



AMG 133 PROGRAM UPDATE

WCIRD C IR CALL

DECEMBER 5, 2022

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SAFE HARBOR STATEMENT

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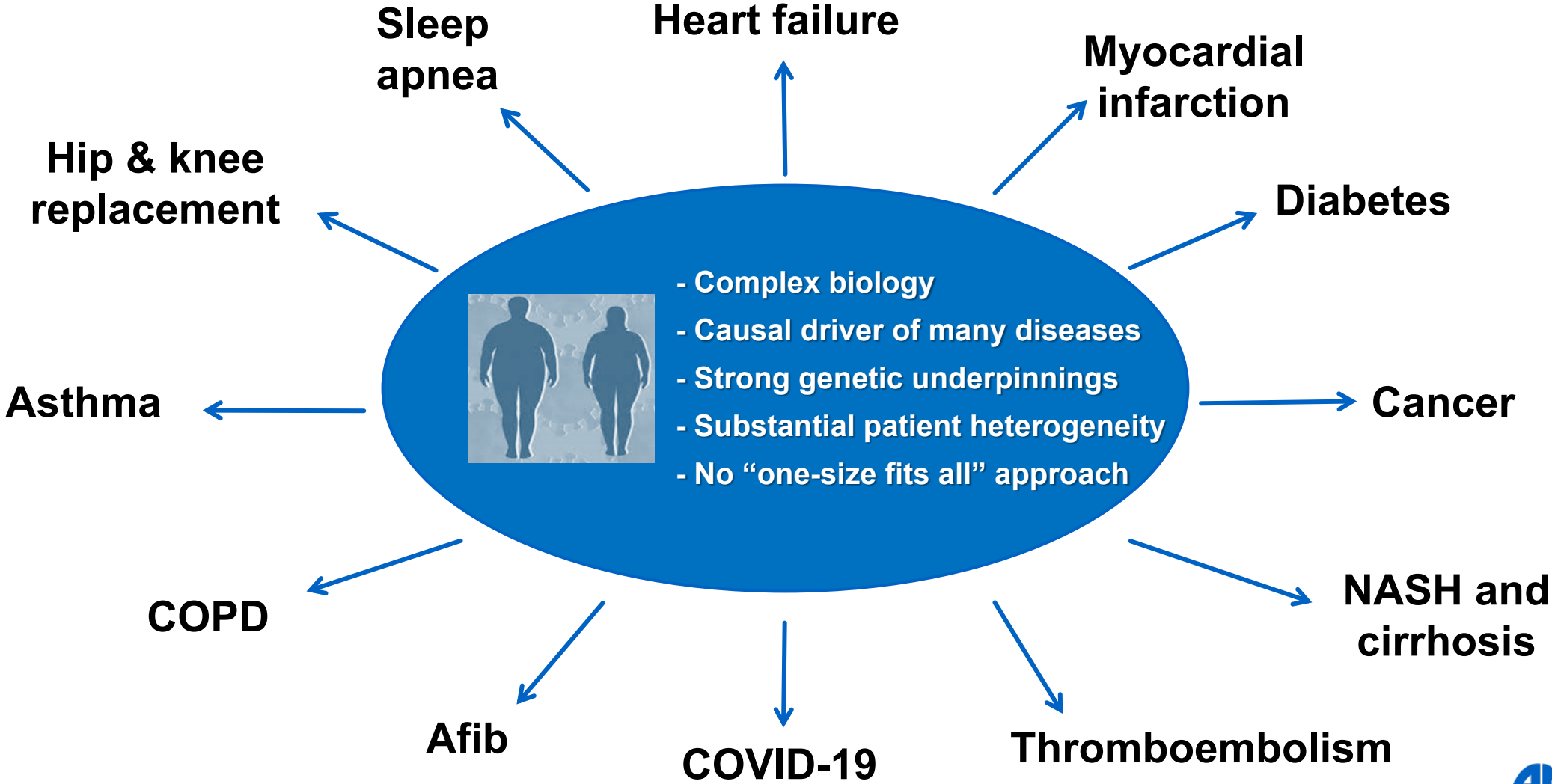
No forward-looking statement can be guaranteed and actual results may differ materially from those we project. Our results may be affected by our ability to successfully market both new and existing products domestically and internationally, clinical and regulatory developments involving current and future products, sales growth of recently launched products, competition from other products including biosimilars, difficulties or delays in manufacturing our products and global economic conditions. In addition, sales of our products are affected by pricing pressure, political and public scrutiny and reimbursement policies imposed by third-party payers, including governments, private insurance plans and managed care providers and may be affected by regulatory, clinical and guideline developments and domestic and international trends toward managed care and healthcare cost containment. Furthermore, our research, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. We or others could identify safety, side effects or manufacturing problems with our products, including our devices, after they are on the market. Our business may be impacted by government investigations, litigation and product liability claims. In addition, our business may be impacted by the adoption of new tax legislation or exposure to additional tax liabilities. If we fail to meet the compliance obligations in the corporate integrity agreement between us and the U.S. government, we could become subject to significant sanctions. Further, while we routinely obtain patents for our products and technology, the protection offered by our patents and patent applications may be challenged, invalidated or circumvented by our competitors, or we may fail to prevail in present and future intellectual property litigation. We perform a substantial amount of our commercial manufacturing activities at a few key facilities, including in Puerto Rico, and also depend on third parties for a portion of our manufacturing activities, and limits on supply may constrain sales of certain of our current products and product candidate development. An outbreak of disease or similar public health threat, such as COVID-19, and the public and governmental effort to mitigate against the spread of such disease, could have a