IR Conference Call on PCSK9

SAR236553/REGN727 PCSK9 Antibody for Hypercholesterolemia Phase 3 ODYSSEY Program Underway

November 5, 2012

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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 labeling 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, the Group's ability to benefit from external growth opportunities, trends in exchange rates and prevailing interest rates, the impact of cost containment policies 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, 2011. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

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Agenda

• **Hypercholesterolemia, and Cardiovascular Disease: Unmet Medical Need**	▸ Dr. Robert Califf, M.D. Vice Chancellor for Clinical and Translational Research Director, Duke Translational Medicine Institute Professor of Medicine, Division of Cardiology, Duke University Medical Center
• **PCSK9 Mechanism of Action and SAR236553/REGN727** • **Dose Selection for ODYSSEY Phase 3**	▸ Bill Sasiela, Ph.D. VP, Program Direction, Regeneron
• **The ODYSSEY Phase 3 Program**	▸ Jay Edelberg, M.D., Ph.D. VP, Head of the PCSK9 Development & Launch Unit, Sanofi
• **Q&A**	▸ Jay Edelberg, M.D., Ph.D., Bill Sasiela, Ph.D., and Dr. Robert Califf, M.D.

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Hypercholesterolemia and Cardiovascular Disease: Unmet Medical Need

Dr. Robert Califf

Vice Chancellor for Clinical and Translational Research

Director, Duke Translational Medicine Institute

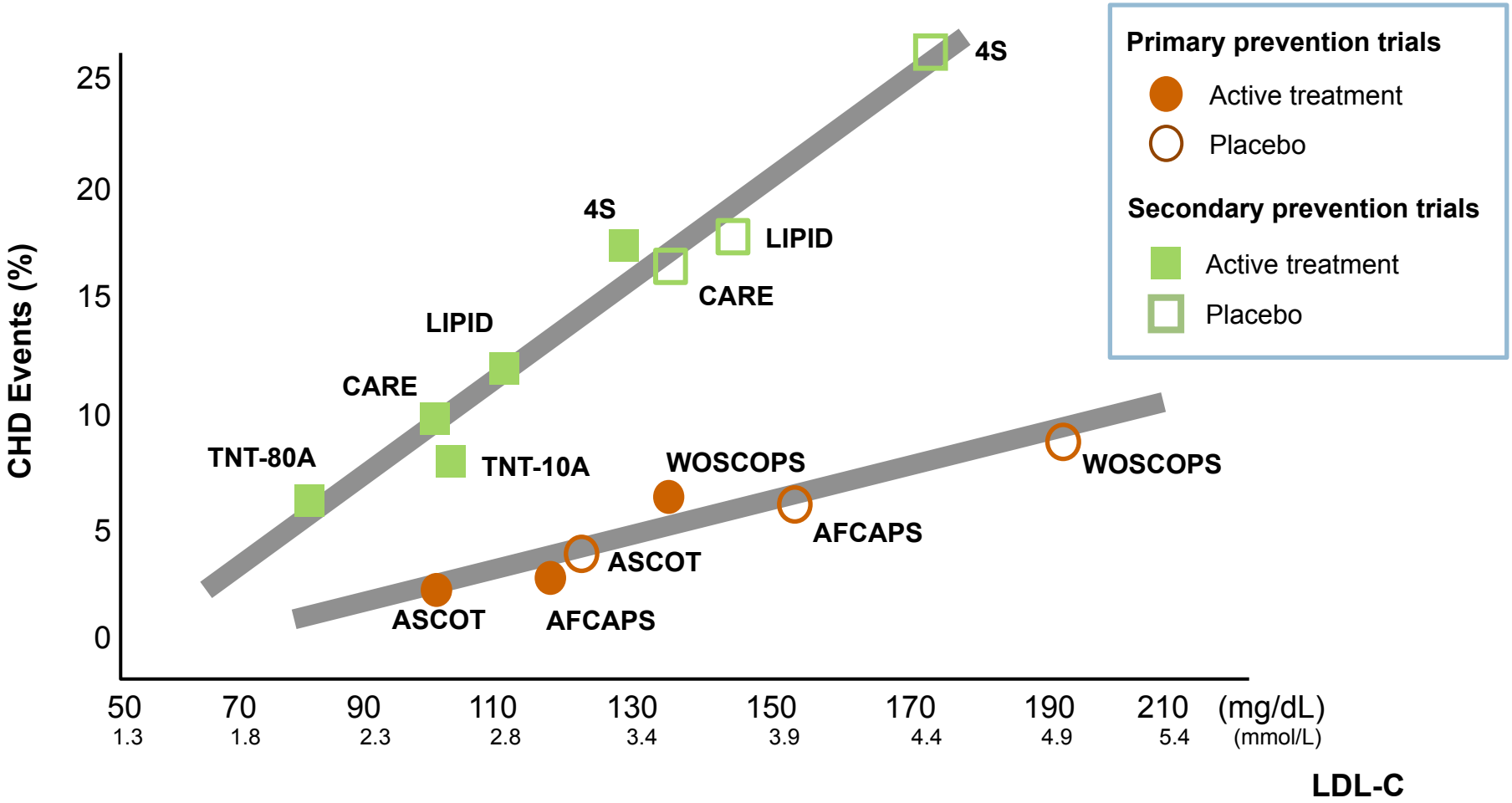
Professor of Medicine, Division of Cardiology, Duke University Medical Center

Hypercholesterolemia and Cardiovascular Disease

- Cardiovascular disease (CVD) remains the leading cause of death and disability in the Western world[1]
  - Based on US data from 2008:[2]
    - >2,200 people die of CVD each day
    - CVD currently claims more lives each year than cancer, chronic lower respiratory disease, and accidents combined
- Hypercholesterolemia (e.g. elevated LDL-C) is a major risk factor for atherosclerosis and CVD[3]
  - Heterozygous familial hypercholesterolemia (HeFH) is an inherited disease that is characterized by elevated LDL-C levels
- LDL-C is identified as the primary target of cholesterol-lowering therapies such as statins[4]

(1) WHO. Cardiovascular diseases (CVDs). Fact sheet N°317. September 2011. Accessed June 2012.
(2) Centers for Disease Control and Prevention. Vital Statistics Public Use Data Files - 2008 Mortality Multiple Cause Files. Accessed May 25, 2012.
(3) Sharrett AR, et al. *Circulation* 2001;104:1108-13.
(4) ESC/EAS Guidelines for the management of dyslipidaemias. *Eur Heart J* 2011;32:1769-818.

Lowering LDL-C with Statins is Effective in Decreasing CV Risk



Adapted from O'Keefe et al. *J Am Coll Cardiol* 2004;43:2142-6; LaRosa JC et al. *N Engl J Med* 2005;352:1425-35.

