

# Capital Markets Day Play to Win

December 10, 2019



## 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, future clinical data and analysis, including post marketing, 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, the absence of guarantee that the product candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic conditions, the impact of cost containment initiatives and subsequent changes thereto, the average number of shares outstanding as well as those 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, 2018. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

## **Additional information**

The tender offer for the outstanding shares of Synthorx common stock ("Synthorx") referenced in this communication has not yet commenced. This communication is for informational purposes only and is neither an offer to purchase nor a solicitation of an offer to sell shares of Synthorx, nor is it a substitute for the tender offer materials that Sanofi and its acquisition subsidiary will file with the U.S. Securities and Exchange Commission (the "SEC") upon commencement of the tender offer. At the time the tender offer is commenced, Sanofi and its acquisition subsidiary will file tender offer materials on Schedule TO, and thereafter Synthorx will file a Solicitation/Recommendation Statement on Schedule 14D-9 with the SEC with respect to the tender offer. THE TENDER OFFER MATERIALS (INCLUDING AN OFFER TO PURCHASE, A RELATED LETTER OF TRANSMITTAL AND CERTAIN OTHER TENDER OFFER DOCUMENTS) AND THE SOLICITATION/RECOMMENDATION STATEMENT WILL CONTAIN IMPORTANT INFORMATION. HOLDERS OF SHARES OF Synthorx ARE URGED TO READ THESE DOCUMENTS WHEN THEY BECOME AVAILABLE (AS EACH MAY BE AMENDED OR SUPPLEMENTED FROM TIME TO TIME) BECAUSE THEY WILL CONTAIN IMPORTANT INFORMATION THAT Synthorx STOCKHOLDERS SHOULD CONSIDER BEFORE MAKING ANY DECISION REGARDING TENDERING THEIR SHARES. The Offer to Purchase, the related Letter of Transmittal and certain other tender offer documents, as well as the Solicitation/Recommendation Statement, will be made available to all holders of shares of Synthorx at no expense to them. The tender offer materials and the Solicitation/Recommendation Statement will be made available to all holders of shares of Synthorx at no expense to them. The tender offer materials and the Solicitation/Recommendation Statement will be made available for free at the SEC's web site at www.sec.gov. Additional copies may be obtained for free by contacting Sanofi at ir@sanofi.com or on Sanofi's website at https://en.sanofi.com/investors.

## Agenda

Strategic outlook	Paul Hudson	Chief Executive Officer		
Margin expansion	Jean-Baptiste de Chatillon	EVP, Chief Financial Officer		
Lead with innovation	John Reed	EVP, Global Head of R&D		
Q&A	Sanofi Executive Committee			
Breakout sessions				



## Strategic outlook

Paul Hudson

**Chief Executive Officer** 



## We hear you

#### Select analyst quotes, 2014-2019



## We see opportunities



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## Play to win



## Our key growth drivers





## Dupixent® targets a central pathway in T2 inflammation



- Type 2 inflammation -
  - Atopic Dermatitis
  - Asthma
  - Nasal Polyps
  - Respiratory / Dermatology adjacencies

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#### Type 2 pathway - transformative potential similar to Type 1

Ankylosing Spondylitis



References: 1. Kaiko GE et al. Immunol 2008; 123: 326–38. 2. Eyerich K & Eyerich S J Eur Acad 2017; 32: 692–703. 3. Raphael I et al. Cytokine 2015; 74: 5–17. 4. Nakayama T et al. Annu Rev Immunol 2017; 35: 53–84. 5. Coates LC et al. Semin Arthritis Rheum 2016; 46: 291–304

## Dupixent<sup>®</sup> has major growth potential in Atopic Dermatitis

## Ambition to become leading biologic with dermatologists

U.S. monthly NBRx at dermatologists<sup>(1)</sup>



## Opportunity to increase uptake and expand to pediatric segments

U.S. population by age group (patients in '000, approximate)<sup>(2)</sup>

	Adults	12-17Y	6-11Y <sup>(6)</sup>	<6Y <sup>(6)</sup>
Prevalence	8,200	2,500	2,500	2,400
Moderate-to-severe	2,600	800	700	700
Biologics eligible <sup>(4)</sup>	1,700	400	90	75
Dupixent <sup>®</sup>	59 <sup>(5)</sup>	5 <sup>(5)</sup>	Submission: 2019e 2022e	
Share of Biologics eligible	3.5%	1.3%		

(1) IQVIA Patient Insights

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(2) Truven Payer Claims Data, IQVIA Sanofi Custom SOB Report, Data on file

(3) FDA approved on March 11, 2019

(4) Moderate-to-Severe uncontrolled for adults and 12-17Y (label population); Conservative assumption for <12Y with severe uncontrolled only

(5) Reflects the number of patients currently on treatment

(6) Estimated regulatory submission timing and data has not been reviewed by any regulatory authority

## Dupixent<sup>®</sup> driving market expansion in Asthma

#### Best uptake among biologics

Cumulative NBRx in Asthma (monthly, all channels)<sup>(1)</sup>



## Expanding biologics market, gaining share and seeking pediatric indication

U.S. population by age group (patients in '000, approximate)<sup>(2)</sup>

	Adults/ 12-17Y	6-11Y <sup>(6)</sup>
Prevalence	23,500	2,400
Moderate-to-severe <sup>(3)</sup>	1,600	200
Biologics eligible <sup>(4)</sup>	900	75
Treated on biologics	118	3
Dupixent®	11 <sup>(5)</sup>	Submission 2021e
Share of Biologics eligible	1.2%	
Share of Biologics class	9.0%	

#### ~80% of Dupixent® asthma patients to date have been naive to biologics



 IQVIA Patient Insights; Dupixent launched in November 2018
 Truven Payer Claims data, IQVIA Sanofi Custom SOB Report, data on file
 Moderate-to-severe with persistent use of medium to high dose ICS or OCS use or biologic

- (4) Uncontrolled despite persistent use of medium to high dose ICS + >1 controller or OCS .
- (5) Reflects the number of patients currently on treatment
- (6) Estimated regulatory submission timing and data has not been reviewed by any regulatory authority

## Dupixent<sup>®</sup>: Significant potential in adjacent indications





Source: epidemiology data primarily from Sanofi Real World Evidence platform

COPD: chronic obstructive pulmonary disease

Note: Allergic Bronchopulmonary Aspergillosis not included subject to regulatory approval as a standalone indication

(1) Investigational program not yet reviewed by any regulatory authority

(2) Approved by FDA

(3) Not included in > $\in$ 10 billion ambition due to heterogeneity of disease

## Vaccines: Strong growth driven by 3 core franchises & RSV





## Accelerate portfolio of potential transformative therapies

Planned submission<sup>(1)</sup> Ambition fitusiran 2021e Delivering on new patient dynamics - convenience 2022e & BIVV001<sup>(2)</sup> 2021e SERD ('859) Master switch for endocrine signaling in HR+ breast cancer 2022e venglustat Leveraging LSD biology in multiple rare diseases and beyond nirsevimab<sup>(3)</sup> 2023e Cost-effective RSV prophylaxis for all infants BTKi ('168)<sup>(4)</sup> 2024e First disease modifying therapy to address MS drivers in the brain

BTKi: bruton tyrosine kinase inhibitor; LSD: lysosomal storage disease; MS: multiple sclerosis; RSV: respiratory syncytial virus; SERD: selective estrogen receptor degrader; HR+: hormone-receptor positive

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First submission for products with multiple potential indications, investigational program not yet reviewed by any regulatory authority (2) In collaboration with SOBI

(3) In collaboration with AstraZeneca(4) In collaboration with Principia

## Hemophilia: Patient experience drives choice

#### Target profiles vs. marketed products



#### Market research

75% patients switched to emicizumab
 due to convenience (less frequent dosing, SC administration)<sup>(6)</sup>

<10% emicizumab patients on monthly dosing<sup>(7)</sup>

~90% emicizumab patients experienced acute bleeds<sup>(6)</sup>

ABR: annualized bleed rate; SC: subcutaneous; BIVV001 is in collaboration with SOBI

