-Telethon Institute for Gene Therapy (1) Steven W. Pipe, John Wiley & Sons Ltd. 2020



### Expanding capabilities COVID-19

Dietmar Berger Global Head of Development, Chief Medical Officer

> John Shiver Global Head of R&D, Sanofi Pasteur



# Expanding R&D capabilities, focusing on Specialty Care and Vaccines

News ways of Digital R&D & Real Focused, simplified **Enhanced patient** working & centricity World Evidence footprint engagement models Patient-related insights DARWIN platform for Simplifying R&D Integrated Development • • . (PROs, tolerability, Real World Evidence footprint, focusing organization health value, etc.) clinical operations where Digital transformation of Fast, rigorous decision-• it matters **Clinical Operations** Patient-centric trial making – taking 'smart' • conduct (leverage Global hubs for priority risks Optimization of telehealth, home Therapeutic Areas development candidates Early engagement of . delivery, digital tools through artificial Investments in leadinginvestigators to optimize when possible) intelligence, indication edge capabilities: study design (#1 Sponsor of Global Clinical Trials)<sup>(1)</sup> E-consent and patient selection, trial biomanufacturing, Gene • portal improving patient optimization, etc. Therapy CMC, evolutive Multiple collaborations experience vaccines facility Digital in CMC and (e.g. BARDA, GSK) **Regulatory Affairs** 

# Ambitious digital transformation across Sanofi R&D

#### **Real World Evidence**

- Commercial value increase of marketed products
- Clinical trial hypotheses support, virtual control arms
- Disease models, biomarker-driven population enrichment
- Search of new indications for development compounds

**Key digital** 

programs

Pharmacovigilance

#### **Digital Research**

- In-silico screening
- Al-driven compound optimization
- *De-novo* antibody design
- ML-driven developability assessment

#### **Digital Clinical Operations**

- Innovative, evidence-based design
- Digital biomarkers, sensors & tools
- Patient engagement platform
- Investigator & site platform
- Real-time data management
- Digital control room

#### **Digital in CMC**

- Paperless CMC labs
- One data platform
- Digitized workflows across all CMC, including external partners
- Process modeling simulation

#### **Digital in Regulatory Affairs**

- Automated document generation
- Language translation
- Cloud-based AI to support document management

SANOFI 🧳 AI: Artificial intelligence; ML: Machine learning; CMC: Chemistry, manufacturing and control

### Improved capabilities and fast execution

### Illustration with BTKi ('168)<sup>(1)</sup>

Phase 1 and 2 conducted 1 year faster than benchmarks Phase 3 studies being launched across the full MS spectrum<sup>(2)</sup>

- Data exchange platform (Patient Site Sponsor) enabling continuous data exchange
- Home delivery of study drug; leverage of telehealth when possible (visits, performance outcomes, etc.)
- Remote site visits enabling business continuity



Trials maintained during COVID-19 97% of patients are on long-term extension study

- Planning Phase 3 studies at risk to start as fast as possible (sites pre-identified and on-boarded)
- Control arm size in PPMS reduced to accelerate study completion while maintaining acceptable statistical power
- Optimized study design through early patient and investigator engagement



First patient enrolled in RMS trial on June 11, despite pandemic

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# 160+ COVID-19 vaccine candidates in development based on multiple technologies

As of June 19, 2020



#### Half of clinical candidates are based on exploratory vaccine platforms



(1) Includes replicating and non replicating (2) Includes viral proteins, subunits, virus-like particles Source: Milken Institutes

# Vaccine platforms: Different safety and efficacy profiles



VAERD: Vaccine-associated enhanced respiratory disease



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# Sanofi is developing two complementary vaccines – each with differentiated profile

Recombinant proteinbased vaccine (Baculovirus)



Protein antigen Adjuvant

mRNA vaccine (natural) mRNA



- Licensed recombinant platform<sup>(1)</sup>
- Existing large-scale capacity
- BARDA collaboration
- Collaboration with gsk for proven AS03 adjuvant
- Innovative approach<sup>(2)</sup> natural mRNA
- Potential for accelerated development
- Significant existing investment in mRNA capacity to be applied towards vaccine

Unknowns

Description

Platform

May require booster dose(s)