significant adverse effect on the supply of materials for our manufacturing activities, the distribution of our products, the commercialization of our product candidates, and our clinical trial operations, and any such events may have a material adverse effect on our product development, product sales, business and results of operations. We rely on collaborations with third parties for the development of some of our product candidates and for the commercialization and sales of some of our commercial products. In addition, we compete with other companies with respect to many of our marketed products as well as for the discovery and development of new products. Discovery or identification of new product candidates or development of new indications for existing products cannot be guaranteed and movement from concept to product is uncertain; consequently, there can be no guarantee that any particular product candidate or development of a new indication for an existing product will be successful and become a commercial product. Further, some raw materials, medical devices and component parts for our products are supplied by sole third-party suppliers. Certain of our distributors, customers and payers have substantial purchasing leverage in their dealings with us. The discovery of significant problems with a product similar to one of our products that implicate an entire class of products could have a material adverse effect on sales of the affected products and on our business and results of operations. Our efforts to collaborate with or acquire other companies, products or technology, and to integrate the operations of companies or to support the products or technology we have acquired, may not be successful. A breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of our systems and our data. Our stock price is volatile and may be affected by a number of events. Our business and operations may be negatively affected by the failure, or perceived failure, of achieving our environmental, social and governance objectives. The effects of global climate change and related natural disasters could negatively affect our business and operations. Global economic conditions may magnify certain risks that affect our business. Our business performance could affect or limit the ability of our Board of Directors to declare a dividend or our ability to pay a dividend or repurchase our common stock. We may not be able to access the capital and credit markets on terms that are favorable to us, or at all.