- (1) emicizumab: 2.1 ABR with q4w; 1.6 ABR with q2w; 0.6 ABR with q1w (Hemlibra prescribing information; median ABR (HAVEN-3 for Q1w & q2w, HAVEN-4 for q4w) (6) 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
- (2) fitusiran: 0.97 ABR with q4w (Phase 2 OLE Interim Results)

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- (3) BIVV001: Target Product Profile aiming for weekly dose, and ~3.5 days with FVIII activity >40%
- (4) Individualized prophylaxis varies from daily to every 4 days and between <1 and >1 ABR
- (5) No H2H studies comparing efficacy of emicizumab and fitusiran or BIVV001 have been conducted

patients and 78 were Hemophilia A caregivers. Patients who switched to emicizumab answered questions specific to their treatment experience (7) 2019 Specialty Pharmacy data obtained through Specialty Pharmacy Distributors, Hemophilia Alliance HTCs and Direct HTCs

## SERD ('859): Potential to improve the treatment of HR+ BC



Al: aromatase inhibitor; BC: Breast Cancer; CDK: cyclin-dependent kinases CT: chemotherapy F: fulvestrant HER2: human epidermal growth factor receptor-2 HR+: hormone-receptor positive mTORi: mammalian target of rapamycin inhibitors Pi3Ki: phosphoinositide 3-kinase inhibitor QTc: QT corrected SoC: standard of care Tam: tamoxifen TNBC: triple negative breast cancer Note: asset under investigation, not approved by regulators (4) Data to be disclosed at an upcoming medical meeting

(5) In vitro activity

(1) Waks AG, et al. JAMA 20019;321:288-300;

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(2) Kantar Health - CancerMpact 2019;

(3) Some patients only receive endocrine therapy, depending on disease staging

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# Venglustat: Leveraging LSD biology in multiple rare diseases

#### GCS inhibition to potentially treat 3 types of disease





LSD: lysosomal storage diseases; GCS: glucosylceramide synthase; ADPKD: autosomal dominant polycystic kidney disease; GBA-PD: Parkinson's disease related to glucocerebrosidase (GBA) gene mutations

(1) Subset of patients being studied in GBA-PD development program

(2) Internal estimates

(3) Potential accelerated submission in the U.S. after Stage 1 of STAGED-PKD

Note: project under investigation, not approved by regulators

# Nirsevimab: Goal to be cost-effective RSV prophylaxis for <u>all</u> infants

### 98% of infants still at risk



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#### High disease burden

- High medical care costs from RSV-related LRTI (\$4.2bn<sup>(4)</sup>)
- Congested ER / ICU during RSV seasons
- Risk of long-term sequelae

#### Nirsevimab has potential to cover all infants through single injection

RSV: Respiratory syncytial virus; LRTI: lower respiratory tract infections; ER: emergency department; ICU: intensive care unit

Estimates based on birth cohort projected in 2024; Lancet Global Health Vol 7 Jan 2019
 U.S. RSV-related infant hospitalizations; Hall, NEJM 2009 Feb 5;360(6):588-98

- (3) Palivizumab eligible population: CHD/CLD & ≤28wGA
- (4) Estimated global costs of in-patient and out-patient management in children <5 years in 2017, unpublished data from Respiratory Syncytial Virus Consortium in Europe
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Note: asset under investigation in collaboration with AstraZeneca, not approved by regulators

# BTKi ('168): Potential to be first DMT to address MS drivers in the brain





## Synthorx acquisition<sup>(1)</sup> perfectly aligned with R&D strategy

Company overview	<ul> <li>Clinical stage biotechnology company</li> <li>Founded in 2014, headquartered in San Diego, CA</li> <li>Listed on NASDAQ under ticker symbol THOR since December 2018</li> </ul>
Lead program	<ul> <li>THOR-707 "not-alpha" IL-2 Synthorin for solid tumors in Phase 1/2</li> <li>Pre-clinical anti-tumor activity alone and in combination with anti-PD-1</li> <li>Very promising profile due to improved pharmacology and dosing</li> </ul>
Expanded Genetic Alphabet platform	<ul> <li>Aims at optimizing therapeutics in oncology and autoimmune disorders</li> <li>Adds new DNA base pair, enabling incorporation of novel amino acids</li> <li>Designed to create optimized biologics referred to as Sythorins</li> </ul>

## Targeting 30% BOI margin by 2022

#### Sanofi expected BOI margin evolution





# Diabetes & cardiovascular cashflow to be maximized in mature markets

### Declining DCV sales<sup>(1)</sup>



### Immediate decisions<sup>(3)</sup>

- Discontinue DCV research
- Optimize commercial model
- No launch of efpeglenatide<sup>(2)</sup>
- Restructure Onduo JV
- Praluent<sup>®</sup> resources right-sized



DCV: diabetes and cardiovascular
(1) Last 12 months sales; Q4 2018 reported sales through Q3 2019 reported sales
(2) Sanofi commits to complete ongoing studies – Sanofi will look for a partner to take over and commercialize efpeglenatide
(3) Subject to consultation with social partners and works councils

## New Global Business Unit organization to support strategy



GBU: Global Business Unit; RBD: Rare Blood Disorder; RD: Rare Disease; PPH: Polio, Pertussis & Hib; IA: Industrial Affairs

Global Business Unit will now include emerging markets sales contributions (2)

Last 12 months sales; Q4 2018 reported sales through Q3 2019 reported sales

Subject to consultation with social partners and works councils

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(3)

## Consumer healthcare – unlocking value

### Mid-term objective



## Sanofi CHC value drivers

- Rx-to-OTC switch growth opportunities
  - Cialis<sup>®</sup> unique product profile in erectile dysfunction
  - Tamiflu<sup>®</sup> for influenza prevention and care in the U.S.
- CHC digital transformation
  - Precision marketing
  - E-commerce
- $\checkmark$
- Standalone unlocking value
- Enhancing speed and agility
- Integrated R&D and manufacturing
- Dedicated support functions and IT

## China: Repositioning for new period of growth

### Driving volume expansion in Established Products & Diabetes

- >60% volume growth in 2020 expected due to VBP bidding wins of Plavix<sup>®</sup> and Co-Aprovel<sup>®</sup>
- Accelerate injectables & new insulins<sup>(1)</sup> growth
- Counties adding a new China by 2030; winning with unique coverage of 1,600 counties
- Reshaping organization in anticipation of VBP



### Major growth opportunity with Specialty and Vaccines

- Dupixent<sup>®</sup> expected launch in Q4 2020, offering therapy for ~0.9m biologics eligible AD patients<sup>(2)</sup>
- 25+ launches in total by 2025 focusing primarily on Rare Disease and Oncology
- Expected strong growth of Vaccines portfolio<sup>(3)</sup>





AD: atopic dermatitis; VBP: Value-based procurement
(1) Leveraging Lantus® and new launches of Toujeo® (2021e) and Soliqua® (2023e)
(2) Severe and moderate adult AD patients in urban population in 2018, failing systemic therapy as of 2018
(3) Flublok®, Hexaxim®, RSV

## **Empowerment and accountability**



## Driving innovation and growth with strategic choices





## Sanofi's value proposition to society





## Margin expansion

Jean-Baptiste de Chatillon

**EVP, Chief Financial Officer** 



## Strategic choices expected to drive margin expansion





# €2 billion savings expected by 2022 to fund growth and drive margin expansion



## We are off to a good start in delivering efficiencies

Operating expense growth YoY at CER<sup>(1)</sup>





## A change of mindset



#### Incentives tied to Free Cash Flow<sup>(4)</sup>



YTD September 2019 vs YTD September 2018
 Video conferencing system
 2019e vs. 2018
 Free Cash Flow definition in Financial appendices

## Smart spending: $\in$ 1.0 Billion savings expected by 2022 (



Spending

#### **Procurement savings**


# Operational excellence in Manufacturing





CMC digitalization acceleration<sup>(1)</sup>: **aims at reducing lead time by 6 months and delivering 9 launches** 