 Unknown safety risks (potentially differentiated safety profile vs. modified mRNA)

Strengths

- Most de-risked technology
- Existing capacities to leverage

- Promising technology
- Only established large scale mRNA
   manufacturing capacity (Translate Bio)



# Baculovirus: Accelerated timeline – earliest approval in June 2021



### Acceleration levers

## Simplification of clinical studies

- Phase 1/2: studying fewer dosages
- Phase 3: selection of adjuvant with highest probability of success

# Uncoupling of R&D and industrial timelines

 'At risk' production of drug substance and drug product

#### Potential for emergency use authorization (up to 100 million doses in January 2021)

SANOFI 🌍 (1) In U.S. and EU; development plans and registration pathway being consolidated with rest of the world

## Baculovirus: Aiming for 1 billion doses in 2021

Variables determining number of vaccine doses



### Final capacity depending on yield and dosing, multiple levers to maximize it

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# Sanofi: Differentiated mRNA candidate





#### **Proprietary LNP**

- Suitable LNP candidate for intramuscular delivery identified and selected from extensive screening
- Formulation optimization completed with large scale LNP process development underway

#### Natural mRNA

- Multiple SARS-CoV-2 antigen
   mRNA constructs identified
- Codon optimized version of naturally occurring mRNA, with no chemically modified nucleotides

# Established manufacturing capabilities

- Expertise in mRNA manufacturing developed over 10+ years: scale designed and built for chronic disease products, transferable to vaccine production

Existing large-scale cGMP manufacturing capacity

- Ongoing 100-gram single-batch mRNA production; demonstrated 250-gram scale
- Expected annual capacity of 90-360 million doses

### First in Human expected in Q4 2020 and earliest approval in H2 2021



Translate

# Conclusion: The world needs multiple vaccines – Sanofi is committed to play a key role in fight against COVID-19

Unprecedented global race to develop vaccines to combat COVID-19 epidemic: >160 vaccine candidates based on established and novel vaccine platforms

Sanofi develops two complementary vaccines, each with differentiated profile

Acceleration of Baculovirus vaccine timelines: Phase 1/2 starting in September with >400 patients – potential launch by H1 2021 with up to 1 billion doses capacity

Potential emergency use authorization by January 2021 with up to 100 million doses of Baculovirus vaccine

Differentiated mRNA candidate to provide additional capacity (90-360 million doses expected annually), increase overall probability of success and strengthen our capabilities to prepare for future pandemics



# Conclusion

John Reed

**Global Head of Research & Development** 



# **Building our presence in Gene Therapy**

Internal pipeline of clinical candidates

- Initial focus on AAV platform
  - Experience in Ophthalmology in the clinic
  - Investigating rare and neurological indications
- Pilot projects on innovative platforms: 3rd-generation lentivirus in Hemophilia, non-viral DNA delivery, mRNA

Standalone Genomic Medicine Unit

- Gene Therapy drug discovery unit in Cambridge (Boston)
  - Vector design
  - Capsid engineering
  - Dedicated capabilities (CMC, Regulatory, Translational Medicine)
- Expanding with new talents

# In-house bioproduction capabilities

#### Leveraging established capacities at Sanofi

- Fully dedicated CMC unit in Boston area
- GMP-grade manufacturing for clinical supply in Lyon Gerland

# Concrete illustrations of Sanofi's approach to R&D

Platforms Expanded tools for drug discovery

Pathways Deep understanding of disease pathways

Patients Relentless patient focus

Capabilities

Leveraging expanding capabilities

### **Synthorx**

Boosting the impact of cancer immunotherapies by expanding the genetic alphabet

### Venglustat

Leveraging our knowledge of disease pathways to invent new medicines applicable to multiple disorders

### Fitusiran & BIVV001<sup>(1)</sup>

Turning cutting-edge protein engineering and new modalities into innovative patient offerings

### COVID-19

Applying our scale and broad platforms to battle a global health crisis
## Key milestones for priority molecules