AGENDA

Topic	Presenter
Introduction	David Reese, MD Executive Vice President, Research and Development, Amgen
AMG 133 Program Update	Narimon Honarpour MD, PhD Vice President, Clinical Development, Amgen
Q&A	All

OBESITY: A COMPLEX AND HETEROGENEOUS DISEASE WITH STRONG GENETIC UNDERPINNINGS THAT CAUSES A WIDE VARIETY OF GRIEVOUS ILLNESSES



NASH = nonalcoholic steatohepatitis; Afib = atrial fibrillation.



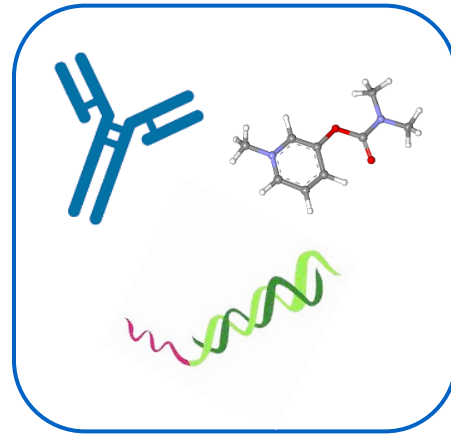
AMGEN IS TACKLING OBESITY USING DIVERSE AND INNOVATIVE APPROACHES

HUMAN GENETIC VALIDATION



- Target discovery
- Unraveling patient heterogeneity

BIOLOGY DRIVES MODALITY CHOICE



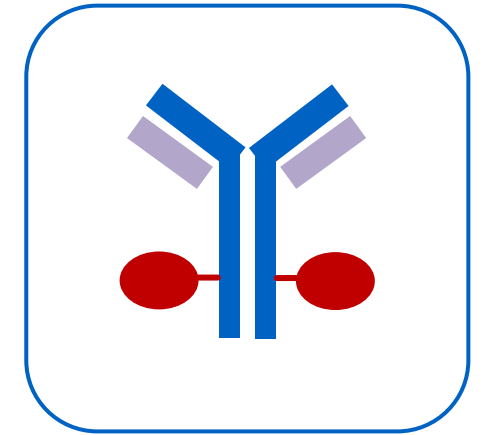
- Large molecule
- Small molecule
- siRNA
- Others

MULTI-ASSET PORTFOLIO



- Incretin based
- Non-incretins
- Novel genetics

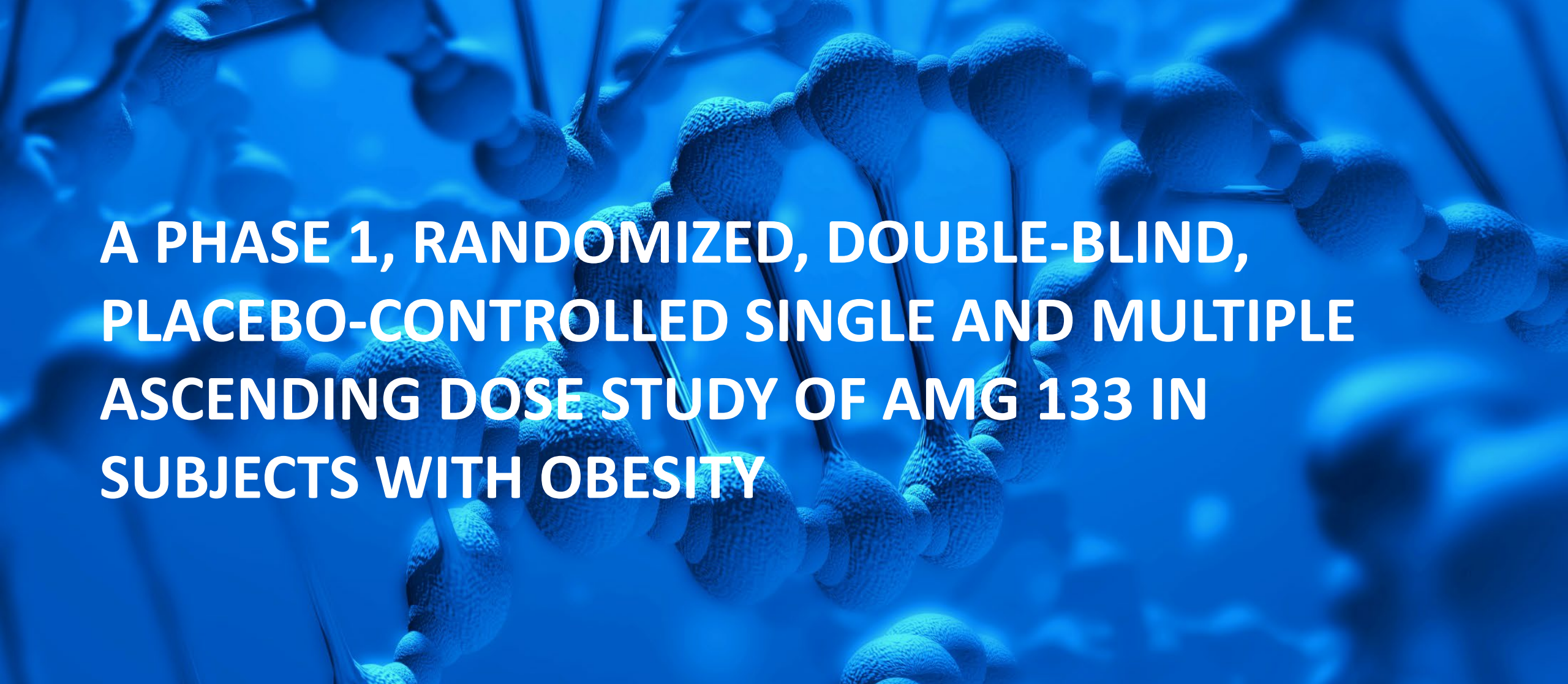
MULTI-SPECIFIC MOLECULES



- e.g., AMG 133

siRNA = small interfering ribonucleic acid.

