

**REGENERON**  
SCIENCE TO MEDICINE®

# REGN-COV2 ANTIBODY COCKTAIL PROGRAM UPDATE

SEPTEMBER 29, 2020



# NOTE REGARDING FORWARD-LOOKING STATEMENTS

This presentation includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("Regeneron" or the "Company"), and actual events or results may differ materially from these forward-looking statements. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," variations of such words, and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements concern, and these risks and uncertainties include, among others, the impact of SARS-CoV-2 (the virus that has caused the COVID-19 pandemic) on Regeneron's and its collaborators' ability to continue to conduct research and clinical programs (including those discussed in this presentation); the nature, timing, and possible success and therapeutic applications of products marketed by Regeneron and/or its collaborators (collectively, "Regeneron's Products") and Regeneron's product candidates and research and clinical programs now underway or planned, including without limitation the development program relating to REGN-COV2 (Regeneron's investigational two-antibody cocktail for the treatment and prevention of COVID-19) discussed in this presentation; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's product candidates (such as REGN-COV2) and new indications for Regeneron's Products; the extent to which the results from the research and development programs conducted by Regeneron and/or its collaborators (including without limitation the results from the initial patient cohort from the seamless Phase 1/2/3 trial evaluating REGN-COV2 discussed in this presentation) may be replicated and/or lead to advancement of product candidates to clinical trials, therapeutic applications, or regulatory approval; safety issues resulting from the administration of Regeneron's Products and product candidates (such as REGN-COV2) in patients, including serious complications or side effects in connection with the use of Regeneron's Products and product candidates in clinical trials; ongoing regulatory obligations and oversight impacting Regeneron's Products, research and clinical programs (such as REGN-COV2), and business, including those relating to patient privacy; determinations by regulatory and administrative governmental authorities which may delay or restrict Regeneron's ability to continue to develop or commercialize Regeneron's Products and product candidates; competing drugs and product candidates that may be superior to, or more cost effective than, Regeneron's Products and product candidates; uncertainty of market acceptance and commercial success of Regeneron's Products and product candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) on the commercial success of Regeneron's Products and product candidates; the availability and extent of reimbursement of Regeneron's Products from third-party payers, including private payer healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicare and Medicaid; coverage and reimbursement determinations by such payers and new policies and procedures adopted by such payers; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; the ability of Regeneron's collaborators, suppliers, or other third parties (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's Products and product candidates; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its financial projections or guidance and changes to the assumptions underlying those projections or guidance; risks associated with intellectual property of other parties and pending or future litigation relating thereto, the ultimate outcome of any such proceedings and investigations, and the impact any of the foregoing may have on Regeneron's business, prospects, operating results, and financial condition; and the potential for any license or collaboration agreement, including Regeneron's agreements with Sanofi, Bayer, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable), as well as Regeneron's collaboration with Roche relating to REGN-COV2, to be cancelled or terminated. A more complete description of these and other material risks can be found in Regeneron's filings with the U.S. Securities and Exchange Commission, including its Form 10-Q for the quarterly period ended June 30, 2020 in the section thereof captioned "Item 1A. Risk Factors." Any forward-looking statements are made based on management's current beliefs and judgment, and the reader is cautioned not to rely on any forward-looking statements made by Regeneron. Regeneron does not undertake any obligation to update (publicly or otherwise) any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.

## KEY TAKEAWAYS FROM TODAY'S UPDATE

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- The REGN-COV2 antibody cocktail reduces viral loads and symptoms vs. placebo in non-hospitalized patients who are infected with SARS-COV2
- Greatest improvements were observed in patients who had not mounted their own effective immune response prior to treatment (antibody seronegative and/or high viral loads at baseline)
- Results are being shared with regulators and will be used to inform next steps

# REGN UTILIZES ITS ANTIBODY TECHNOLOGIES TO FIGHT COVID19

## REGN has been a pioneer in antibody and antibody-like technologies for decades

- Resulting in many important new medicines: e.g., for fighting blindness (EYLEA), allergic diseases such as asthma and atopic dermatitis (DUPIXENT), heart disease (PRALUENT) and cancer (LIBTAYO)