	Dupixent <sup>®(1)</sup>	Pivotal results in Asthma 6-11 years old	<b>H</b> 2 2020					
		Pivotal results in PN and CSU	H2 2021					
	Fitusiran & BIVV001 <sup>(2)</sup>	Fitusiran & BIVV001 pivotal results in Hem A/B & Hem A	<b>H1/H2 2021</b>					
	SERD '859	Proof of Concept in combination with CDK4/6i and adjuvant BC	<b>H</b> 2 2020					
VenglustatProof of Concept in GBA-PDNirsevimab(3)Phase 2b data to be presented at		Proof of Concept in GBA-PD	N1 2021					
		Phase 2b data to be presented at dedicated Sanofi event	H2 2020					
	BTKi '168 <sup>(4)</sup>	First patient in for all Phase 3 studies	<b>H</b> 2 2020					
	PN: Pruring podularis: CSU: Chronic spontaneous urticaria: CDK: Cyclin-dependent kinase: RC: Breast cancer: PD: Parkinson disease: Hem: Hemophilia: PoC: Proof of							

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PN: Prurigo nodularis; CSU: Chronic spontaneous urticaria; CDK: Cyclin-dependent kinase; BC: Breast cancer; PD: Parkinson disease; Hem: Hemophilia; PoC: Proof c concept, clinical and commercial evidence to initiate pivotal study
 (1) In collaboration with Regeneron (2) In collaboration with Sobi (3) In collaboration with AstraZeneca (4) In collaboration with Principia

### **Upcoming milestones**

😭 Priority assets	— H2 2020 →	— H1 2021 →	———— H2 2	2021	———— FY 2	022
Regulatory	Sutimlimab Cold agglutinin disease	Sarclisa <sup>®</sup> Refractory MM	Libtayo <sup>®(1)</sup> 2L BCC	Dupixent®(1) Asthma 6-11yo	Sarclisa <sup>®</sup> 1L ND-MM Ti (IMROZ)	Dupixent <sup>®(1)</sup> Chronic spontaneous urticaria
(Unless specified	Flublok <sup>®</sup> EU approval	Baculovirus Recomb. Vx COVID-19	Libtayo® <sup>(1)</sup> 1L NSCLC monotherapy	mRNA Vaccine COVID-19	SERD '859 2L-3L monotherapy BC	Olipudase alfa Niemann-Pick type B
otherwise, indicates first potential approval		MenQuadfi™ ≥12 months EU approval	Avalglucosidase alfa Pompe disease		Dupixent <sup>®(1)</sup> Prurigo nodularis	Fitusiran Hemophilia A/B
in the U.S. or EU)		Shan 6 DCGI license			Libtayo <sup>®(1)</sup> 1L NSCLC in combo with CT	Shan 6 WHO pre-qualification