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**A PHASE 1, RANDOMIZED, DOUBLE-BLIND,
PLACEBO-CONTROLLED SINGLE AND MULTIPLE
ASCENDING DOSE STUDY OF AMG 133 IN
SUBJECTS WITH OBESITY**

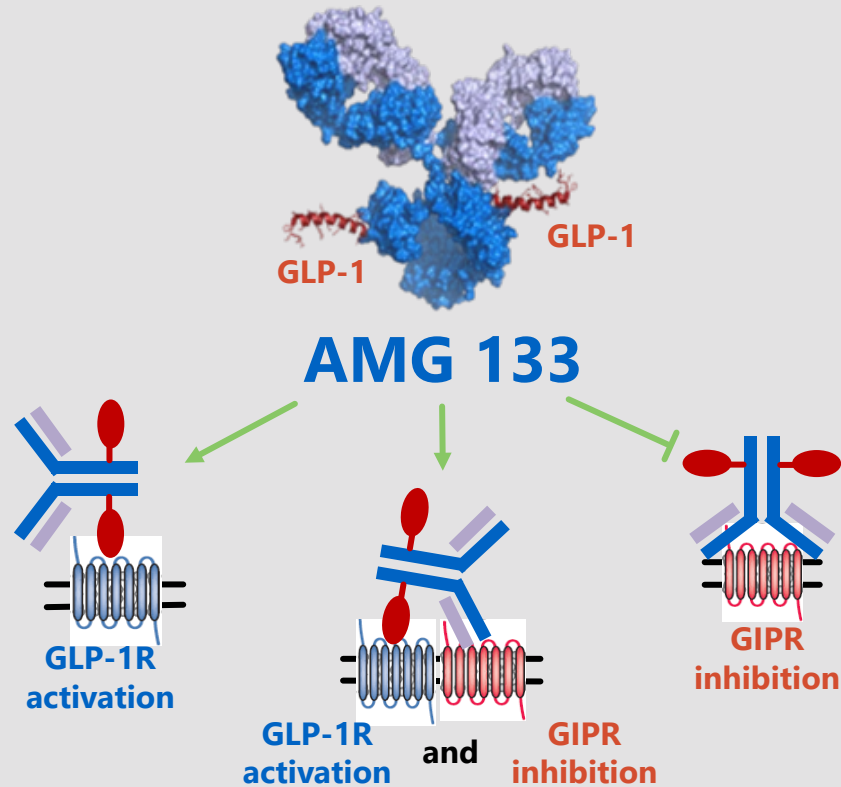
NARIMON HONARPOUR

VICE PRESIDENT CLINICAL DEVELOPMENT

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AMG 133, A FIRST-IN-CLASS ANTIBODY-PEPTIDE CONJUGATE TARGETING OBESITY

GIPR INHIBITORY ANTIBODY



STUDY POPULATIONS OF GIPR VARIANTS

Japanese
Genome-wide association study¹

European
Genome-wide association study^{2,3}

Whole exome sequencing
in UK-Biobank and N. America⁴

↓ GIPR expression

↓ BMI

GIPR= Gastric Inhibitory Polypeptide Receptor; GLP-1= Glucagon-like peptide-1; GLP-1R= Glucagon-like peptide-1 receptor.

GIPR= Gastric Inhibitory Polypeptide Receptor; BMI= body mass index

1. Nature Genetics 2012; 44 (3):302-6
2. Nature Genetics 2010; 42 (11):937-48 (deCODE is collaborator)
3. Nature Genetics 2013; 45 (5):501-12 (deCODE is collaborator)
4. Science 2021; 373 (6550)