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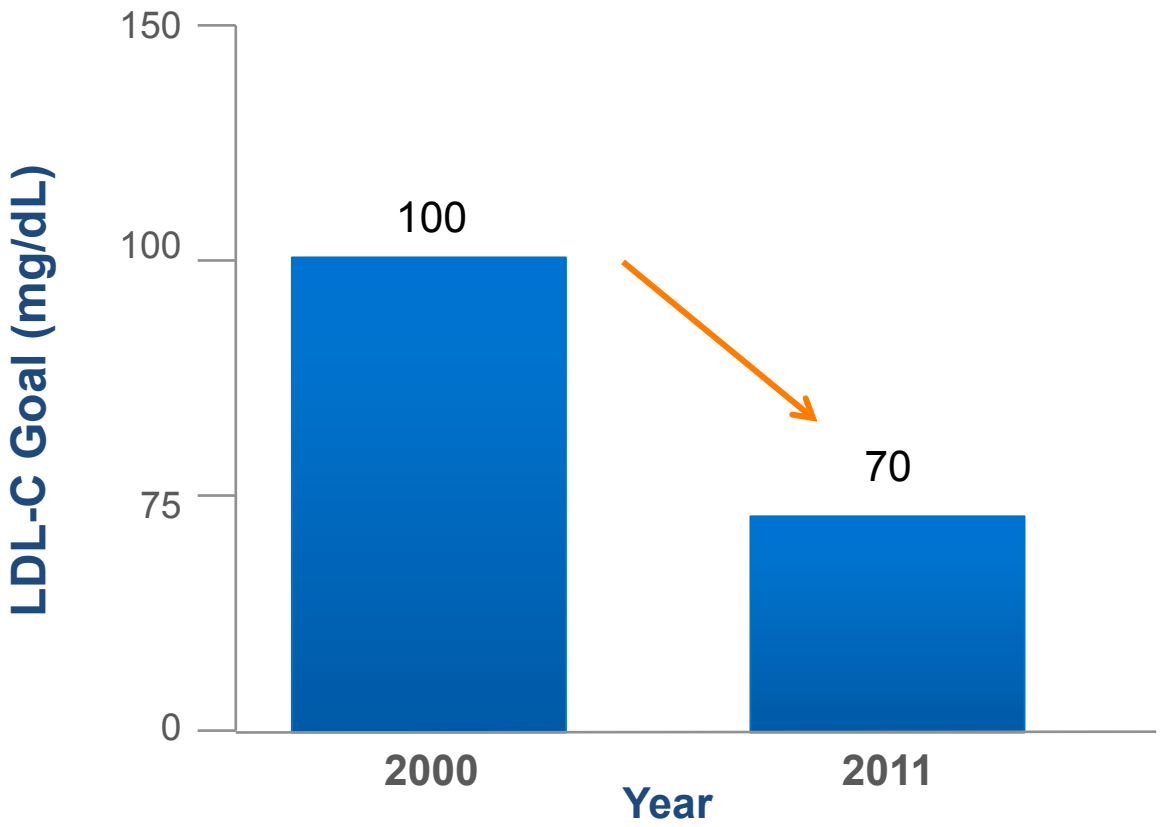
LDL-C Guidelines Have Evolved to More Rigorous Goals



These guidelines have identified people with documented CHD or CHD risk equivalents as most at risk of CHD

Sources: Grundy SM, et al. *Circulation* 2004;110:227-39., ESC/EAS Guidelines for the management of dyslipidaemias. *Eur Heart J* 2011;32:1769-818., Gitt AK, et al. *Clin Res Cardiol* 2010;99:723-33.

Hypercholesterolemia and Cardiovascular Disease

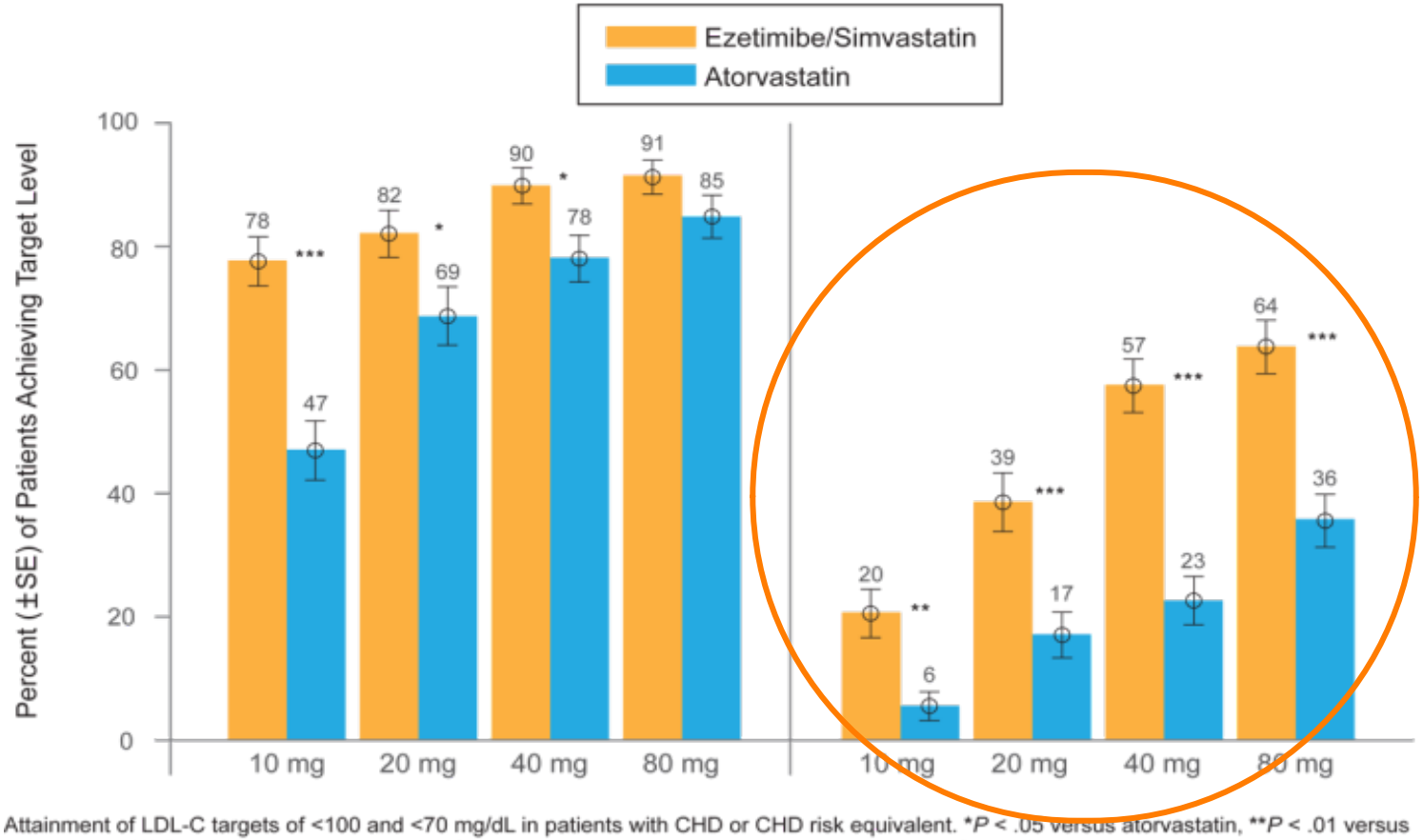
- Despite the availability of statins, many patients with hypercholesterolemia are not reaching their recommended LDL-C goal with current therapy[1,2]
  - US: ~63 million patients with elevated LDL-C, 12 million patients not at goal[3]
- Globally, 21 million patients are estimated to not be at goal LDL-C levels[4]

(1) ESC/EAS Guidelines for the management of dyslipidaemias. *Eur Heart J* 2011;32:1769-818.
(2) Hermans MP, et al. *Curr Med Res Opin* 2010;26:445-54.
(3) Seidah NG, et al. *Nat Rev Drug Discov*. 2012;11:367-83.
(4) Adapted from Decision Resources 2008, Decision Resources 2010 and CVReg 2011.

Despite Existing Therapy, Many Patients Fail to Reach LDL-C Goals

N=1,850 (~230/arm); Baseline LDL-C = ~175-180 mg/dL

LDL-C < 100 mg/dL **LDL-C < 70 mg/dL**



Attainment of LDL-C targets of <100 and <70 mg/dL in patients with CHD or CHD risk equivalent. *$P < .05$ versus atorvastatin, **$P < .01$ versus atorvastatin, *** $P < .001$ versus atorvastatin. Statin doses are listed on the x-axis; ezetimibe is a fixed 10-mg dose.

Ballantyne CM, et al. *Am Heart J* 2005;149:470.