Submission	Sarclisa <sup>®</sup> Refractory MM (IKEMA)	Dupixent <sup>®(1)</sup> Asthma 6-11yo	Olipudase alfa Niemann-Pick type B	Dupixent <sup>®(1)</sup> Prurigo nodularis ☆	Dupixent <sup>®(1)</sup> Chronic spontaneous urticaria	Dupixent <sup>®(1)</sup> AD 6mo-5yo
	Libtayo <sup>®(1)</sup> 1L NSCLC monotherapy	Baculovirus Recomb. Vx COVID-19	FitusiranHemophilia A/B	mRNA Vaccine COVID-19	Anti-CEACAM5 '701 2/3L NSCLC monotherapy (LC03)	Dupixent <sup>®(1)</sup> Eosinophilic esophagitis
	Libtayo <sup>®(1)</sup> 2L BCC		SERD '859 2L-3L monotherapy BC		Venglustat ADPKD	Dupixent <sup>®(1)</sup> Bullous pemphigoid
	Avalglucosidase alfa Pompe disease		Libtayo <sup>®(1)</sup> 1L NSCLC in combo with CT		BIVV001 <sup>(2)</sup> Hemophilia A	Libtayo <sup>®(1)</sup> 2L Cervical cancer
	Shan 6 DCGI submission				Sarclisa <sup>®</sup> 1L ND-MM Ti (IMROZ)	
Pivotal results	Dupixent <sup>®(1)</sup> Asthma 6-11yo	Fitusiran 😭	Libtayo <sup>®(1)</sup> 1L NSCLC in combo with CT	BIVV001 <sup>(2)</sup> Hemophilia A	Venglustat ADPKD	Dupixent <sup>®(1)</sup> Eosinophilic esophagitis
		SERD '859 2L-3L monotherapy BC	Dupixent <sup>®(1)</sup> Prurigo nodularis	Sarclisa <sup>®</sup> 1L ND-MM Ti (IMROZ)	Anti-CEACAM5 '701 2/3L NSCLC monotherapy (LC03)	Dupixent <sup>®(1)</sup> Bullous pemphigoid
			Dupixent <sup>®(1)</sup> Chronic spontaneous urticaria	Libtayo <sup>®(1)</sup> 2L Cervical cancer	Dupixent <sup>®(1)</sup> AD 6mo-5yo	Nirsevimab <sup>(4)</sup> RSV
					VerorabVax <sup>®</sup> Rabies	
Proof of	SERD '859 1L mBC in combo with CDK4/6i	SHP2 '720 <sup>(3)</sup> Solid tumors	T-cell eng. CD3/CD123 '234 Acute myeloid leukemia	SERD '859 2L mBC in combo with Pi3Ki	Anti-CEACAM5 '701 2/3L NSCLC with ramucirumab	aCD38 mAb Fc '085 Multiple myeloma
Concept	SERD '859 Adjuvant BC	ST400 <sup>(6)</sup> Beta thalassemia	TGFb '459 NSCLC, MM, CRC, MuC	Sarclisa <sup>®</sup> Kidney transplant	Anti-CEACAM5 '701 1L NSCLC in combo with PD-1	miRNA-21 '375 Alport syndrome
		BIVV003 <sup>(6)</sup> Sickle cell disease	Sarclisa <sup>®</sup> Peripheral T-cell lymphoma	Sarclisa <sup>®</sup> SC formulation	THOR-707 Monotherapy in Solid tumors	Fluzone <sup>®</sup> HD QIV pediatrics
		VenglustatGBA-PD	BIVV020 Cold agglutinin disease		SKYPAC (PCV) <sup>(5)</sup> Pneumococcal	RSV active immunization RSV