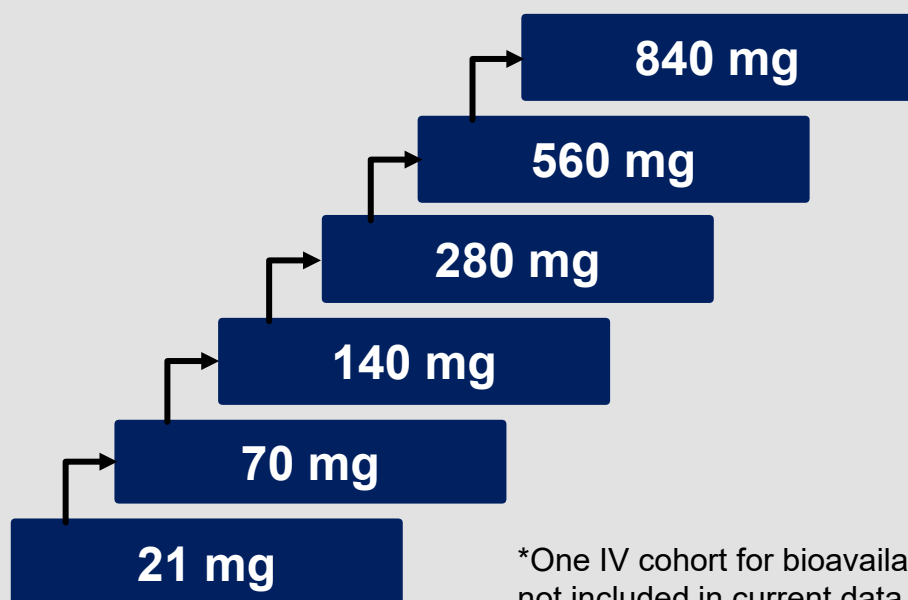
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AMG 133 PHASE 1 STUDY DESIGN AND OBJECTIVE

- **A Phase 1 randomized, double-blind, placebo-controlled study with single and multiple ascending dose cohorts.**
- **Enrolled obese subjects (BMI \geq 30.0 kg/m² to \leq 40.0 kg/m²) without other medical conditions to receive either subcutaneous AMG 133 or placebo.**
- **Evaluated safety, tolerability, pharmacokinetics, and pharmacodynamics of AMG 133 in subjects with obesity and without other medical conditions.**
- **Reporting on safety, pharmacokinetic parameters, and pharmacodynamics (body weight change).**

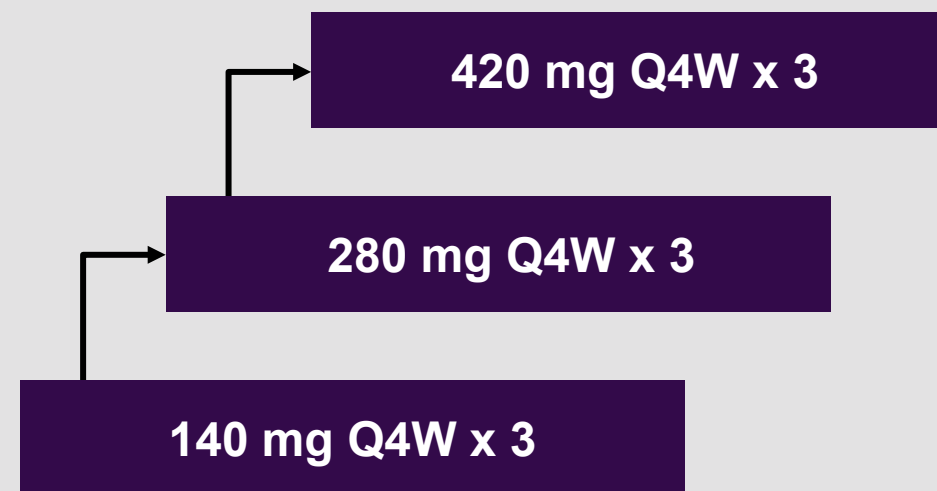
STUDY SCHEMA

Single Ascending Dose Cohorts* AMG 133:Placebo (6:2) SC x 1



*One IV cohort for bioavailability not included in current data set

Multiple Ascending Dose Cohorts** AMG 133:Placebo (6:2) SC Q4W x 3



**3 cohorts not included due to ongoing trial/analysis; 1 with digital tools and 2 with 2- or 4-week dose escalation strategies