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Important Unmet Needs in Patients Already Treated with Lipid Lowering Therapies

Countries	Patient type	Goal	% Uncontrolled
U.S.	20,000 veterans with coronary heart disease[1]	<70 mg/dL	59%
Canada and 11 EU countries	22,000 non-diabetic/ non-metabolic syndrome statin-treated outpatients[2]	<97 or <116 mg/dL, based on patient risk category	52%
8 EU countries	15,000 patients receiving lipid-lowering drugs[3]	<97 or <116 mg/dL, based on patient risk category	45%

In addition, ~5-10% of patients treated with statins are intolerant[4,5]

(1) Hermans MP, et al. *Curr Med Res Opin* 2010;26:445-54.
(2) Virani SS, et al. *Am Heart J* 2011;161:1140-6.
(3) Leiter LA, et al. *Diabet Med* 2011;28:1343-51.
(4) Nair JK, et al. *Br J Cardiol* 2008;15:158-60.
(5) Bruckert E, et al. *Cardiovasc Drugs Ther* 2005;19:403-14.

Recent Studies Show Therapeutic Regimens Resulting in Lower LDL-C Levels Lead to Further Reductions in CV Events in a Variety of Patient Populations

Trial	Patient Population	Number of Patients	Comparator LDL-C	Treatment LDL-C	% RRR in CV Events
PROVE-IT / TIMI-22	Acute Coronary Syndrome	4,162	95 mg/dL	**62 mg/dL**	**25%**
TNT	Secondary Prevention	10,001	101 mg/dL	**77 mg/dL**	**22%**
JUPITER	Primary Prevention (+ Risk Factors)	17,802	110 mg/dL	**55 mg/dL**	**44%**

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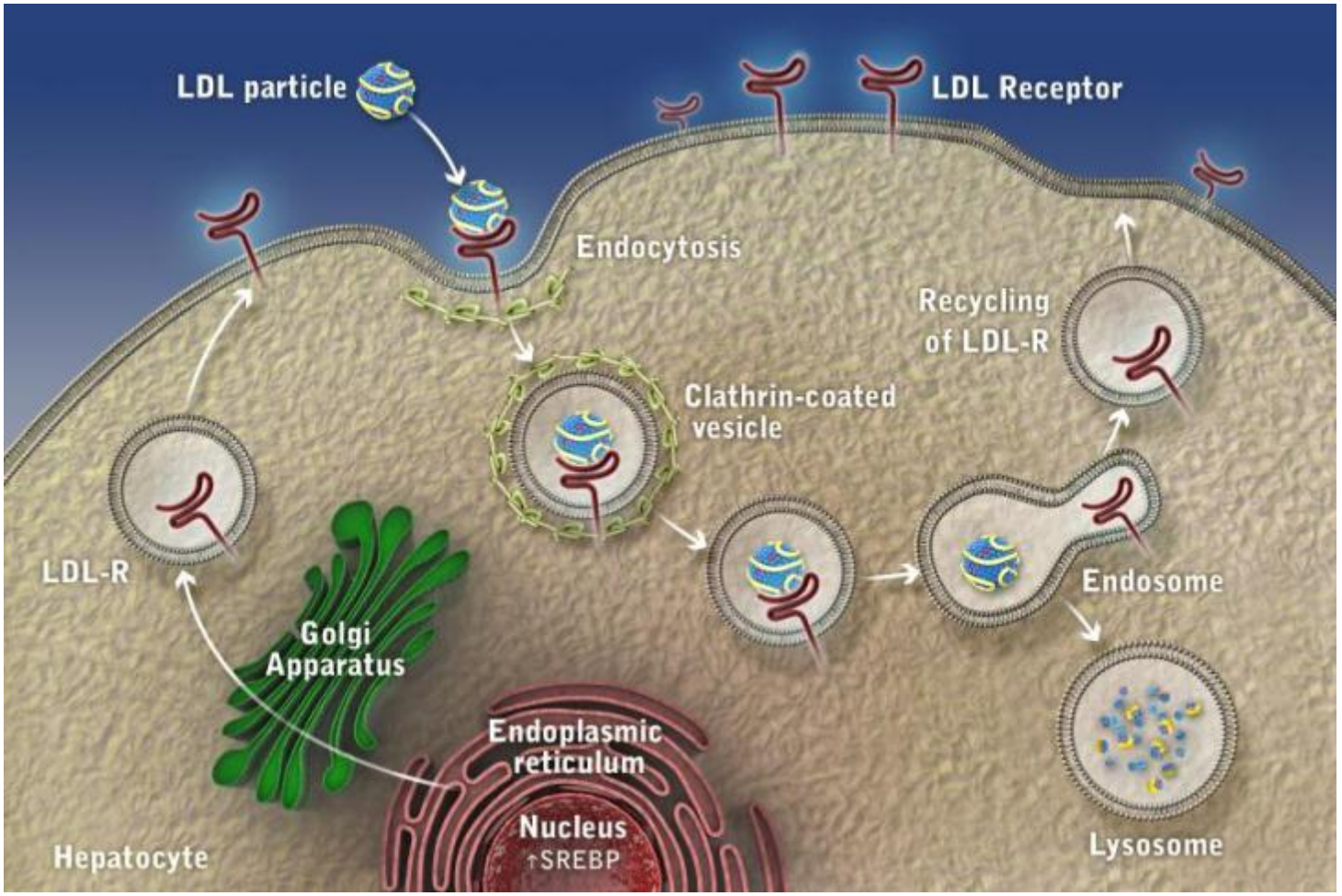
PCSK9 Mechanism of Action and Introduction to SAR236553/REGN727

Bill Sasiela, Ph.D.

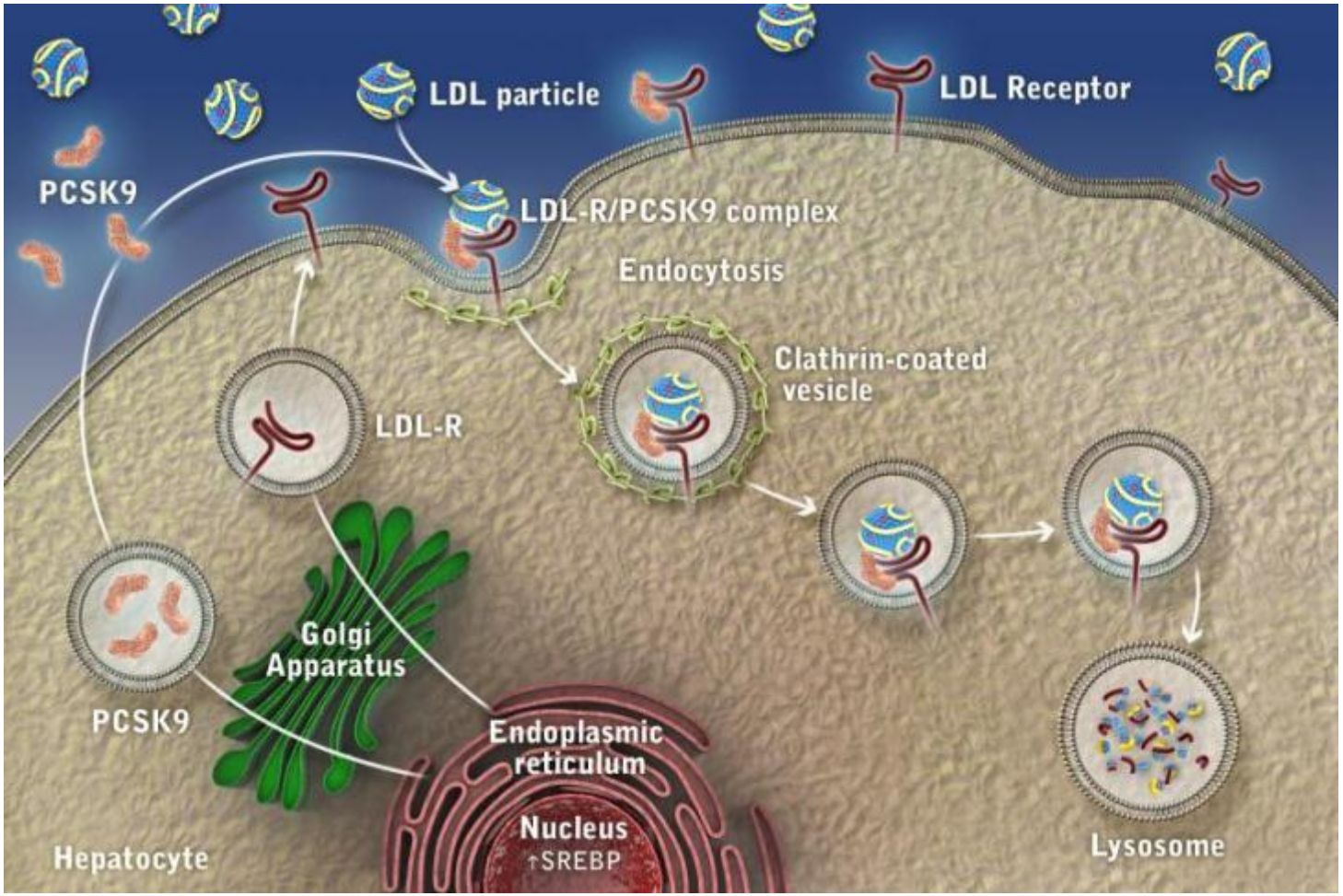
Vice President, Program Direction, Regeneron