AD: Atopic dermatitis; BC: Breast cancer; PD: Parkinson disease; m: metastatic; ADPKD: Autosomal dominant polycystic kidney disease; BCC: Basal cell carcinoma; NSCLC: Non-small-cell lung carcinoma; NDMM: Newly diagnosed multiple myeloma; SC: Subcutaneous; MM: Metastatic melanoma; CRC: Colorectal cancer; MuC: Metastatic urothelial carcinoma; MM: Multiple myeloma; DCGI: Drug Controller General of India; WHO: World Health Organization (1) In collaboration with Regeneron (2) In collaboration with Sobi (3) In collaboration with Revolution Medicines (4) In collaboration with AstraZeneca (5) In collaboration with SK (6) In collaboration with Sangamo

# Sanofi positioned to deliver the next-generation of medicines and vaccines

#### **Platforms**

- Unique blend of cutting-edge technologies
- **Demonstrated platforms:** Nanobodies®, Multispecifics, Antibody Drug Conjugates, Vaccines...
- Exploratory platforms: Synthorins, mRNA, Gene Therapy...

#### **Pathways**

- Advancing human immunology
   across multiple areas of high
   unmet need
- Pioneering history in monogenic disorders
- Bringing Sanofi's heritage in LSD beyond rare diseases

#### **Patients**

- Connecting with patients
   through digital technologies
- Breaking the barriers of today's standard of care
- Leveraging real world evidence to make a real difference in patient day-to-day lives

#### **Expanding capabilities**

- Digital R&D
- Faster Clinical Operations

#### Everything begins and ends with the patient





Michael | Kidney Transplant | U.S.



Shannae | MPS I | Australia



Tucker | Hemophilia B | U.S.



James | Prostate Cancer | U.S.



Heather | aTTP | U.S.



Nancy | AD | U.S.



Sami | Pompe | Palestine



Laurie | RA | Canada



Grethe | Multiple Sclerosis | Denmark

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MPS: Mucopolysaccharidosis; AD: Atopic Dermatitis; aTTP: Acquired thrombotic thrombocytopenic purpura; CAD: Cold agglutinin disease; RA: Rheumatoid arthritis

Gary | CAD | U.S.