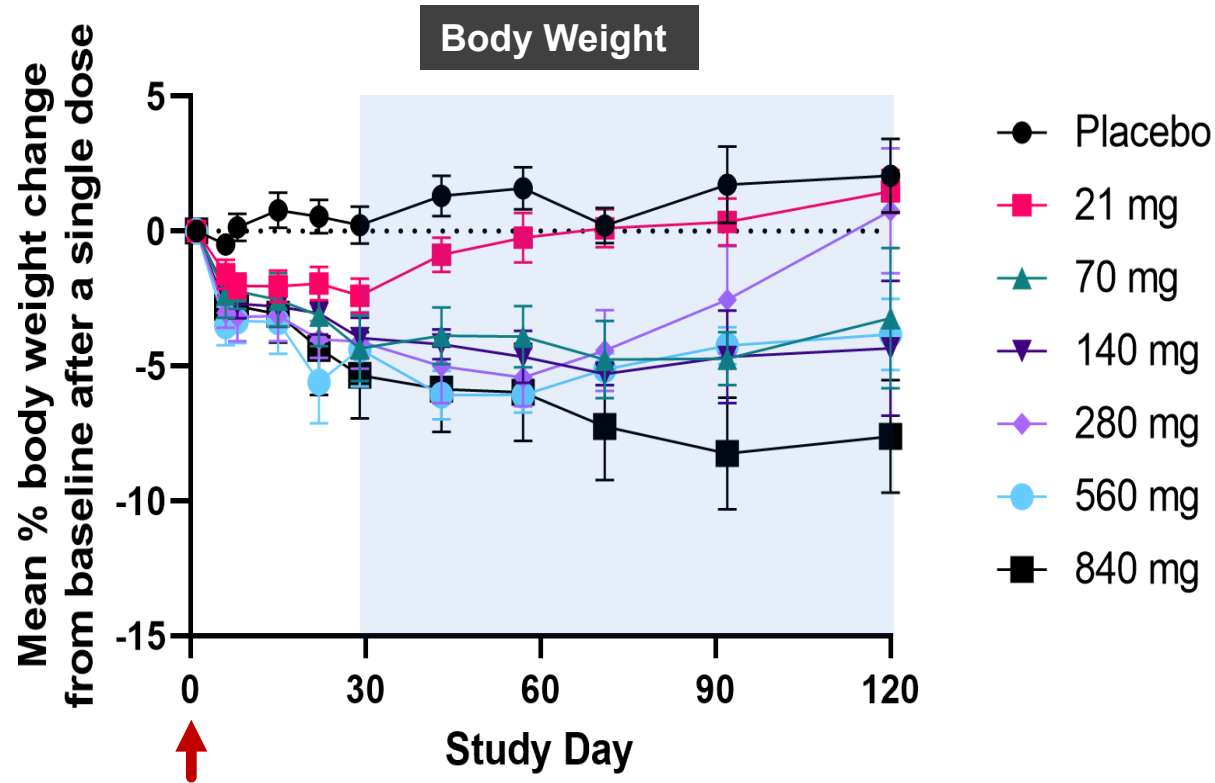
SC, subcutaneous; IV, intravenous; mg = milligram; Q4W, every 4 weeks.