LDL Receptors Remove Free LDL-C from the Bloodstream[1-5]



(1) Tibolla G et al. *Nutr Metab Cardiovasc Dis* 2011;21:835-43. (2) Akram ON et al. *Arterioscler Thromb Vasc Biol* 2010;30:1279-81.
(3) Duff CJ et al. *Expert Opin Ther Targets* 2011;15:157-68. (4) Horton JD et al. *J Lipid Res* 2009;50 Suppl:S172-7. (5) Cariou B et al. *Atherosclerosis* 2011;216:258-65.

PCSK9 Prevents Re-cycling of LDL-R, Leading to Elevated LDL-C Levels[1-5]



(1) Tibolla G et al. *Nutr Metab Cardiovasc Dis* 2011;21:835-43. (2) Akram ON et al. *Arterioscler Thromb Vasc Biol* 2010;30:1279-81.
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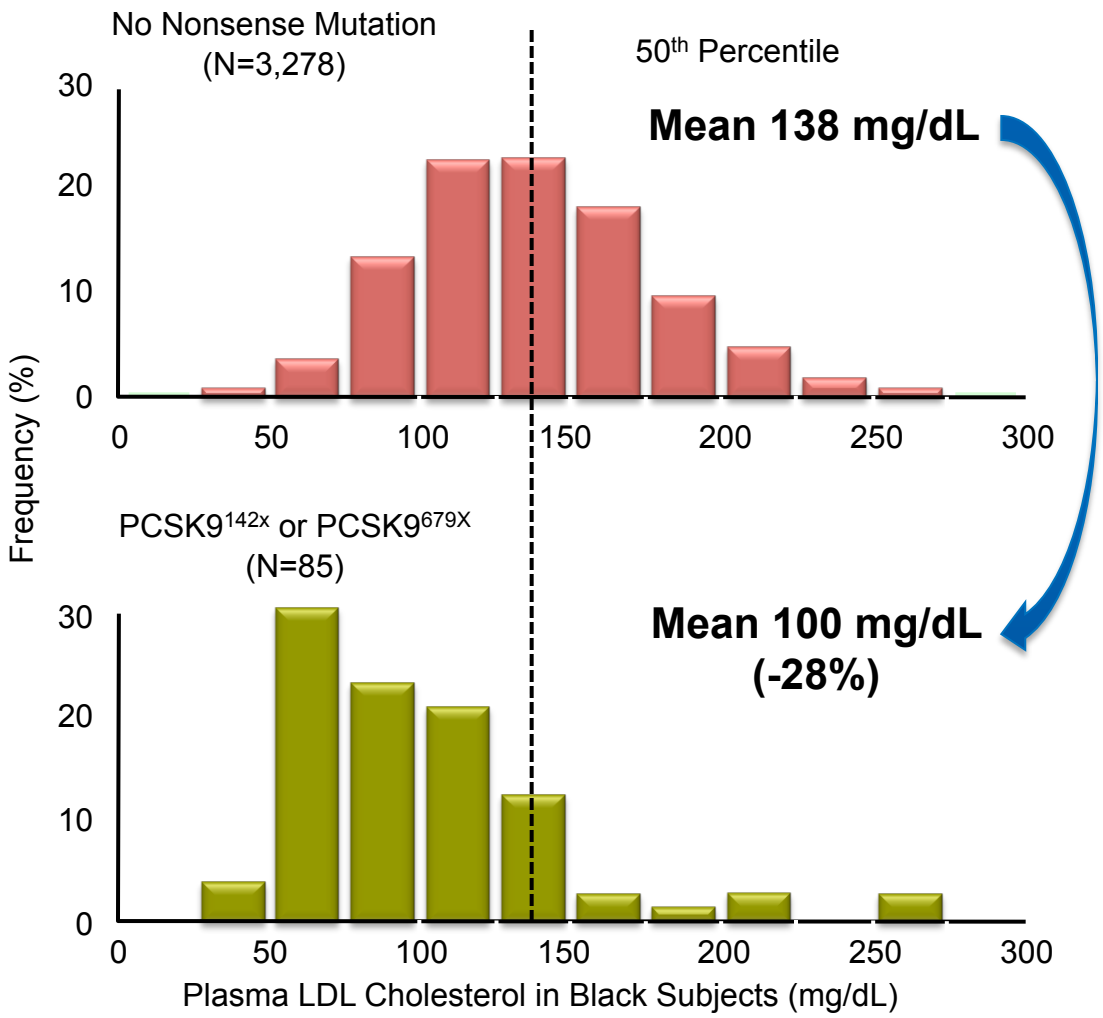
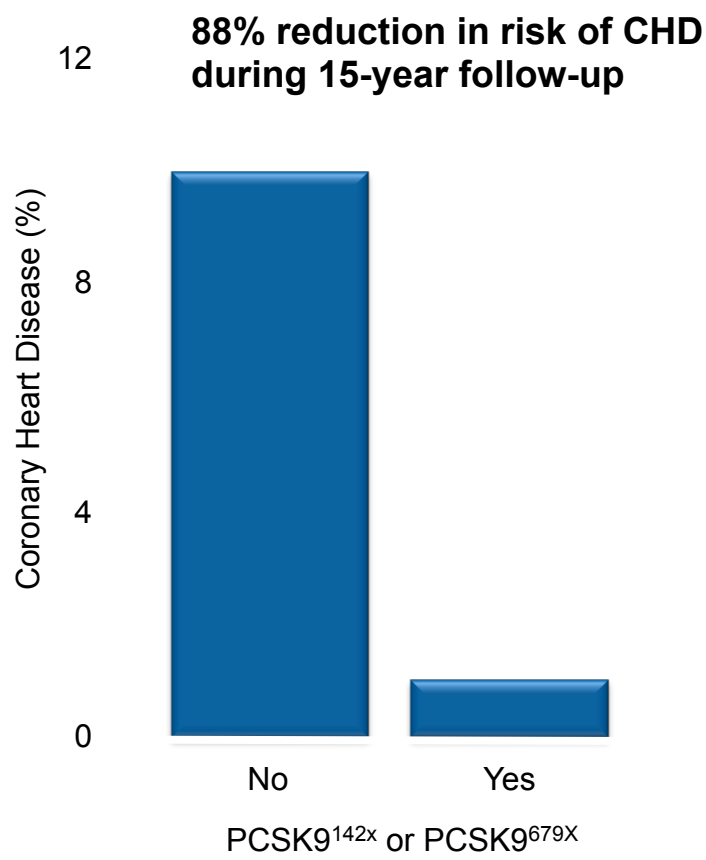
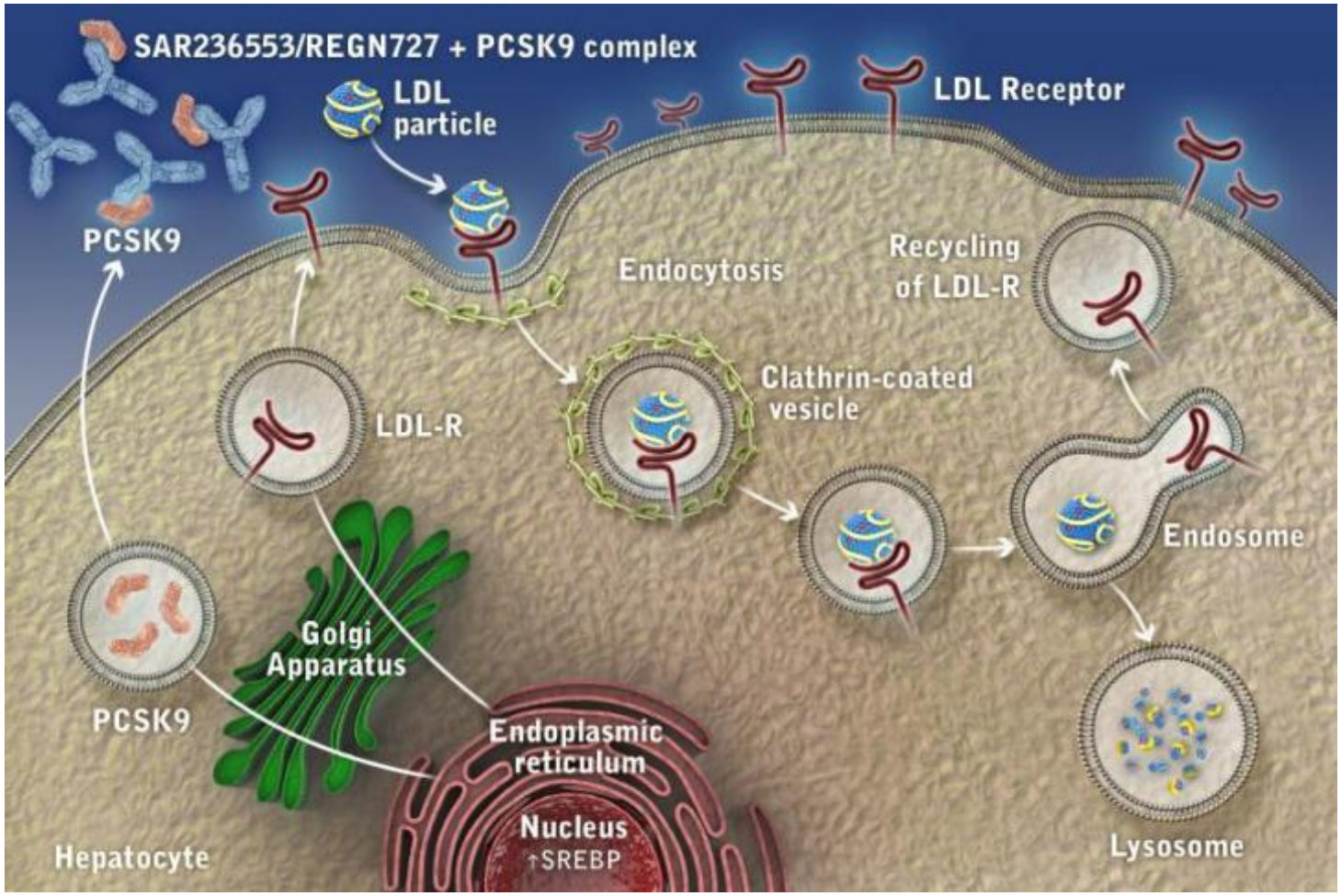
Loss of Function Mutation Demonstrates Role of PCSK9 in Regulating LDL-C