#### Q&A session 2



Paul Hudson Chief Executive Officer



John Reed Global Head of R&D



Jean-Baptiste de Chatillon Chief Financial Officer



**Bill Sibold** Global Head of Sanofi Genzyme



**Thomas Triomphe** Global Head of Sanofi Pasteur



**Dietmar Berger** Global Head of Development



Yong-Jun Liu Global Head of Research



Marcos Milla Chief Scientific Officer, Synthorx



Karin Knobe TA Head, RD and RBD Development



Pablo Sardi TA Head, RND Research



**Robert Peters** TA Head, RBD Research



Vanessa Wolfeler Global Franchise Head, RBD



Shannon Resetich Global Franchise Head, RD



John Shiver Global Head of R&D, Sanofi Pasteur



## **R&D Investor Event**

#### **Appendices**

June 23, 2020



### R&D Pipeline – New Molecular Entities<sup>(\*)</sup>

Pha (Tota	se 1 1:21)	Pha	se 2 al : 5)	Phase 3 (Total : 7)	Registration (Total : 2)	
SAR441344 <sup>(**)(1)</sup> Anti-CD40L mAb Multiple Sclerosis	<b>ST400</b> <sup>(۳)(5)</sup> <i>Ex Vivo</i> ZFN Gene-Edited Cell Therapy, Beta thalassemia	SAR440340 <sup>(**)(11)</sup> Anti-IL33 mAb COPD	R SAR439859 SERD Metastatic Breast Cancer 2/3L	SAR442168 <sup>(**)(13)</sup> BTK inhibitor Multiple Sclerosis	SAR341402 (insulin aspart) Rapid acting insulin Type 1/2 Diabetes (EU)	
SAR439459, mono & with cemiplimab <sup>(**)(11)</sup> , anti-TGFb mAb Advanced Solid Tumors	BIVV003 <sup>(**)(5)</sup> Ex Vivo ZFN Gene-Edited Cell Therapy, Sickle Cell Disease	<b>romilkimab</b> Anti-IL4/IL13 bispecific mAb Systemic Scleroderma	<b>SAR339375</b> miRNA-21 Alport Syndrome	<b>avalglucosidase alfa</b> Neo GAA Pompe Disease	<b>sutimlimab</b> Anti Complement C1s mAb Cold Agglutinin Disease	
REGN5458 <sup>(**)(2)</sup> Anti-BCMAxCD3 bispecific mAb Relapsed Refractory MM	BIVV020 Complement C1s inhibitor	R olipudase alfa rhASM ASMD <sup>(12)</sup> ad+ped		venglustat Oral GCS inhibitor ADPKD <sup>(14)</sup>		
Anti-MUC16xCD3 bispecific mAb Ovarian Cancer	SAR443060(**%6) RIPK1 inhibitor <sup>(7)</sup> Amyotrophic Lateral Sclerosis			fitusiran RNAi targeting anti-thrombin Hemophilia A and B		
SAR442720 <sup>(**)(3)</sup> SHP2 inhibitor Solid Tumors	SAR443122 <sup>(**)(6)</sup> RIPK1 inhibitor <sup>(7)</sup> Inflammatory indications			BIVV001( <sup>™)(15)</sup> rFVIIIFc − vWF − XTEN <sup>(16)</sup> Hemophilia A		
SAR440234 T cell engaging multi specific mAb Leukemia	<b>SAR441169</b> <sup>(۳)(8)</sup> RORC (ROR gamma T) antagonist, Psoriasis			<b>nirsevimab<sup>(**)(17)</sup></b> Respiratory syncytial virus Monoclonal Antibody		
SAR441000 <sup>(**)(4)</sup> , mono & with PD1, Cytokine mRNA Solid tumors	<b>SAR441236</b> Tri-specific neutralizing mAb HIV	<ul><li>R Registrational Study (other the O Opt-in rights products for which other the O Opt-in rights products products for which other the O Opt-in rights products products</li></ul>	an Phase 3) h rights have not been exercised yet	SAR408701 Maytansin-loaded anti-CEACAM5 mAb, NSCLC 2/3L		
<b>SAR442085</b> Anti CD38 mAb Fc engineered Multiple Myeloma	Next Gen PCV <sup>(**)(9)</sup> Pneumococcal Conjugate Vaccines	Immuno-inflammation Oncology Rare Diseases	MS & Neuro Diabetes Cardiovascular & metabolism			
O REGN5459 <sup>(**)(2)</sup> Anti-BCMAxCD3 bispecific mAb Relapsed Refractory MM	Herpes Simplex Virus Type 2 <sup>(**)(10)</sup> HSV-2 therapeutic vaccine	(1) Developed in collaboration with Imn (2) Renearan product for which Sand	Vaccines nunext	(14) Autosomal Dominant Polycystic K	idney Disease	
SAR444245 (THOR-707), mono & combo, Non-alpha IL-2 Solid tumors	<b>Respiratory syncytial virus</b> Infants 4-month and older Vaccines	Developed in collaboration with Rev     Developed in collaboration with Bio     Developed in collaboration with San     Developed in collaboration with D	rolution Medicines NTech ggamo ali	<ul> <li>Developed in contaboration with Sool</li> <li>Recombinant Ccagulation Factor VIII Fc – von Willebrand Factor – XTEN Fusion prot</li> <li>Developed in collaboration with AstraZeneca</li> <li>Phase of projects determined by clinicalitis.gov disclosure timing when relevant</li> <li>Partnered and/or in collaboration – Sanofi may have limited or shared rights on some of these products</li> <li>mono = monotherapy; mAb = monoclonal antibody; RRMM = Relapsed Refractory Multiple Myelon</li> <li>GCS = glucosylceramide synthase; N-H Lymphoma = Non-Hodgkin Lymphoma</li> </ul>		
SAR442257 Anti-CD38xCD28xCD3 trispecific mAb, MM / N-H Lymphoma		(/) Receptor-interacting serine/threonit (8) Developed in collaboration with Lea (9) Developed in collaboration with SK (10) Developed in collaboration with Rmr (11) Developed in collaboration with Rmr	ne-protein kinase 1 d Pharma mune Design/Merck generon			
SANOFI 🎝		<ul> <li>Acid Sphingomyelinase Deficiency a</li> <li>Developed in collaboration with Print</li> </ul>	also known as Niemann Pick type B ncipia		79	