BASELINE CHARACTERISTICS AND SUBJECT DISPOSITION

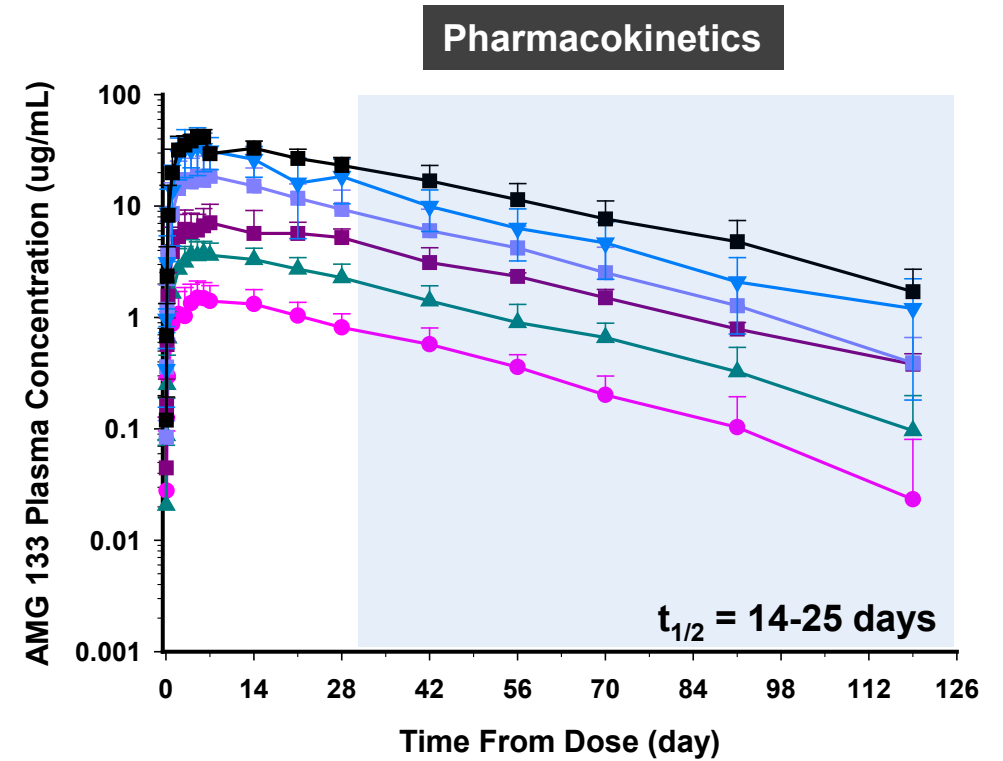
Characteristic	Single Ascending Dose (N = 49)		Multiple Ascending Dose (N = 26)	
	Placebo (N = 12)	AMG 133 (N = 37)	Placebo (N = 6)	AMG 133 (N = 20)
Age, mean \pm SD, y	45.7 \pm 13.4	48.5 \pm 10.9	45.7 \pm 14.0	46.1 \pm 4.4
Males, n (%)	8 (66.7)	24 (64.9)	2 (33.3)	10 (50.0)
Weight, mean \pm SD, kg	97.2 \pm 12.4	100.3 \pm 14.0	98.9 \pm 15.8	96.3 \pm 12.4
BMI, mean \pm SD, kg/m ²	32.8 \pm 2.1	33.6 \pm 3.0	34.2 \pm 3.7	33.3 \pm 2.9
Hemoglobin A1C, mean \pm SD, %	5.38 \pm 0.35	5.52 \pm 0.41	5.50 \pm 0.20	5.58 \pm 0.34

N, total number of subjects treated in each cohort. n, number of patients with observed data. BMI, body mass index; SD, standard deviation.