Cohen JC. *N Engl J Med* 2006;354:1264-72

Blocking PCSK9 can Potentially Lower LDL-C Levels[1-5]



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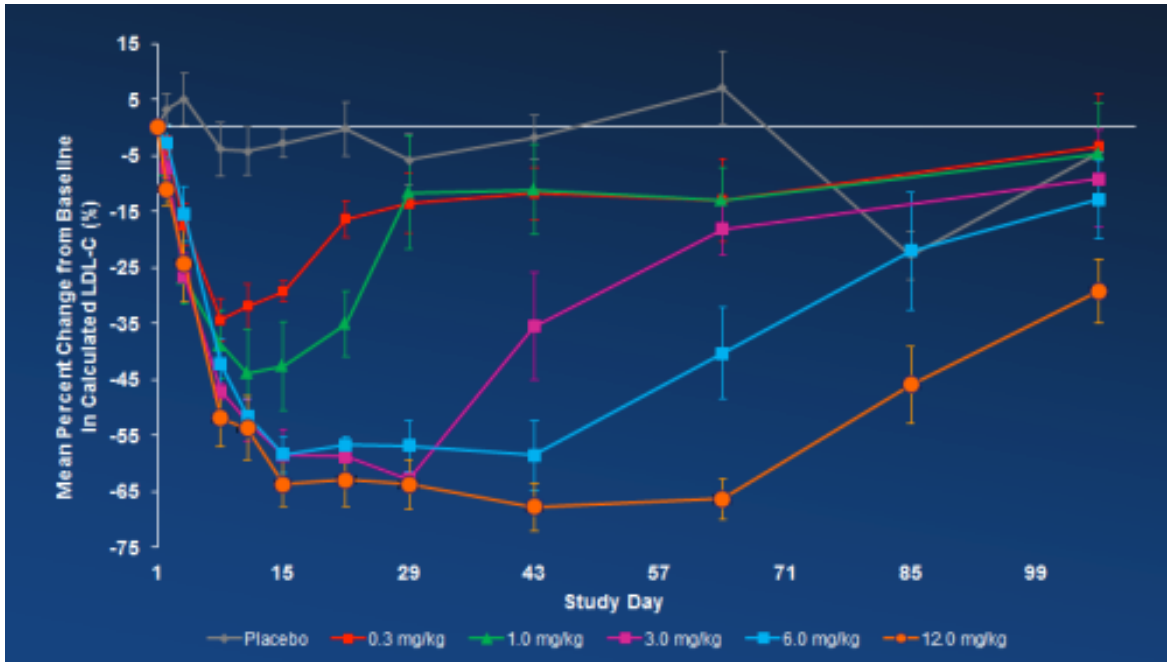
Phase 1 Data in Healthy Volunteers: Dose Dependent and Sustained Reductions in LDL-C