Factory of the future

Sanofi Manufacturing system

Supply chain

Shift to 2nd generation processes<sup>(2)</sup>: 6 'lighthouse' digital sites<sup>(3)</sup>: decrease of plant cycle time by 20%

Top decile<sup>(4)</sup> performance program expansion: **39 sites already enrolled, 49 by 2022** 

Digitalization and AI forecasting to reduce inventory level by 20 days

# Manufacturing procurement

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Optimization of CMOs and suppliers: reduce baseline by 20%

CMO: Contract Manufacturing Organization; AI: Artificial intelligence; CMC: Chemistry, Manufacturing and Controls

(1) ILAB

(2) For Vaccines & Biologics

(3) Framingham (US), Toronto (CA), Suzano (BR), Sisteron (FR), Hangzhou (CN), Waterford (IE)
 (4) Based on POBOS benchmark of manufacturing costs and productivity versus peers

# Streamline Established Products portfolio (

#### Number of product families



- Driving simplicity and agility
- Improving gross margin ratio
- Greater commercial focus on top products

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• ~€1.5bn cash proceeds expected in 2019-2025

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# Objective to increase Free Cash Flow<sup>(1)</sup> by ~50% by 2022<sup>(2)</sup>

#### Free Cash Flow<sup>(1)</sup> evolution



- Grow net sales
- Improve working capital
- Prioritize investments
- Expand margin



# **Capital allocation**



### Key messages







# Lead with innovation

John Reed

EVP, Global Head of R&D



# Next chapter for Sanofi R&D



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# Potential transformative therapies

Ambition

Planned initial submission<sup>(5)</sup>

Dupixent <sup>®(1)</sup>	Maximize patient benefit across type 2 inflammatory diseases	Launched
Fitusiran & BIVV001 <sup>(2)</sup>	Delivering on new patient dynamics – convenience	2021e/2022e
SERD ('859)	Master switch for endocrine signaling in HR+ breast cancer	2021e
venglustat	Leveraging LSD biology in multiple rare diseases and beyond	2022e
nirsevimab <sup>(3)</sup>	Cost-effective RSV prophylaxis for <u>all</u> infants	2023e
BTKi ('168) <sup>(4)</sup>	First disease modifying therapy to address MS drivers in the brain	2024e



BTKi: bruton tyrosine kinase inhibitor; LSD: lysosomal storage diseases; MS: multiple sclerosis; RSV: respiratory syncytial virus; SERD: selective estrogen receptor degrader; HR+: hormone receptor-positive (1) In collaboration with Regeneron

(2) In collaboration with SOBI

(3) In collaboration with AstraZeneca

(4) In collaboration with Principia

(5) Planned submission for first indication, not reviewed by regulators

# Priority assets fit with our long-term R&D objectives



(1) This includes assets discovered internally or wholly owned through acquisition and assets in-licensed at an early stage and for which Sanofi retains the majority of the share of the economics



(2) In collaboration with Regeneron, profit and loss split

(3) In collaboration with Sobi, holds commercial rights for Europe, North Africa, certain

countries in Middle East, Russia

- (4) In collaboration with AstraZeneca, profit and loss split
- (5) In collaboration with Principia, Sanofi has led Ph2 MS development and Ph3 planning. Principia was responsible for Ph1 in healthy subjects

# Dupixent<sup>®(1)</sup>: IL-4 & IL-13, central drivers of T2 inflammation



- Atopic Dermatitis
- Asthma
- CRSwNP
- Bullous Pemphigoid
- Prurigo Nodularis
- Chronic Spontaneous Urticaria
- Eosinophilic Esophagitis
- Allergic Bronchopulmonary Aspergillosis
- Chronic Obstructive Pulmonary Disease
- Additional indications



T2: type 2; Th2: T helper 2; ILC2: group 2 innate lymphoid cells; IL: interleukin; IgE: immunoglobulin E;, CRSwNP: Chronic Rhinosinusitis with Nasal Polyposis (1) In collaboration with Regeneron Dupixent® approved in atopic dermatitis, asthma and CRSwNP. Dupixent® in development for all other indications listed and not approved by regulators

# Dupixent<sup>®(1)</sup>: Greater specificity enabling safe profile



#### X Cytokine blockade

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# Dupixent<sup>®(1)</sup>: Safety supports pediatrics expansion

#### Robust safety<sup>(2)</sup>

9,300+ patients Studied across 23 clinical programs

6,500+ patients Treated >1year

**76-week** long-term safety data In adults (>18 years)

**52-week** long-term safety data In adolescents (12-17 years)

# Clinical practice

Clinical

trials

**125,000+** patients Treated globally since launch

 Expanding to pediatrics		
	Target regulatory submission	
AD 6-11 years Breakthrough designation	2019e	
AD <6 years	2022e	
Asthma 6-11 years	2021e	
Asthma <6 years	Under discussion	



# Dupixent<sup>®(1)</sup>: Expanding into adjacent Type 2 indications



Dupixent® is not approved by regulators in any of the indications listed Photos are not indicative of responses in all patients

(1) In collaboration with Regeneron

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- (2) Patients inadequately controlled by topical corticosteroids
- (3) Patients uncontrolled on anti-histamines/current SOC excluding biologics
- (4) Patients on chronic oral corticosteroids
- (5) Patients uncontrolled on high-dose proton pump inhibitor and topical steroid slurry and elimination diet / trigger avoidance
- (6) Uncontrolled type 2 inflammation population

# Hemophilia: Patient experience drives choice

#### Target profiles vs. marketed products



#### Different patients, different needs

- Patients choosing SC monthly dosing (convenience)
  - Fitusiran aiming for ABR<1</li>
  - Feasible with emicizumab only at ABR>2
- Patients choosing "active lifestyle" (efficacy)
  - BIVV001 is the only treatment to allow ~3.5 days of near-normal FVIII activity, allowing lifestyle similar to non-hemophilia patients
  - Current therapies may limit physical exercise from low FVIII activity levels and high dosing burden

- ABR: annualized bleed rate; SC: subcutaneous; BIVV001 is in collaboration with SOBI Fitusiran and BIVV001 are not approved by regulators
- **SANOFI** (1) emicizumab: 2.1 ABR @q4w; 1.6 ABR @q2w; 0.6 ABR @q1w (Hemlibra prescribing information; median ABR (HAVEN-3 for Q1w & q2w, HAVEN-4 for q4w)
  - (2) Individualized prophylaxis varies from daily to every 4 days and between <1 to >1 ABR
- (3) No H2H studies comparing efficacy of emicizumab and fitusiran or BIVV001 have been conducted
- (4) fitusiran: 0.97 ABR @q4w (Phase 2 OLE Interim Results);
- (5) BIVV001: Target Product Profile aiming for weekly dose, and ~3.5 days with FVIII activity >40%

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# Fitusiran: Potential first high-efficacy monthly therapy

	PatientsemicizumabWith & without inhibitors		<b>fitusiran</b> All Hemophilia patients • Hemophilia A & B • With & without inhibitors			
Patients						
Ffficacy	q4w	q2w	q1w	q4w	q2w	q1w
(ABR) <sup>1</sup>	2.10	1.60	0.60	0.97	n/a	n/a
Safety	Profile evolving: thrombosis, TMAs No antidote available		Profile evolving: thrombosis (ph. 3 ongoing Antidote available			
Convenience	<ul> <li>Subcutaneous</li> <li>Up to 4 injections</li> <li>Weight-based vs fixed dose</li> <li>Increasing up to 4 ml for monthly dose<sup>(2)</sup></li> <li>Cold chain required</li> <li>No pre-filled syringe</li> </ul>		<ul> <li>Subcutaneous</li> <li>Single injection</li> <li>Fixed dose</li> <li>Low volume &lt;1ml</li> <li>No cold chain</li> <li>Pre-filled syringe</li> </ul>			
ABR: annualized b	leed rate; TMA: thrombotic r	nicroangiopathy		median ABR (19 subjects with	out inhibitors)	

(2) Weight-based dosing

Fitusiran is not approved by regulators

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No H2H studies comparing efficacy of fitusiran and emicizumab have been conducted (1) Patients without inhibitors: Hemlibra prescribing information (USPI 2018), median ABR (HAVEN-3 for q1w & q2w, HAVEN-4 for q4w); fitusiran Phase 2 OLE interim results,