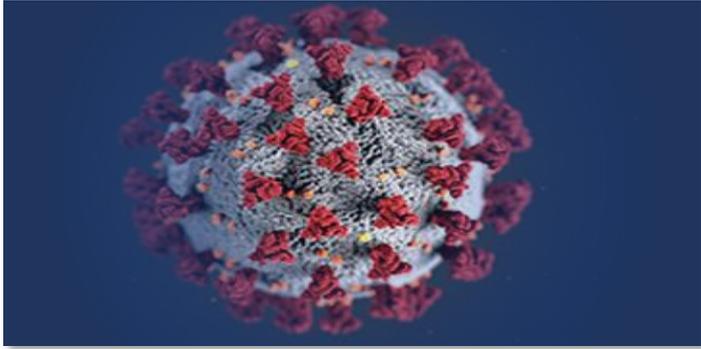
## REGN technologies delivered an effective “Antibody Cocktail” treatment for Ebola

- WHO trial showed REGN “antibody cocktail” had marked survival benefit in patients already infected with Ebola virus
- REGN “Antibody Cocktail” on track to be first approved Ebola treatment, with PDUFA date in October

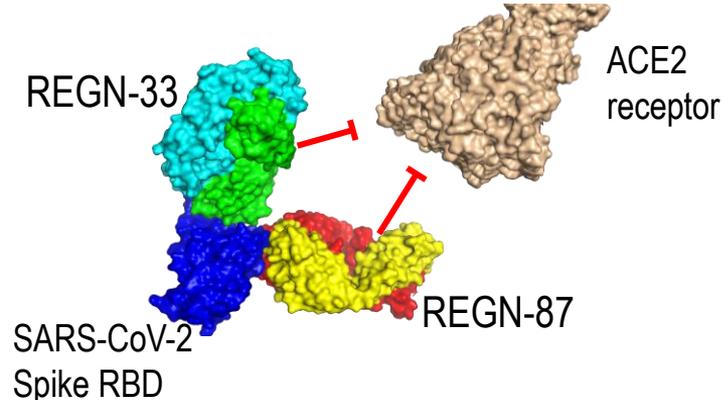
## REGN used its technologies to develop “Antibody Cocktail” for COVID19

- REGN scientists showed “antibody cocktail” targeting critical “spike” protein blocked infectivity, and prevented emergence of viral resistant mutants (**Science** 369:1010, 2020; **Science** 369:1014, 2020)
- Non-human primate data provide evidence of antiviral activity both when given as a preventative, and as a therapeutic (**BioRxiv**; **Science**, in revision)

# REGN-COV2: A HIGHLY POTENT COCKTAIL OF TWO NON-COMPETING, NEUTRALIZING ANTIBODIES AGAINST SARS-COV2



- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a (+) strand single-stranded RNA virus that is the causative agent of the coronavirus disease 2019 (COVID-19) pandemic
- It is genetically similar to SARS and bat coronaviruses
- A single glycoprotein on the surface of the virus (the “Spike” protein) is required for interaction with the host receptor (ACE2), fusion and entry into susceptible cells
- Infections with SARS-CoV-2 were first reported at the end of 2019 in China
- WHO declared a SARS-CoV-2 pandemic on March 11, 2020



- REGN scientists generated two highly-potent, non-competing, neutralizing human antibodies:
  - Bind to the receptor binding domain (RBD) of the Spike protein
  - Block virus binding to the ACE receptor, thereby blocking viral entry into cells
  - Viral/antibody complex is then cleared by the immune system
- Preclinical data show that REGN-COV2 blocks infection when administered prior to exposure to SARS-COV2 in animals AND
- Preclinical data show that REGN results in faster viral clearance in animals already infected with SARS-COV2

# REGN-COV2 HAS A BROAD ONGOING CLINICAL DEVELOPMENT PROGRAM

## STUDY 2066 - Hospitalized (IV): Seamless P1/2/3

- Four Cohorts (N=390/cohort)
  - No O2 requirement
  - Low flow O2
  - High flow O2
  - Mechanical ventilation