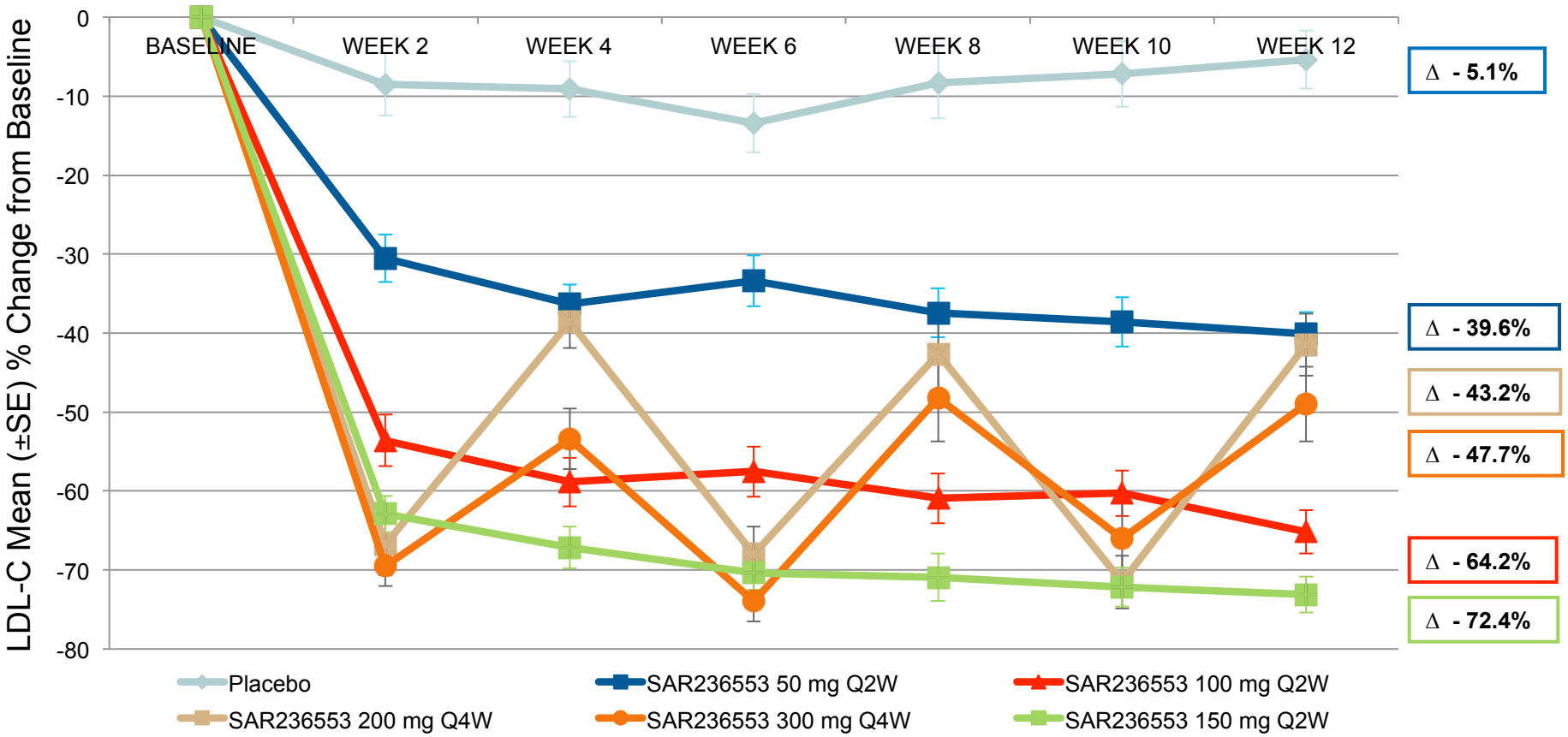
- In Phase 1 trials in healthy volunteers, familial and non-familial hypercholesterolemia:
  - SAR236553/REGN727 dose-dependently reduced LDL-C with or without atorvastatin
  - No discontinuations
  - Small number of mild injection-site reactions when administered subcutaneously
  - Headache was most common TEAE



Stein EA, et al. *N Engl J Med* 2012;366:1008-118.

Phase 2 Data Demonstrated Significant LDL-C Reduction

Q2W Dosing Provides Consistent and Sustained Effect



Mean percentage change in calculated LDL-C from baseline to weeks 2, 4, 6, 8, 10, and 12 in the modified intent-to-treat (mITT) population, by treatment group. Week 12 estimation using LOCF method.

McKenney JM, et al. *J Am Coll Cardiol* 2012;59:2344-53.

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Phase 2 Data Demonstrated Significant LDL-C Reduction

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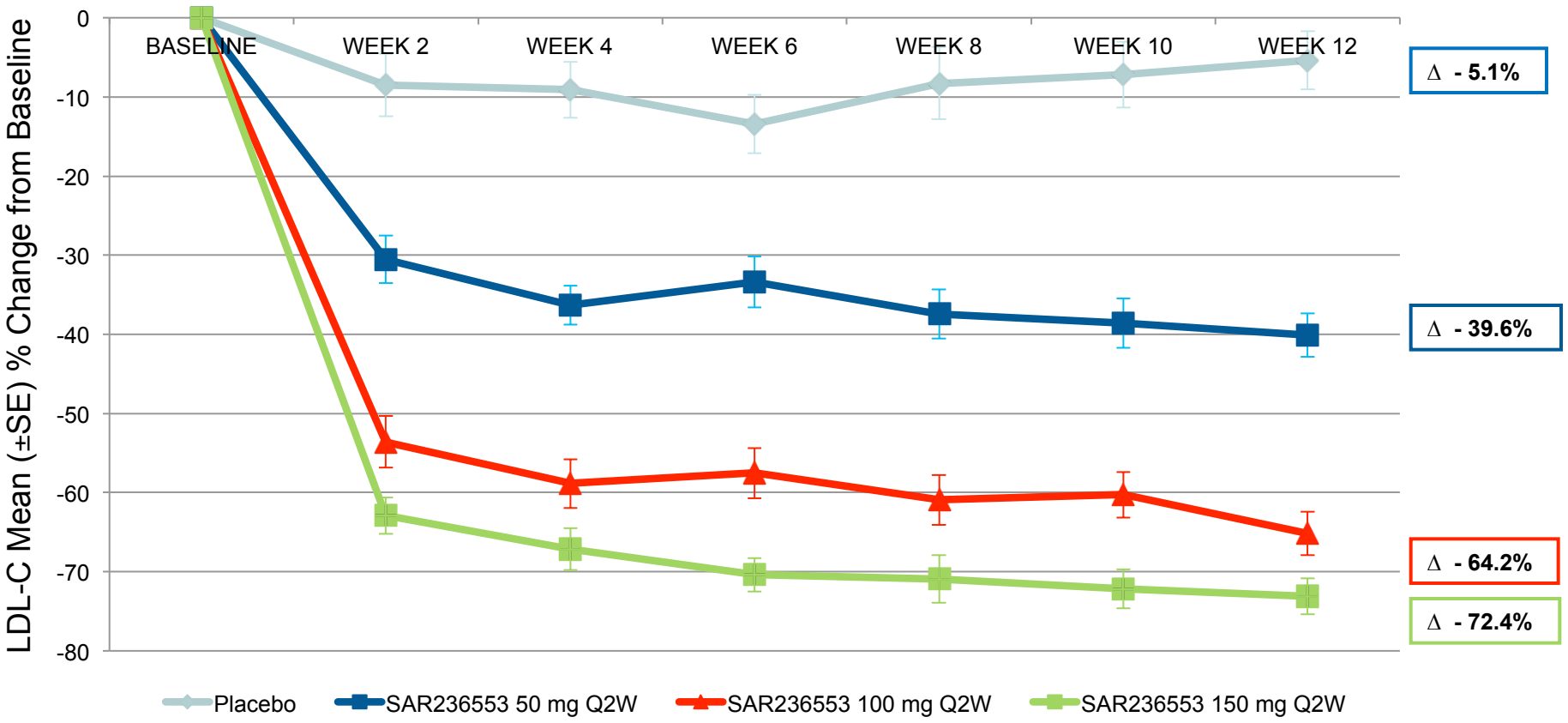

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Summary & Conclusions from Completed Clinical Studies