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# Fitusiran: >70% enrollment achieved in ATLAS Ph3 program



#### U.S. submission expected 2021



# BIVV001: Potential to allow more active lifestyle



Carter, 19, is attending Vanderbilt University where he plays volleyball He has severe Hemophilia A

FVIII activity (%), logarithmic scale



 (1) 50 IU/Kg every seven days after fourth dose (n=9) – aPTT assay (aPTT: activated partial thromboplastin time)
 (2) Mahlangu, J., *et al*, Blood, 123(3), 317–325.
 Sources: Konkle et al, oral presentation at ISTH, July 2019; Issltchkov et al, poster at ISTH, July 2019; F Peyvandi, I Garagiola, and G Young. Lancet 2016; 388: 187–97
 BIVV001 is in collaboration with Sobi and is not approved by regulators FVIII: Factor 8; IU/kg: international unit per kilogram

# **BIVV001: Registration study initiated**

#### Phase 3 study in previously treated patients $\ge$ 12 years (n=150)

- Primary endpoint: ABR in Arm A<sup>(1)</sup>
- Novel endpoints include joint health via ultrasound and physical activity monitoring
- Dose: 50 IU/kg once per week
- Rapid enrollment expected (prospective study + community excitement)



#### U.S. submission expected H1 2022



ABR: annual bleed rate; FVIII: Factor 8; IU/kg: international unit per kilogram BIVV001 is in collaboration with Sobi and is not approved by regulators (1) Estimation approach for ABR in prophylaxis arm with success criteria defined as less than or equal to an upper bound confidence interval

# SERD ('859): Aiming for new standard of care in HR+ BC

# MoA: completely shutting down estrogen signaling



#### In vitro activity similar to fulvestrant<sup>(1)</sup> but orally administered

**Preclinical data** 





HR+ BC: hormone receptor-positive breast cancer; MoA: mechanism of action; IM: intramuscular; ER: estrogen receptor; SERD: selective estrogen receptor degrader (1) Data on file SERD ('859) not approved by regulators

# SERD ('859): Early data supporting best-in-class ambition

#### Full ER degradation<sup>(1)</sup>

#### Lesion signals blocked<sup>(2)</sup>

# Before treatment After treatment



#### Promising Ph1 results<sup>(3)</sup>

- Promising early efficacy
- Favorable safety and tolerability
  - No related Grade 3 events
  - No bradycardia
  - No QTc prolongation
- FDA Fast Track granted

#### Favorable safety / tolerability profile supporting ambition of potential endocrine backbone



FES-PET: [18]F-fluoroestradiol positron-emission tomography;, ER: estrogen receptor SERD ('859) not approved by regulators

(2) TED14856: DL2bis (150mg) - Pt# 009

(3) To be presented at upcoming medical conference

(1) TED14856; Patient 840-0002020-06; T1= C2D15, 400mg QD

# SERD ('859): Potential to move quickly to early lines







# Nirsevimab<sup>(1)</sup>: Aiming for cost-effective RSV prophylaxis

# Strong risk reduction in healthy pre-term infants 29-35 weeks



# Flexible dosing to cover all infants during their first RSV season

- Single injection
- Administration independent of gestational age
  - At birth for born-in-season infants
  - Just prior to RSV season for born out-of-season infants to ensure protective Ab titer through the season

#### FDA breakthrough therapy designation and EMA Priority Medicine



Ab: antibody; LRTI: lower respiratory tract infections; RSV: Respiratory syncytial virus Note: infants with CLD/CHD will also be eligible in their 2nd season; one season lasts 5 months (1) In collaboration with AstraZeneca, not approved by regulators (2) https://academic.oup.com/ofid/article/6/Supplement 2/S27/5604259

# Nirsevimab<sup>(1)</sup>: Addressing shortfall of active immunization



#### Passive 'immunization' is the only approach to provide sufficient Ab titer when risk is highest

SANOFI SANOFI Ab: antibody (1) In collaboration with AstraZeneca, not approved by regulators (2) Stockman, 2012; Hall 2013
(3) e.g. Sanofi's Respiratory syncytial virus (RSV) vaccine in Phase 1

## Nirsevimab<sup>(1)</sup>: Submission expected by 2023

	MELODY	MEDLEY	
Phase	Phase 3	Phase 2/3	
Endpoint	Safety and efficacy	Safety	Target
Control	Placebo	palivizumab	2023e
Patients	>35wk healthy infants (n=3,000)	High-risk infants (n=1,500)	
Study end <sup>(2)</sup>	2023e	2021e	



# Venglustat: Leveraging LSD biology in multiple rare diseases and beyond





LSD: lysosomal storage diseases; GCS: glucosylceramide synthase; (GL-1): glucosylceramide; LacCer: lactosylceramide; GL-3: globotriaosylceramide; ADPKD: autosomal dominant polycystic kidney disease; GBA-PD: Glucocerebrosidase Parkinson's disease Venglustat not approved by regulators

# Venglustat: Mechanism already validated in LSDs

#### Gaucher disease type 3

- Potential first-in-class neurologic GD-3 treatment
- ~300 diagnosed patients in U.S., Europe & Japan

Mean change of biomarkers from



#### Fabry disease

- Potential best-in-class oral therapy option<sup>(2)</sup>
- ~10,000 diagnosed patients in U.S., Europe & Japan

Plasma GL-3 (n=7)<sup>(3)</sup> globotriaosylceramide (µg/ml)



#### >250 patients treated across 5 indications, extended safety data up to 3 years for some patients



LSD: lysosomal storage diseases; GD-3: Gaucher Type 3; CSF: cerebrospinal fluid; GL-3: (1) globotriaosylceramide (2) Venglustat not approved by regulators (3)

- ) LEAP Phase 2 oral presentation WORLD Feb 2019, R. Schiffmann
- ) Irrespective of genotype
- ) Phase 2 poster presented at SSIEM Sep 2019, P. Deegan

# Venglustat: Transformative potential in ADPKD

#### High unmet need

- ~340,000 patients in U.S., Europe & Japan, ~37% rapidly progressing<sup>(1)</sup>
- Significant tolerability issues of current therapies (e.g., polyuria, dehydration) End-stage ADPKD:



#### Robust pre-clinical data in validated animal model<sup>(2)</sup>



Age (weeks)



Venglustst not approved by regulators, ADPKD: autosomal dominant polycystic kidney disease; MRI: magnetic resonance imaging; GlcCer: glucosylceramide Picture from *Nature Genetics*, 2013 (1) Mayo Clinic Classification 1C-1E (2) Nat Med. 2010 July ; 16(7): 788–792

# Venglustat: STAGED-PKD – potential submission by 2022e





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 TKV: total kidney volume; eGFR: estimated glomerular filtration rate
 Venglustat not approved by regulators
 (1) Mayo model classified ADPKD patients by age-adjusted TKV into 5 groups (1A through 1E)
 (2) Selected dose = highest dose that is safe and well tolerated in Stage 1

64

## Venglustat: Potential first DMT for genetically defined Parkinson's disease subpopulation



#### ~20% of idiopathic PD patients anticipated to be included in phase 3 (FDA recommendation)



CSF: cerebrospinal fluid; GSL: glycosphingolipid; GCase: glucocerebrosidase; GCS: glucosylceramide synthase; GBA-PD: Glucocerebrosidase Parkinson's disease Venglustat not approved by regulators (1) MOVES-PD part 1 data presented at WORLD 2019 for 32 weeks of treatment, pool Japan + RoW

# BTKi ('168)<sup>(1)</sup>: MS patients still accumulate disability

#### EDSS worsening over time<sup>(2)</sup>

#### SPMS conversion over time<sup>(4)</sup>



Time since eligible for treatment<sup>(3)</sup>

Disease duration (years)

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EDSS: expanded disability status scale; SPMS: secondary progressive multiple sclerosis (1) In collaboration with Principia, not approved by regulators