## STUDY 2067 Outpatient (IV): Seamless P1/2/3

- **Symptomatic – Initial Data Available Today**
- Asymptomatic

## STUDY 2069 Household contacts prophylaxis (SQ) P3

## STUDY 2093 Normal human volunteer multidose PK/Safety (SQ)

## UK/NHS RECOVERY Phase 3 Hospitalized Study (IV)

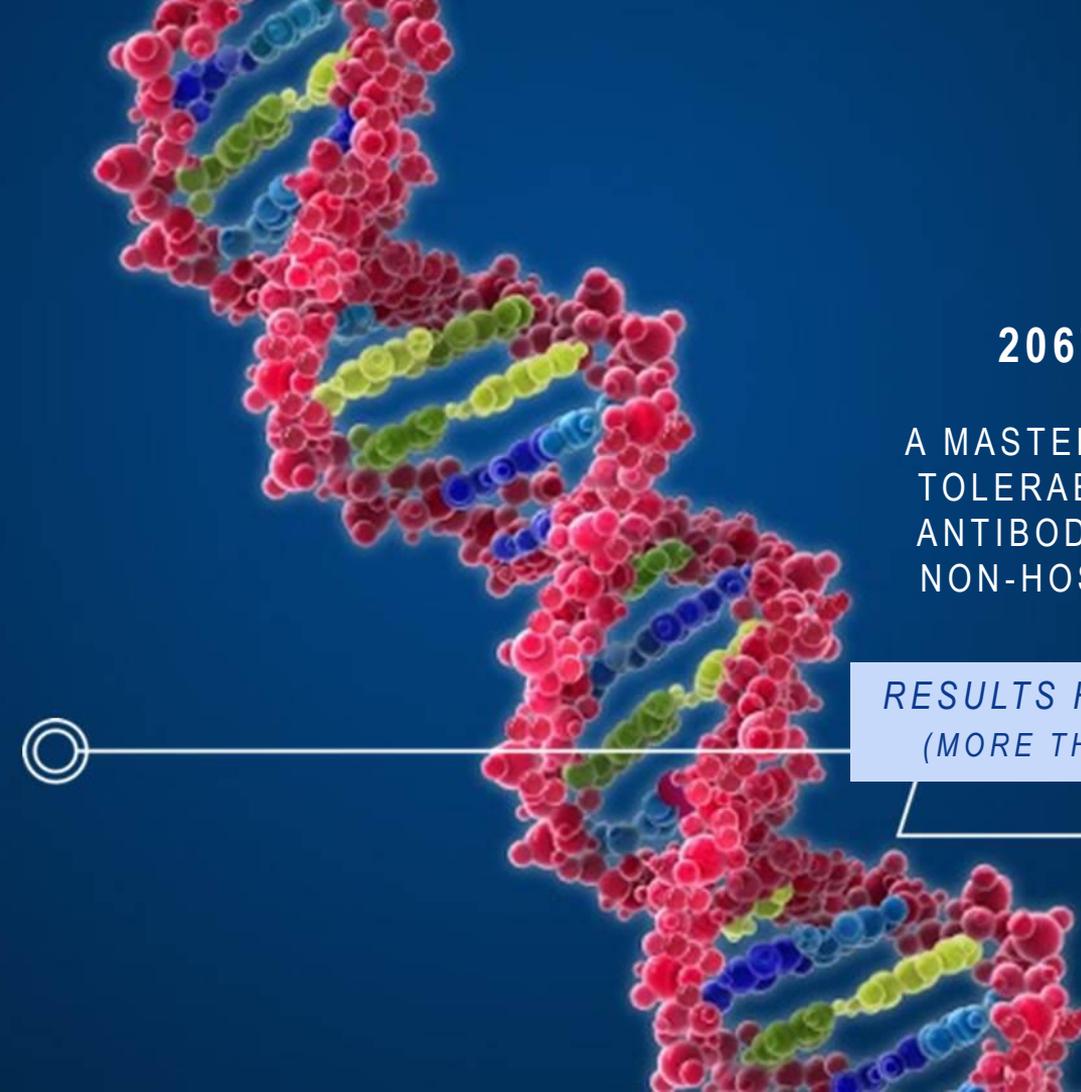
Approximately 2000 patients enrolled to date

Independent Data Review Committees are watching the trials to evaluate safety and have recommended to continue the trials as designed

No safety concerns have been noted with treatment of COVID 19 in hospitalized and ambulatory patients and prophylaxis treatment with SC formulation in both household exposed subjects and healthy volunteers.

Few patients experienced IRRs or ISR events; mainly mild to moderate in intensity.