A SINGLE DOSE OF AMG 133 PROMOTES SUSTAINED WEIGHT LOSS



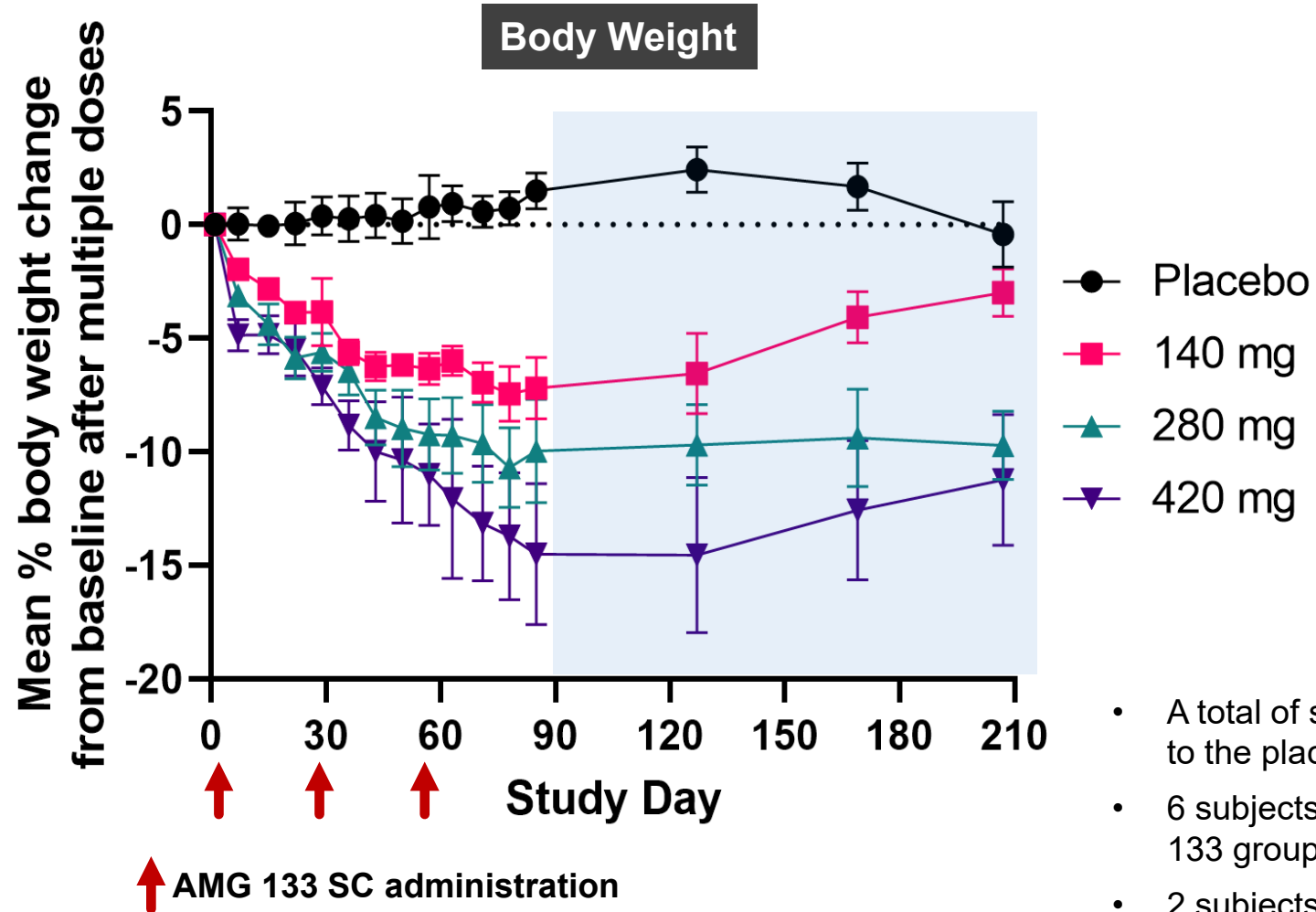
↑ AMG 133 SC administration



A total of 12 subjects were randomized to the placebo group across cohorts
 6 subjects were randomized to the AMG 133 group at each dose level
 1 subject was replaced in the 140 mg dose group

SC = subcutaneous; $t_{1/2}$ = half-life; mg = milligram.

RAPID AND SUBSTANTIAL WEIGHT LOSS WITH DURABILITY OF EFFECT AFTER LAST DOSE ADMINISTERED



- A total of six subjects were randomized to the placebo group across cohorts
- 6 subjects were randomized to the AMG 133 group at each dose level
- 2 subjects were replaced in the 420 mg dose group

SC = subcutaneous; mg = milligram.

SAFETY AND TOLERABILITY FROM SINGLE AND MULTIPLE ASCENDING DOSE COHORTS

- **No safety concerns were identified that would preclude further development**
- **The majority of TEAEs were mild and resolved within 48 hours**
- **Most TEAEs were GI-related with the most common being nausea and vomiting**
- **Among subjects with > 1 dose of AMG 133 (N=22):**
 - **> 90% of GI-related AEs were after the first dose**
 - **All GI-related AEs in this group were mild**

***Per protocol, no education or dietary guidance was given to subjects**

TEAE – treatment-emergent adverse event; GI = gastrointestinal; N = number of subjects treated; AE = adverse event.

SUMMARY AND CONCLUSION



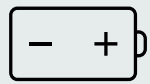
AMG 133 is a GIPR antagonist + GLP1 agonist antibody-peptide conjugate taken into human testing based on human genetic insights and preclinical evidence.



The pharmacokinetics and pharmacodynamics of AMG 133 support dosing intervals of every 4 weeks or longer



Reductions in body weight were dose proportional with up to 14.5% body weight loss at d85 following three monthly subcutaneous doses of 420 mg, each 4 weeks apart.



Durable weight loss with reductions observed for up to 150 days after the final (third) AMG 133 administration at higher doses



Most TEAEs were mild, transient and associated with the first dose administered. TEAEs were most commonly GI-related.



The safety, tolerability and PK profile as well as the magnitude, rapidity, and durability of weight loss support further clinical development of AMG 133



QUESTIONS?

DAVID REESE, MD

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