(2) Tilling K et al. Health Technol Assess 2016:20:1-48

(3) Criteria for eligibility: age ≥18 years, EDSS score ≤6.5, occurrence of ≥2 relapses in

the previous 2 years

(4) Manouchehrinia A et al. Mult Scler 2017;23:1488-95; Kaplan-Meier estimates based on 8526 patients in Swedish MS registry (SMSreg)

# BTKi ('168)<sup>(1)</sup>: Best-in-class potential in DMT segment

Phase 1 results<sup>(2)</sup>

#### Competitive profile<sup>(3)</sup>



#### Time (hr)

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DMT: disease modifying therapy; BTK: bruton tyrosine kinase; CNS: central nervous system

(1) In collaboration with Principia, not approved by regulators

2) Human ph. 1 results presented at ACTRIMS forum 2019

(3) Aspirational, no direct comparison studies have been performed

(4) Phase 1 data

# BTKi ('168)<sup>(1)</sup>: Ready to launch trials across full MS spectrum



Go/no-go decision (efficacy & safety)



# Expected next steps for potentially transformative assets

	Upcoming milestones	Next steps	Acceleration potential
fitusiran – Hem A/B	1H-21 Pivotal results	2H-21 Submission	Earlier submission for inhibitor population, potential priority review
BIVV001 – Hem A	Dec '19 Phase 3 initiation (achieved)	2H-21 Pivotal results 1H-22 Submission	
venglustat <sup>(1)</sup> – ADPKD	2H-20 Futility analysis	2H-21 Pivotal results 1H-22 Submission	Dates reflect accelerated approval strategy for U.S. <sup>(2)</sup>
venglustat <sup>(1)</sup> – GBA-PD	1H-21 PoC (MOVE-PD)	2H-21 Pivotal study start 2025 Pivotal results 2025 Submission	
SERD ('859) – HR+BC (all lines)	2H-19 PoC (achieved)	1H-21 Pivotal results (2L/3L mono) 2H-21 Submission (2L/ 3L mono) 2024 Pivotal results (1L/2L combo)	Potential accelerated U.S submission by 2H-23 for 1L/2L combo Exploring fast route to early BC
nirsevimab – infant RSV prophylaxis	1H-23 Pivotal data	2023 Submission	Potential for priority review
BTKi ('168) – MS (all forms)	1H-20 PoC	2H-20 Pivotal study start (RMS, PPMS, SPMS) 2024 Pivotal results	Potential for priority review



Assets under investigation, not approved by regulators. RSV: Respiratory syncytial virus; (1) Also planned for venglustat: submissions for GD3 (1H-23), GM2 (2H-23) and Fabry BIVV001 in collaboration with Sobi, nirsevimab in collaboration with AZ, BTKi in collaboration with Principia

disease (2H-23)

(2) Accelerated approval based on total kidney volume, submission for full approval based on TKV & eGFR earliest in 2H-23

# Synthorx promising assets synergistic with Sanofi pipeline



Significant synergies with Sanofi R&D novel platforms (i.e. drug conjugates, protein fusions, multi-specific biologics, and nanobody<sup>®</sup> technology)

# Dual Strategy for THOR-707: Exploit T and NK cell



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## Recent accomplishments from our late-stage pipeline

#### Ambition

**Sarclisa<sup>®</sup>** 

Sutimlimab

Olipudase alfa

Differentiated CD-38 in relapsed refractory multiple myeloma

First-in-class treatment for CAD New SOC for refractory ITP

First ERT in ASMD

Pending FDA decision

Presented positive Ph3 results in CAD and PoCC in ITP at ASH 2019

Pivotal topline results to be released Jan 2020



SOC: standard of care; PoCC: proof of clinical & commercial concept; ERT: enzyme replacement therapy; CAD: cold agglutinin disease; ITP: immune thrombocytopenic purpura ASMD: Acid Sphingomyelinase Deficiency Sarclisa® is the brand name for Isatuximab; Sarclisa®, sutimlimab, olipudase alfa not approved by regulators
## Sutimlimab pivotal data presented at ASH

#### Serious autoimmune hemolytic anemia

- Diagnosed patients: ~10,000 in U.S., EU5, JP<sup>(1)</sup>
- Chronic hemolytic anemia, independent of season
- Debilitating fatigue and impaired QoL
  - Increased outpatient, inpatient, and ER utilization
- Hemolysis in CAD is driven by the classical complement pathway
- No currently approved therapies
- Sutimlimab selectively targets C1 in the classical complement pathway leaving the lectin and alternative pathways intact
- U.S. submission expected in Q1 2020

#### Rapid, sustained hemolysis resolution and QoL benefit (n=22)<sup>(2)</sup>



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CAD: Cold Agglutinin Disease; TE: Thromboembolic Event; QoL: Quality of Life; EU: All of Europe; JP: Japan Sutimlimab is not approved by regulators 1) Haematologica. 2006;91(4):460-466

(2) Phase 3 results, ASH 2019, late-breaker presentation





Continuing transformation of Sanofi R&D

Resources allocated to priority areas

Focus on transformative therapies (T2 biology and priority assets)

Execute to secure accelerated time to market



## Capital Markets Day Financial appendices

December 10, 2019



### Definitions

#### **Free Cash Flow**

Free Cash Flow is a non-GAAP financial performance indicator which is reviewed by our management, and which we believe provides useful information to measure the net cash generated from the Company's operations that is available for strategic investments<sup>1</sup> (net of divestments<sup>1</sup>), for debt repayment, and for capital return to shareholders. Free Cash Flow is determined from the Business Net Income adjusted for depreciation, amortization and impairment, share of profit/loss in associates and joint ventures net of dividends received, gains & losses on disposals, net change in provisions including pensions and other post-employment benefits, deferred taxes, share-based expense and other non-cash items. It comprises net changes in working capital, capital expenditures and other asset acquisitions<sup>2</sup> net of disposal proceeds<sup>2</sup>, and payments related to restructuring and similar items. Free Cash Flow is not defined by IFRS and it is not a substitute measure for the IFRS aggregate net cash flows in operating activities. <sup>1</sup>Amount of the transaction above €500 million; <sup>2</sup>Not exceeding €500 million

#### **Business Operating income (BOI)**

Sanofi reports segment results on the basis of "Business Operating income". Business Operating income is a is a non-GAAP financial performance indicator. This indicator is used internally by Sanofi's chief operating decision maker to measure the performance of each operating segment and to allocate resources. Business operating income is derived from Operating income, adjusted as follows:

- the amounts reported in the line items Restructuring costs and similar items, Fair value remeasurement of contingent consideration and Other gains and losses, and litigation are eliminated;
- amortization and impairment losses charged against intangible assets (other than software and other rights of an industrial or operational nature) are eliminated;
- the share of profits/losses from investments accounted for using the equity method is added;
- · net income attributable to non-controlling interests is deducted;
- other acquisition-related effects (primarily the workdown of acquired inventories remeasured at fair value at the acquisition date, and the impact of acquisitions on investments accounted for using the equity method) are eliminated;
- · restructuring costs relating to investments accounted for using the equity method are eliminated.