## Additional Indications(\*)

Phase 1 (Total : 6) Phase 2 (Total : 18)		Phase 3 (Total : 25)		Registration (Total : 3)	
Cemiplimab <sup>(**)(1)</sup> + REGN4018 <sup>(**)(2)</sup> Ovarian Cancer	dupilumab <sup>(**)(1)</sup> Grass pollen allergy	<b>isatuximab + cemiplimab<sup>(**)(1)</sup></b> Relapsed Refractory MM	Dupixent <sup>@(*)(1)</sup> Asthma 6 - 11 years old	isatuximab Newly Diag. MM Te <sup>(8)</sup> (GMMG)	MenQuadfi™ U.S. 2y+ , EU 1y+
SAR439859 + palbociclib <sup>(3)</sup> Metastatic Breast Cancer	<b>R</b> sarilumab <sup>(**)(1)</sup> Polyarticular Juvenile Idiopathic Arthritis	<b>isatuximab + cemiplimab<sup>(∞)(1)</sup></b> Lymphoma	<b>dupilumab<sup>(™)(1)</sup></b> Eosinophilic Esophagitis	<b>isatuximab</b> 2L RRMM (IKEMA)	Dupixent <sup>®(**)(1)</sup> AD 6 – 11 years old (U.S., EU)
sutimlimab Immune Thrombocytopenic Purpura	R sarilumab <sup>(**)(1)</sup> Systemic Juvenile Arthritis	<b>isatuximab + atezolizumab</b> <sup>(6)</sup> mCRC	Dupixent <sup>@(**)(1)</sup> AD 6 months - 5 years old	<b>isatuximab</b> 1L Newly Diag. MM Ti <sup>(9)</sup> (IMROZ)	<b>Aubagio<sup>®</sup></b> Relapsing MS – Pediatric
SAR442720 <sup>(**)(4</sup> ) + cobimetinib <sup>.</sup> Relapsed Refractory solid tumors	<b>SAR440340<sup>(**)(1)</sup></b> Asthma	<b>isatuximab + atezolizumab</b> <sup>(6)</sup> Solid Tumors	dupilumab <sup>(**)(1)</sup> COPD	isatuximab Smoldering multiple myeloma	
SAR443060 <sup>(**)(5)</sup> Multiple sclerosis	<b>dupilumab<sup>(**)(1)</sup></b> Peanut Allergy	SAR408701 + ramucirumab NSCLC 2/3L	<b>dupilumab</b> <sup>(**)(1)</sup> Bullous pemphigoid	Lemtrada <sup>®</sup> Relapsing Remitting MS - Pediatric	
Yellow Fever Vaccine (Vero cell)	R cemiplimab <sup>(**)(1)</sup> 2-L Basal Cell Carcinoma	<b>venglustat</b> Fabry Disease	dupilumab <sup>(**)(1)</sup> Chronic spontaneous urticaria	<b>Cerdelga®</b> Gaucher T1, ERT switch Pediatric	
	SAR439859 Breast Cancer adjuvant	<b>venglustat</b> Gaucher Type 3	<b>dupilumab</b> <sup>(**)(1)</sup> Prurigo nodularis	venglustat GM2 gangliosidosis	
	isatuximab 1-2L AML / ALL pediatrics	venglustat GBA-PD <sup>(7)</sup>	<b>sarilumab</b> <sup>(**)(1)</sup> Giant Cell Arteritis	<b>Praluent<sup>® (**)(1)</sup></b> LDL-C reduction - Pediatric	
	isatuximab patients awaiting kidney transplantation	<b>SP0173</b> Tdap booster US	<b>sarilumab</b> <sup>(**)(1)</sup> Polymyalgia Rheumatica	<mark>MenQuadfi™</mark> 6w+ (US / EU)	
			cemiplimab <sup>(**)(1)</sup> 1L NSCLC	Shan 6 Pediatric hexavalent vaccine	Immuno-inflammation
R Registrational study (other than Phas	se 3)		cemiplimab <sup>(**)(1)</sup> + chemotherapy 1L NSCLC	VerorabVax <sup>®</sup> (VRVg) Purified vero rabies vaccine	
Opt-in rights products for which rights     Developed in collaboration with Regene     (2) Regeneron product for which Sanofi ha	Opt-in rights products for which rights have not been exercised yet         Studies in collaboration with Regeneron         (6)         Studies in collaboration with Genentech Inc. (atezolizumab)           Regeneron product for which Sanofi has opt-in rights         (7)         Parkinson's Disease with an associated GBA mutation           Prizer product (palbocicitib)         (8)         Transplant eligible           Developed in collaboration with Revolution Medicines –         (9)         Transplant ineligible           Developed in collaboration with Denali         Eveloped in collaboration with Denali         Eveloped in collaboration with Denali			<b>fitusiran</b> Hemophilia A and B pediatric	Oncology Rare Diseases
<ol> <li>Pfizer product (palbocicilib)</li> <li>Developed in collaboration with Revolu cobimetinib is a Genentech product</li> <li>Developed in collaboration with Denali</li> </ol>					Rare Blood Disorders MS & Neuro
(*) Phase of projects determined by clinical (**) Partnered and/or in collaboration - Sanc COPD = chronic obstructive pulmonary disease; AN MM = multiple myloma;; RRMS = Relapsing / Remit	Itrials.gov disclosure timing when relevant ofi may have limited or shared rights on some of the AL = acute myeloïd leukemia; ALL = acute lymphobl ting Multiple Sclerosis	se products astic leukemia;			Diabetes Cardiovascular & metabolism Vaccines

## Expected submission timeline<sup>(1)</sup>



## Pipeline movements since Q1 2020

	Additions / Moves		Removals from	Sanofi pipeline
Registration	sutimlimab Anti Complement C1s mAb Cold Agglutinin Disease			
	Aubagio® Relapsing MS – Pediatric			
Phase 3	SAR442168 <sup>(**)(1)</sup> BTK inhibitor Multiple Sclerosis		Pediatric pentavalent vaccine <sup>(**)(2)</sup> Japan	
Phase 2	SAR408701 + ramucirumab NSCLC 2/3L			
Phase 1	SAR442257 Anti-CD38xCD28xCD3 trispecific mAb, MM / N-H Lymphoma			