Efficacy:

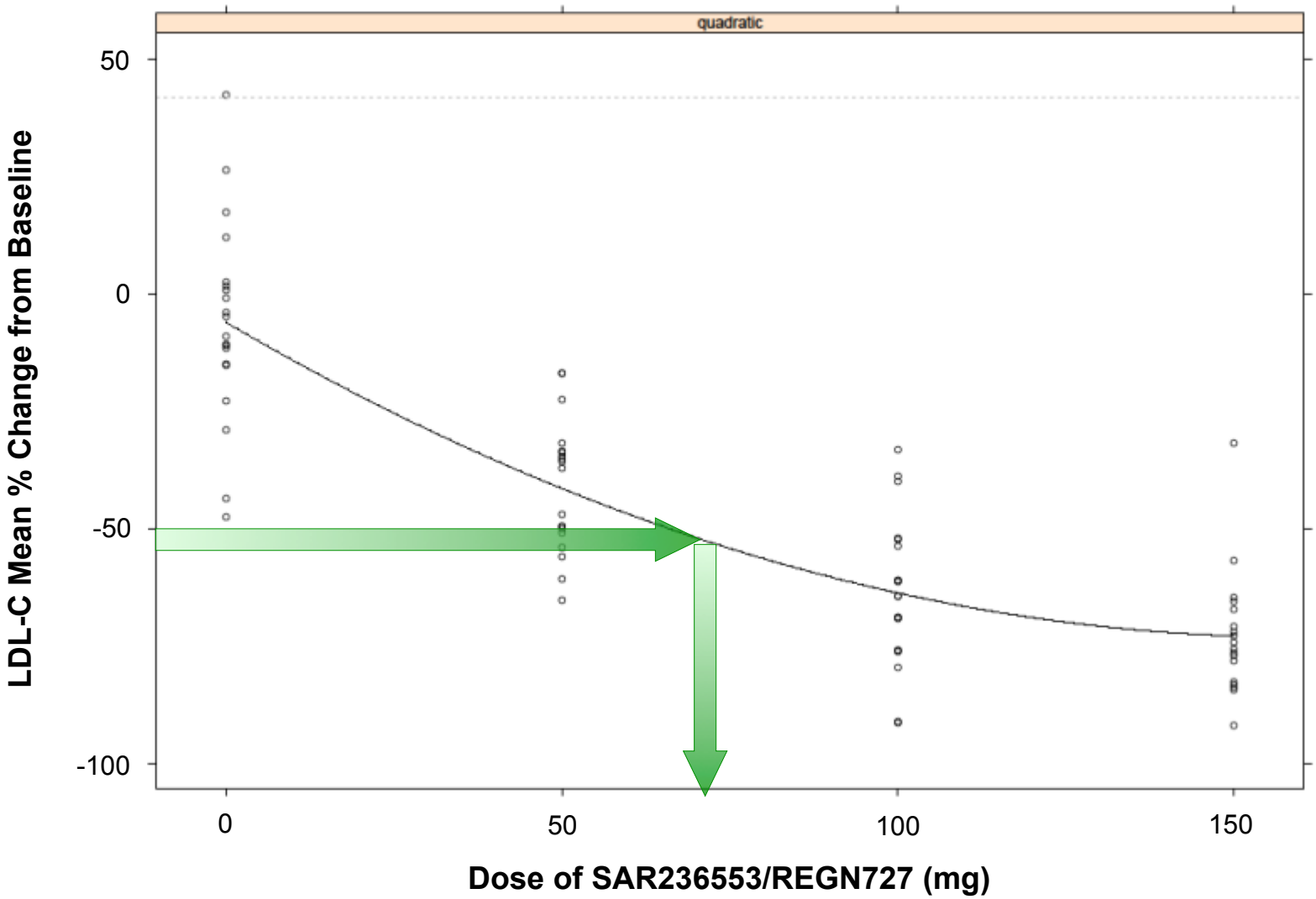
- Reductions in LDL-C of up 66.2% to 72.4% with 150 mg Q2W; consistent effects in HC and HeFH patients
- Q2W dose provides more stable/consistent reductions over time compared to Q4W dosing
- Corresponding reductions in TC, apoB (up to 56%) and non-HDL-C (up to 63%)
- Reductions in Lp(a) of up to 30+%
- Evidence for modest reductions in TGs and increases in HDL-C

Safety and tolerability – Experience to date:

- No deaths
- Discontinuations:
  SAR236553/REGN727 →8/275 (2.9%);
  PBO →4/77 (5.2%)
- SAEs:
  SAR236553/REGN727 → 4/275 (1.5%)
- Arthralgia, COPD, leucocytoclastic vasculitis, humerus fracture
  PBO → 2/77 (2.6)%

- TEAEs
  - Slightly higher TEAE rate observed with SAR236553/REGN727
  - Most common TEAE: mild injection site reaction
  - No persistent/prevalent liver or skeletal muscle safety signals

SAR236553/REGN727: Dose Response Quadratic Model Prediction



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Phase 2 Data Inform Phase 3 Dose Selection: Sustained and Consistent LDL-C Lowering

75mg and 150mg Q2W

- 150 mg demonstrated ~70% LDL-C reduction in Phase 2
- Modeling indicates that 75 mg expected to provide ~50% LDL-C reduction

Ability to Up-Titrate

- Up-titration provides ability for physicians to adjust dose to achieve individual patients goals

Evaluation of Consistency of Response

- The goal is to develop two doses that provide consistent reductions in LDL-C at all post-dose time points in combination with any and all background lipid-lowering therapies

1 mL volume in sub-cutaneous, auto-injector being evaluated in Phase 3

The ODYSSEY Phase 3 Program

Jay Edelberg, M.D., Ph.D.

VP, Head of the PCSK9 Development & Launch Unit, Sanofi

ODYSSEY – A Large Phase 3 Clinical Trial Program Initiated Across a Broad Patient Population