# Sanofi accounting of Antibody License and Collaboration Agreement with Regeneron<sup>(1)</sup>

		U.S. Ex-U.S.			
Net sales		Sanofi consolidates worldwide net sales			
Cost of sales		Sanofi consolidates worldwide cost of sales			
R&D expense <sup>(2)</sup>		Development costs funded upfront by Sanofi until first positive Phase 3; subsequent costs funded 80% Sanofi / 20% Regeneron Regeneron 20% reimbursement recorded as a reduction of Sanofi R&D expense			
SG&A expense		Sanofi expenses 100% of its commercial expenses			
Other operating income and expenses	1. Regeneron SG&A spend	Sanofi reimburses Regeneron for 100% of Regeneron's commercial expenditures To date Regeneron has exercised its right to copromote in U.S. only; Sanofi leads all ex-U.S. activities			
	2. Development balance	Regeneron reimburses 50% of cumulative development costs quarterly once collaboration profitable <sup>(3)</sup> ; Reimbursement capped at 10% of Regeneron's share of profit per quarter on all Antibody products combined			
	3. Collaboration profitable	Outflow: Sanofi expenses 50% of profit; paid to Regeneron	Outflow: Sanofi expenses 35% to 45% of profit; paid to Regeneron		
	4. Collaboration in a loss	Inflow: Sanofi recognizes reimbursement of 50% loss from Regeneron	Inflow: Sanofi recognizes reimbursement of 45% loss from Regeneron		
Amortization of intangibles (IFRS)	Sales Milestones	Regeneron entitled to receive up to \$250m in milestones starting from \$1bn ex-US sales			

(1) Following expiry of the Antibody Discovery Agreement in December 2017, Praluent<sup>®</sup>, Dupixent<sup>®</sup>, Kevzara<sup>®</sup> and IL- (2) 33 / SAR440340 continue to be developed and commercialized with Regeneron under the Antibody License and Collaboration Agreement (LCA) signed in November 2007, Amended and Restated November 2009

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and further amended May 2013 and July 2015 For discovery and pre-clinical activities, Sanofi funded \$120m per year between 2007-2009; up to \$160m per year between 2010-2014; up to \$160m per year between 2015-2017, less \$75m reallocated to the immunology-oncology agreement spread over 20152017; Discovery agreement expired December 31, 2017

 (3) As of December 31, 2018, Sanofi has incurred \$6.8bn;
 \$3.4bn to be reimbursed, of which \$2.8bn remains outstanding

### Sanofi Libtayo<sup>®</sup> accounting pursuant to immuno-oncology global collaboration<sup>(1,2)</sup>

		U.S.	Ex-U.S.		
Net sales		Consolidated by Regeneron	Consolidated by Sanofi		
Cost of sales		Consolidated by Regeneron	Consolidated by Sanofi		
R&D expenses		Sanofi reimburses 50% of development expenses incurred during quarter <sup>(3</sup>			
SG&A expenses		Sanofi expenses 100% of its commercial expenses			
	1. SG&A reimbursement	Inflow: Regeneron reimburses 100% of Sanofi's U.S. commercial expenses	Outflow: No Regeneron commercial expenses ex-US		
Other operating Income and expenses	2. Development balance	Regeneron reimburses 50% of pre-POC development costs <sup>(4)</sup> quarterly, once collaboration profitable <sup>(5)</sup>			
	3. Collaboration profitable	Inflow: Sanofi recognizes 50% of collaboration's profits Outflow: Sanofi expenses 50% of profi			
	4. Collaboration in a loss	Outflow: Sanofi expenses 50% of losses; to be paid to Regeneron	Inflow: Sanofi recognizes reimbursement of 50% of collaboration's losses		
Amortization of intangibles (IFRS)	Sales milestones	Regeneron to receive \$375m milestone when sales of Libtayo <sup>®</sup> , including sales of future opt-ins under the IO LCA <sup>(6)</sup> sold for use in combination with Libtayo <sup>®</sup> , exceed \$2bn over any consecutive 12-month period			
(1) On July 1, 2015, Sanofi and Regeneron entered into an (2) Libtayo <sup>®</sup> collaboration unaffected by the Amended I-O (4) As of December 31, 2018, amounts to \$58m primarily					

Immuno-Oncology (IO) Discovery and Development Agreement and an IO License and Collaboration Agreement (IO LCA). Sanofi made a \$640m upfront payment. The companies agreed to reallocate \$75m (spread over three vears) to IO R&D from Sanofi's \$160m annual contribution to SANOFI 🎝 their existing antibody discovery agreement. The companies (3) agreed to invest \$1bn from discovery through POC, to be funded 25% by Regeneron and 75% by Sanofi.

Discovery and Development Agreement effective December 31, 2018. Revision provides for ongoing collaborative development of two clinical-stage bispecific antibody programs: (1) BCMAxCD3 and (2) MUC16xCD3 Agreement

In January 2018, Sanofi and Regeneron announced the Libtavo<sup>®</sup> budget through 2022 was increased from \$650m to \$1.64bn, funded equally by the two companies

for bi-specifics, LAG3 and CTLA-4 development programs

- (5) Capped at 10% of Regeneron profit share per quarter
- (6) Sanofi has opt-in rights with respect to each of the 2 bispecifics antibodies (BCMAxCD3 or MUC16xCD3) covered by the Amended and Restated IO Discovery Agreement

## Sanofi's ownership of Regeneron

Ownership of	<ul> <li>As of December 31, 2018 Sanofi owned 21.7% of Regeneron pursuant to the investor</li></ul>
Regeneron	agreement signed in 2007 and amended in January 2014
Accounting of	<ul> <li>Sanofi's share of Regeneron's profit / losses are presented on the Income Statement within</li></ul>
Ownership	Share of profit/(loss) from investments accounted for using the equity method
	<ul> <li>Pursuant to the January 2018 Letter Agreement, Sanofi may elect to sell Regeneron shares every quarter starting from 2018 to the end of 2020</li> </ul>
Ability to Sell	<ul> <li>Maximum number of shares allowed to be sold under the 2018 Letter Agreement is 1.4 million,</li></ul>
Shares	approximately 1% of the share capital
	<ul> <li>In 2018, Sanofi sold shares with a carrying amount of €24 million</li> </ul>

# Synthorx acquisition<sup>(1)</sup> bringing significant value creation potential

Acquisition Price	<ul> <li>Synthorx shareholders to receive \$68 per share in cash</li> <li>Values Synthorx at approximately \$2.5 billion on a fully diluted basis</li> </ul>
Financials	<ul> <li>Expected to be slightly dilutive to Business EPS in 2020 and 2021<sup>(2)</sup></li> <li>IRR expected to be well in excess of cost of capital over time</li> </ul>
Timing	<ul> <li>Transaction unanimously approved by the Boards of both companies</li> <li>Expected to close by the end of Q1 2020<sup>(1)</sup></li> </ul>





## Capital Markets Day R&D appendices

December 10, 2019



## Dupixent<sup>®(1)</sup>: Development plan for adjacent indications

	Indication	Unmet need	Study start	# patients	Outcome measures	Expected read-out
Dermatology	Prurigo Nodularis	No approved therapy	Dec-19	150 + 150 <sup>(2)</sup>	Improvement in worst itch NRS	Mid-2021
	Chronic Spontaneous Urticaria	Additional treatment options needed	Dec-19	80 + 104 <sup>(2)</sup>	Improvement in weekly itch severity score (ISS7)	Mid-2021
	Bullous Pemphigoid	No approved therapy	Jan-20	80	Sustained remission	Mid-2022
	[				Deele eesekeeseel	
	Eosinophilic Esophagitis	No systemic therapy Long-term safety issues of local/swallowed steroids	Dec-18	425	Peak esophageal intraepithelial eos count Improvement in dysphagia symptoms	Part A: mid-2020 Part B: H2 2022
Respiratory & Gastro- Intestinal	Allergic Bronchopulmonary Aspergillosis	No approved therapy	May-20	170	Exacerbation reduction	Mid-2023
	Chronic Obstructive Pulmonary Disease	No biologic therapy approved	May-19	924 + 924 <sup>(2)</sup>	Exacerbation reduction FEV1 improvement	Mid-2023 (for 2 <sup>nd</sup> study)

IgE: immunoglobulin; NRS: numeric rating scale; ISS: itch severity scale; FEV1: forced expiratory volume in one second

(1) In collaboration with Regeneron

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(2) Two studies for Prurigo Nodularis, Chronic Spontaneous Urticaria and Chronic Obstructive Pulmonary Disease None of these indications are approved for Dupixent by regulators

### **Expected upcoming milestones**

**H1** H2 2021 2022 2020 2020 BTKi ('168)<sup>(1)</sup> Dupixent<sup>®(2)</sup> venglustat Dupixent<sup>®(2)</sup> PoCC in RMS | Q1 AD adult China approval | Q3 PoCC in GBA-PD | Q1 Pivotal results in AD 6m-5vol H1 Libtavo<sup>®(2)</sup> venalustat SERD ('859) fitusiran PoCC in GD 3 | Q1 PoCC in mono, combo & adjuvant BC | H2 Pivotal results in Hemophilia A/B | H1 1L NSCLC mono OS results | H1 olipudase alfa Dupixent<sup>®(2)</sup> Dupixent<sup>®(2)</sup> Libtayo<sup>®(2)</sup> Pivotal results in PN, CSU | H2 Pivotal results in ASMD | Q1 Pivotal results in Asthma 6-11 yo | Q4 1L NSCLC combo OS results | H2 **Flublok**<sup>®</sup> avalglucosidase alfa **BIVV001**<sup>(3)</sup> Pivotal results in LOPD | Q2 EU approval | Q4 Pivotal results in Hemophilia A | H2 Sarclisa® sutimlimab SERD('859) Pivotal results in 2L RRMM | Q1 Cold Agglutinin Disease U.S. approval | Q3 Pivotal results in 3L-2L mono BC | H1 Sarclisa® MenQuadfi™ venalustat 3L RRMM U.S. approval | Q2 ≥12 months EU approval | Q4 Pivotal results in ADPKD | Q4 Dupixent<sup>®(2)</sup> Libtayo<sup>®(2)</sup> AD 6-11 yo U.S. approval | Q2 BCC 2L U.S. approval | H2 MenQuadfi™ ≥2 yo U.S. approval | Q2 Fluzone QIV HD<sup>®</sup> ≥65 yo EU approval | Q2

Note: assets under investigation, not approved by regulators



PoCC: proof of clinical & commercial concept: AD: atopic dermatitis: RRMM: relapsed refractory multiple myeloma; ASMD: acid sphingomyelinase deficiency; BCC: basal cell carcinoma; RMS: Relapsing Multiple Sclerosis; LOPD: late onset Pompe disease; BC: breast cancer; GD: Gaucher Disease; GBA-PD: Parkinsons Disease with an associated GBA mutation; CSU: Chronic Spontaneous Urticaria;

PN: Prurigo Nodularis; ADPKD: Autosomal Dominant Polycystic Kidney Disease; RSV: Respiratory syncytial virus: NSCLC: non small cell lung cancer

- (1) In collaboration with Principia
- (2) Developed in collaboration with Regeneron
- (3) Developed in collaboration with SOBI

## Oncology pipeline potential to drive growth





Cemiplimab, BCMA-CD3 and MUC16-CD3 in collaboration with Regeneron; Cytokine mRNA in collaboration with BioNtech, SHP2i in collaboration with Revolution Apart from cemiplimab approved in advanced CSCC, all other assets and indications have not been approved by regulators

## Sarclisa®: Large opportunity for differentiated 2<sup>nd</sup> in class

Limited penetration in early lines

<20% of U.S. patients in 1-2L exposed to Darzalex® or Pd



Patients in 1-2L, k (U.S.)<sup>(1)</sup>





## Sarclisa®: Expanding from late lines to early lines

U.S. & EU5<sup>(1)</sup>





## Venglustat: >240 patients enrolled in MOVES-PD



#### ~20% of idiopathic PD patients anticipated to be included in phase 3 (FDA recommendation)

SANOFI Venglustat not approved by regulators

## Sutimlimab: Potentially new SOC for refractory ITP patients

#### Significant unmet need for stable or Rapid and sustained platelet count increased platelet counts increase in Phase 1<sup>(2)</sup> U.S., EU5, Japan patients<sup>(1)</sup> Mean platelet count (x 10<sup>9</sup>/L) 250 -**Diagnosed adult ITP** ~142K Washout First Dose Patients 200 150 ~71K Treated 100 x 10<sup>9</sup>/L 100 50 50 x 10<sup>9</sup>/L Multi-Refractory ~16K (Failed 2 or more lines of therapy) Screening () 147 1 7 Study day

#### Generally well-tolerated<sup>(2)</sup> with Phase 3 expected to begin H1 2021



SOC: Standard of Care; ITP: immune thrombocytopenic purpura;
(1) Feudjo-Tepie, M. A., et al. J Thromb Haemost 2008, 6: 711-712; Sanofi analysis
(2) Phase 1 results, ASH 2019 oral presentation (including in patients that failed TPO mimetics)
Sutimilimab is not approved by regulators

## Olipudase alfa: Potential first and only therapy for ASMD

#### High unmet medical need

#### Ultra-rare progressive genetic disorder

- Results from a deficient activity of the enzyme acid sphingomyelinase, which is found in lysosomes and is required to breakdown lipids called sphingomyelin
- Also known as Niemann-Pick Disease Type B
- Prevalence: ~2,000 patients in U.S., Europe & Japan<sup>(1)</sup>

#### No approved treatment

~3% of patients die each year due to respiratory or liver failure

## FDA BTD, EMA PRIME & Japan SAKIGAKE designations granted

#### Pivotal top line results Jan 2020

#### Promising phase 1 results<sup>(2)</sup>



Acceptable safety profile, well tolerated

#### Phase 2/3 topline results (ASCEND) Jan 2020

- 36 patients, 52-week period
- Primary efficacy endpoints
  - % change in spleen volume
  - % change in Dlco

#### Regulatory submissions expected to begin Q4 2020



Olipudase is not approved by regulators. ASMD: acid sphingomyelinase deficiencies; BTD: breakthrough designation; PRIME: priority medicines; DLco: diffusion capacity of the lungs for carbon monoxide

(1) Sanofi estimate

2) Pediatric preliminary data from DFI13803/LTS13632 (n=12); Adult preliminary data from DFI13412 (Phase 1b)/LTS13632 (n=5)

## Avalglucosidase alfa: Investigational ERT for Pompe Disease

#### Progressive, often fatal myopathy

## Pompe disease: rare, inherited and often fatal lysosomal storage and neuromuscular disorder

- Caused by mutations in the GAA gene, resulting in accumulation of glycogen
- Disease spectrum:
  - LOPD: progressive damage to skeletal & respiratory muscle, significant disability, premature death within muscle cells
  - IOPD: rapidly progressive myopathy, respiratory failure, often fatal in first year of life
  - Prevalence: ~10,000 patients in U.S., Europe & Japan<sup>(1)</sup>

## Respiratory failure is the most common cause of mortality in Pompe disease<sup>(2)</sup>

#### Promising pre-clinical<sup>(3)</sup> & PoC data<sup>(4)</sup>

- rhGAA conjugated with bisM6p residues
- Engineered to increase cellular uptake<sup>(4)</sup>



#### **Enrolled studies**

- Ph. 3 LOPD, COMET study (n=100):randomized head to head against alglucosidase Alfa powered to test for superiority. read-out Q2 2020
- Ph. 1/2 IOPD, mini-COMET (n=22): read-out Q1 2020

#### Orphan drug designation in U.S. & EU

#### U.S. & EU submissions expected H2 2020

Avalglucosidase alfa is not approved by regulators. ERT: enzyme replacement therapy; LOPD: Late-Onset Pompe Disease; IOPD= Infantile -nset Pompe Disease; PoC = proof of concept; rhGAA: recombinant human acid α-glucosidase

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- (1) Sanofi estimate
  - (2) Winkel, L. P., Hagemans, M. L., et al. (2005). J Neurol and Mellies, U. and Lofaso, F. (2009). Respir Med
- (3) Compared to Myozyme®, ~5x greater clearing of glycogen from heart, diaphragm, skeletal muscle based on pre-clinical data. Zhu Y. J Biol Chem. 2004, Zhu Y. Mol Ther. 2009 and Zhou Q. Bioconjug Chem. 2011, 2013
- (4) Positive response on respiratory function observed in NEO1 phase 1/2 study. Pena L., et al. Neuromuscul Disord. 2019



## Capital Markets Day Vaccines

December 10, 2019



## Our key growth drivers





## Vaccines: Strong growth driven by 3 core franchises & RSV





### PPH / Boosters: Worldwide pediatric combinations leader

Large potential in both primary & booster vaccination



## Influenza: Growth driven by differentiated vaccines



#### Ongoing geographic expansion of differentiated flu vaccines

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 TIV: Trivalent Influenza Vaccine; QIV: Quadrivalent Influenza Vaccine; SD: Standard-dose; (2)
 Not approved