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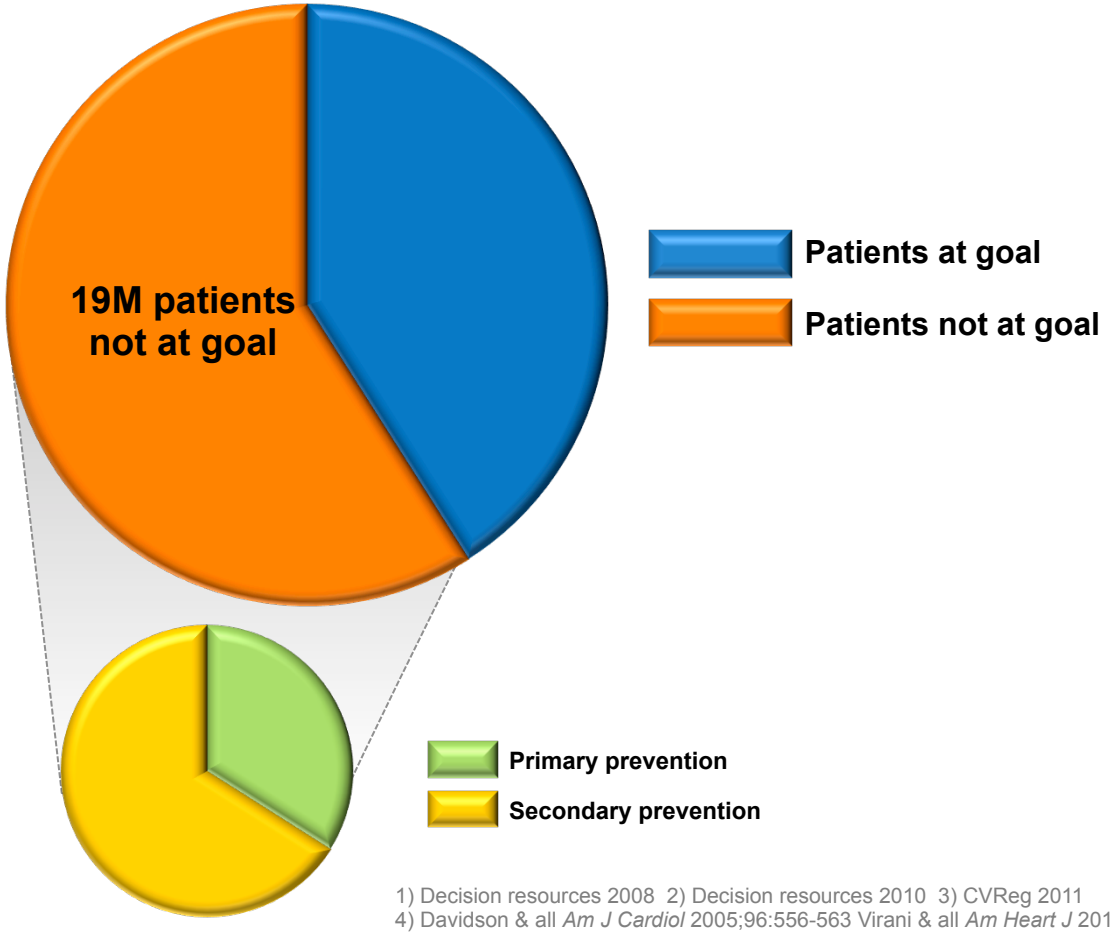
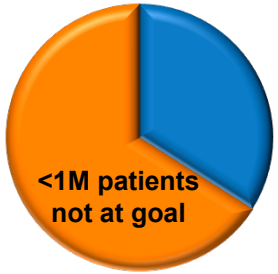
Population (No. of patients in trials)	**Clinical setting**	**Studies**
Heterozygous familial hypercholesterolemia (n=826)	• On top of standard of care	FH I, FH II, HIGH FH
High CV risk (n=3,716) • MI, Stroke, T2D, CKD	• On top of standard of care • Comparison vs. ezetimibe • Comparison vs. statin up-titration	COMBO I, LONG TERM, COMBO II, OPTIONS I, OPTIONS II, OPTIONS I, OPTIONS II
Statin intolerant (n=250)	• Comparison vs. ezetimibe and atorvastatin	ALTERNATIVE
Primary hypercholesterolemia (n=100)	• Comparison vs. ezetimibe	MONO
High Risk CV (n=18,000) • Recent ACS	• On top of standard of care	OUTCOMES

Despite Existing Therapy, Many Patients Fail to Reach LDL-C Goals[1-4]

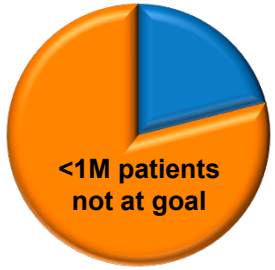
HC at high CV risk population



Statin Intolerant



HeFH population



1) Decision resources 2008 2) Decision resources 2010 3) CVReg 2011
4) Davidson & all *Am J Cardiol* 2005;96:556-563 Virani & all *Am Heart J* 2011;161:114

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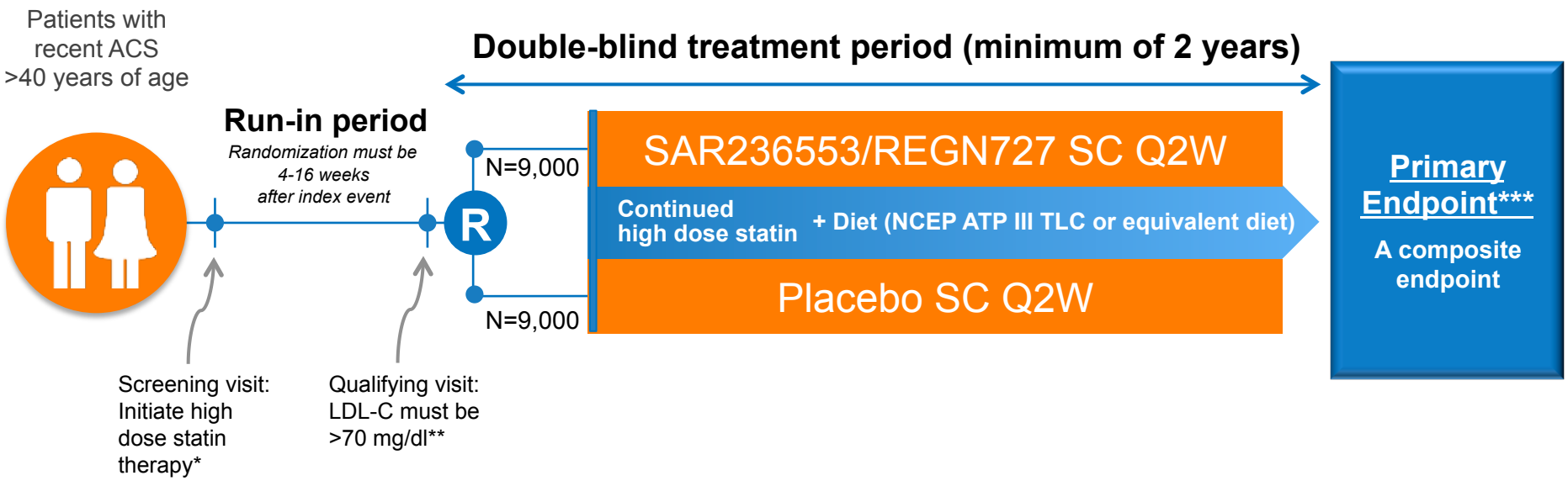
Overview of ODYSSEY OUTCOMES Phase 3 Clinical Trial

A randomized, double-blind, placebo-controlled study (NCT01663402), sponsored by Sanofi and Regeneron, to evaluate the safety and efficacy of (SAR236553/REGN727) in patients who have recently experienced an Acute Coronary Syndrome (ACS)



*High intensity statin therapy include atorvastatin 40/80 mg or rosuvastatin 20/40 mg
** Patients can also qualify with apoB>80 mg/dl or non-HDL-C > 100 mg/dl
***Primary endpoint is a composite endpoint of coronary heart disease (CHD) death, non-fatal myocardial infarction (MI), fatal and non-fatal ischemic stroke, and unstable angina requiring hospitalization

ODYSSEY Phase 3 Clinical Trial Program: Expected Timeline

2012 2013 2014 2015 2016 2017 2018

Enrollment in all Phase 3 trials has initiated

- First Phase 3 program to study the effect of blocking PCSK9 on lipids and CV outcomes

Regulatory approval in US and EU is expected based on LDL-C primary endpoint

- Assumes acceptable safety profile and no change in view of LDL-C as a valid surrogate endpoint for approval
- First launch expected by the end of 2015 with global launch in 2016

Outcomes trial expected to conclude in 2018

- Timing dependent on enrollment and event rate

The ODYSSEY Phase 3 Clinical Trial Program

Summary

- CVD is leading case of death and morbidity in the Western World
- Despite available therapies, many patients unable to reach their LDL-C goals
- PCSK9 represents a novel pathway to potentially achieve lower LDL-C levels
- SAR236553/REGN727 is a novel, fully human, subcutaneously administered monoclonal antibody directed against PCSK9
- A 22,000 patient Phase 3 program—ODYSSEY—is underway across multiple patient types
  - LDL-C is the primary endpoint for initial regulatory filings
  - Includes ODYSSEY OUTCOMES, a CV outcomes trial, which will enroll approximately 18,000 patients
- Evaluating a 1mL auto-injector for both Q2W doses, 75mg and 150mg, in our Phase 3 program

Q&A