 HD: High-dose
 (3)
 Not approved

 (1)
 Not approved outside of the U.S.
 (3)

Not approved in all countries Not approved by regulators in pediatrics

## Fluzone® High-Dose: Superior efficacy in landmark trial

#### Pivotal efficacy trial results, age 65+

Fluzone®	Fluzone®	Superior Relative Efficacy: %95 Cl		
Vaccine ( <i>standard d</i> ose) Subjects	Vaccine High-Dose (standard dose) Vaccine Subjects Subjects	Primary Endpoint <sup>(1)</sup> associated with protocol- defined influenza –like illness	Secondary Endpoint <sup>(2)</sup> associated with modified CDC- defined influenza –like illness	
15,993	15,990	<b>24.2%</b> (9.7;36.5)	<b>51.1%</b> (16.8;72.0)	

- Large 2-season efficacy trial of 32,000 patients; published in New England Journal of Medicine
- Fluzone<sup>®</sup> High Dose is used in U.S. & Canada
- Nearly 2/3 of immunized seniors in U.S. receive Fluzone High-Dose
- Launches in Europe & Asia: 2021e+ pending regulatory review

References: DiazGranados CA, et al. N Engl J Med. 2014;371(7):635-645. 2. Fluzone High-Dose vaccine [Prescribing Information]. Swiftwater, PA: Sanofi Pasteur Inc.; 2016.
 Primary endpoint: Occurrence, at least 14 days post-vaccination, of lab-confirmed influenza caused by any viral type or subtype (regardless of similarity to vaccine components)
 Secondary endpoint: Occurrence of culture-confirmed influenza caused by viral types/subtypes antigenically similar to those contained in the vaccine in association with a modified CDC-defined ILI

# Fluzone<sup>®</sup> High-Dose reduces cardio-respiratory hospitalizations

Relative vaccine effectiveness<sup>(1)</sup> of Fluzone<sup>®</sup> High-Dose vs standard dose vaccine: Cardio-respiratory hospitalizations



- 3.6M subjects total; 357K hospitalized due to cardio-respiratory event over 5 seasons
- Consistent reduction of cardio-respiratory hospitalization, a critical medical & health-economic issue for seniors

# Flublok<sup>®</sup>: 1<sup>st</sup> recombinant flu vaccine showing better efficacy in adults 50+

#### Pivotal efficacy trial results, age 50+

Fluarix <sup>®</sup> Vaccine <i>(standard dose)</i> Subjects	Flublok®	Relative Efficacy: %95 Cl		
	Vaccine Subjects	Primary Endpoint PCR confirmed + protocol- defined influenza-like illness	Secondary Endpoint Culture confirmed + protocol- defined influenza-like illness	
4,344	4,328	<b>30%</b> (10;47)	<b>43%</b> (21;59)	

- 1 season efficacy trial of 9,000 patients; published in New England Journal of Medicine
- Comparable safety to standard dose vaccines
- First recombinant influenza vaccine
- Baculovirus expression vector system
- Launches in Europe & Asia: 2021e+ pending regulatory review

## Innovative prospective real world data generation

Sanofi Pasteur is pursuing leading-edge, innovative real world data to reinforce value of our differentiated flu vaccines & support clinical decision making



## Meningitis<sup>(1)</sup>: Strong MenQuadfi<sup>™</sup> results

#### MenQuadfi™: Better immunogenicity profile<sup>(2)</sup>

- Pivotal trials completed for first submissions in the U.S., EU and international regions
- All primary objectives met
  - Non-inferiority to comparator vaccines
  - · Co-administration data with routine vaccines
- Good safety profile
- FDA action date April 2020<sup>(3)</sup>

## MET50: Adolescents achieving seroprotection hSBA titers ≥1:8 at D30<sup>(4)</sup>



#### Pivotal trial results

Menquadfi<sup>™</sup> is not approved by regulators

- (1) Serogroups ACWY
- (2) Compared to Menactra and Menveo

(3) 2 years+

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(4) D30, day 30; hSBA, serum bactericidal assay using human complement; M, number of subjects with valid serology results; n, number of subjects achieving hSBA titers ≥1:8; N, total number of subjects in group; per-protocol analysis set for assessing response to MenACWY and Tdap responses. Data (MenACYW-TT and MenACWY-CRM). EU Clinical Trials Register. 2016-001963-35 (MET50) results summary. January 2019. Available at: https://www.clinicaltrialsregister.eu/ctr-search/trial/2016-001963-35/results [accessed April 2019]. Poster presented at the 37th Annual meeting of the European Society for Paediatric Infectious Diseases, May 6-11 2019, Ljubljana. Slovenia

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## Meningitis<sup>(1)</sup>: Expanding in new age groups & geographies





## Accelerating innovation in Vaccines



SANOFI SANOFI SINCE Respiratory Syncytial Virus; PCV: Pneumococcal Conjugate Vaccine

# Nirsevimab: Goal to be cost-effective RSV prophylaxis for <u>all</u> infants

#### 98% of infants currently not eligible



#### High disease burden

- High medical care costs from RSV-related LRTI (\$4.2bn<sup>(2)</sup>)
- Congested ER / ICU during RSV seasons
- Risk of long-term sequelae

#### Nirsevimab has potential to cover all infants through single injection

RSV: Respiratory syncytial virus; LRTI: lower respiratory tract infections; ER: emergency department; ICU: intensive care unit

(1) Palivizumab eligible population: CHD/CLD & ≤28wGA

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(2) Estimated global costs of in-patient and out-patient management in children <5 years in 2017, unpublished data from Respiratory Syncytial Virus Consortium in Europe Note: asset under investigation in collaboration with AstraZeneca, not approved by regulators

## Nirsevimab<sup>(1)</sup>: Aiming for cost-effective RSV prophylaxis

## Strong risk reduction in healthy pre-term infants 29-35 weeks



## Flexible dosing to cover all infants during their first RSV season

- Single injection
- Administration independent of gestational age
  - At birth for born-in-season infants
  - Just prior to RSV season for born out-of-season infants to ensure protective Ab titer through the season

#### FDA breakthrough therapy designation and EMA Priority Medicine



Ab: antibody; LRTI: lower respiratory tract infections; RSV: Respiratory syncytial virus Note: infants with CLD/CHD will also be eligible in their 2nd season; one season lasts 5 months (1) In collaboration with AstraZeneca, not approved by regulators (2) https://academic.oup.com/ofid/article/6/Supplement 2/S27/5604259

## Nirsevimab<sup>(1)</sup>: Addressing shortfall of active immunization



#### Passive 'immunization' is the only approach to provide sufficient Ab titer when risk is highest

 
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 Ab: antibody (1)
 Ab: antibody

 (1)
 In collaboration with AstraZeneca, not approved by regulators
 (2) Stockman, 2012; Hall 2013
(3) e.g. Sanofi's Respiratory syncytial virus (RSV) vaccine in Phase 1

### Nirsevimab<sup>(1)</sup>: Submission expected by 2023

	MELODY	MEDLEY	
Phase	Phase 3	Phase 2/3	
Endpoint	Safety and efficacy	Safety	Target
Control	Placebo	palivizumab	2023e
Patients	>35wk healthy infants (n=3,000)	High-risk infants (n=1,500)	
Study end <sup>(2)</sup>	2023e	2021e	





## **Capital Markets Day** General Medicines and CHC

December 10, 2019



## **China: Building our Specialty franchises**



SANOFI 🧊 EP: Established Products; I&I: Inflammation & Immunology; RD: Rare Diseases; RBD: Rare Blood Disorders; MS: Multiple Sclerosis
## Game-changing first-in-category switch opportunities



- Rx-to-OTC switches are an engine of growth in large U.S. market
- Sanofi has proven global switch expertise (Allegra<sup>®</sup>, Nasacort<sup>®</sup>, Xyzal<sup>®</sup>)
- Evolving regulatory environment favorable, discussions on track
- Innovative digital techniques employed to secure switch success

Disruptive growth tapping into new CHC categories

## SANOFI 🎝



## Capital Markets Day Play to Win

December 10, 2019



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