We want to thank BARDA for their ongoing support of this program



**REGENERON**  
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## 2067 SEAMLESS PH1/2/3 TRIAL

A MASTER PROTOCOL ASSESSING THE SAFETY, TOLERABILITY, AND EFFICACY OF REGN-COV2 ANTIBODY COCKTAIL FOR THE TREATMENT OF NON-HOSPITALIZED PATIENTS WITH COVID-19

*RESULTS FROM INITIAL COHORT OF 275 PATIENTS  
(MORE THAN 900 PATIENTS CURRENTLY ENROLLED)*



# RESULTS FROM INITIAL COHORT OF 275 PATIENTS FROM 2067 SEAMLESS PH1/2/3 TRIAL IN OUTPATIENTS

## **Primary objectives were to establish safety, antiviral activity as well as clinical benefits**

- Since little is firmly established about the detailed time course and natural history in this patient population, our strategy was to perform a descriptive analysis on the first ~275 patients
- We prospectively hypothesized that many patients would recover based upon their own individual immune response, and that any anti-virus effect and/or associated clinical benefit would most likely be greatest in patients who had not yet mounted a strong immune response.
- We hoped these data, if robust, could support an EUA, and provide the criteria for formal analysis plan in next larger cohort of patients (already enrolled) that would allow rapid replication

## **We confirmed some very important aspects of COVID19 outpatient disease**

- As we hypothesized, these patients consist of two different populations: those who have already mounted an effective immune (antibody) response, and those who have yet to do so
  - Patients who have already mounted their own immune response have substantially lower viral load at baseline, and resolve their symptoms quickly
  - Medical complications in our study population are uncommon, occurring in less than 10% of patients treated with standard care, but they overwhelmingly occur (at ~10X higher rates) in patients yet to mount immune response

# PROSPECTIVE HYPOTHESIS REGARDING PATIENTS MOUNTING THEIR OWN IMMUNE RESPONSE TO VIRUS

**Before treatment, serology was used to divide patients into those who were “SeroAb-Positive” (had measurable endogenous Abs to COVID19) vs those “SeroAb-Negative” (no measurable Abs)**

- As expected, “SeroAb-Positive” patients had much lower viral levels at baseline compared to “SeroAb-Negative” patients ( $p < 0.0001$ ), and rapidly achieved viral loads approaching “LLQ” even without treatment
- In contrast, “SeroAb-Negative” patients had significantly higher viral levels at baseline, and cleared virus more slowly in the absence of treatment
  - The median viral load in SeroAb-negative patients was  $17 \times 10^6$  copies/mL, whereas in the SeroAb-positive patients it was only  $8.9 \times 10^3$  copies/mL.
  - 93% of the SeroAb-Negative population had viral titers  $> 10^5$  copies/mL, compared to only 28% in the SeroAb-Positive group
- “SeroAb-Positive” patients also had strong trend for faster alleviation of their symptoms (in  $\sim 7$  days) than “SeroAb-Negative” patients (in  $\sim 13$  days)

# BASELINE SEROLOGY STATUS CORRELATES WITH VIRAL LOAD (P<0.0001)

## Serostatus at baseline

Seronegative: 113/275 (41%)

Seropositive\*: 123/275 (45%)

Other\*\*: 39/275 (14%)

\*\*includes borderline serostatus or missing data

## Viral load (median) in NP swab

Seroneg: 7.18 log<sub>10</sub> copies/mL

Seropos: 3.49 log<sub>10</sub> copies/mL

## Mean days of COVID-19

symptoms before randomization:

3.5 days

Table 14.1.1.1-2 Summary of Demographics and Baseline Characteristics by Baseline Serology Status  
Full Analysis Set (FAS)

Baseline Serology Status: Negative					
	Placebo (N=33)	R10933+R10987 2.4 g IV (N=41)	R10933+R10987 8.0 g IV (N=39)	R10933+R10987 Combined (N=80)	Total (N=113)
SARS-CoV-2 - NP Swab (log <sub>10</sub> copies/mL)					
n	31	37	36	73	104
Mean (SD)	6.63 (1.716)	6.36 (1.833)	6.82 (1.252)	6.59 (1.580)	6.60 (1.613)
Median	7.15	6.35	7.51	7.20	7.18
Min : Max	0.0 : 7.9	0.0 : 7.9	4.1 : 7.9	0.0 : 7.9	0.0 : 7.9
Baseline Serology Status: Positive					
	Placebo (N=47)	R10933+R10987 2.4 g IV (N=37)	R10933+R10987 8.0 g IV (N=39)	R10933+R10987 Combined (N=76)	Total (N=123)
SARS-CoV-2 - NP Swab (log <sub>10</sub> copies/mL)					
n	47	36	37	73	120
Mean (SD)	3.42 (2.088)	3.42 (2.409)	3.05 (1.979)	3.23 (2.194)	3.30 (2.146)
Median	3.68	3.61	3.24	3.35	3.49
Min : Max	0.0 : 7.9	0.0 : 7.9	0.0 : 7.9	0.0 : 7.9	0.0 : 7.9
Baseline Serology Status: Other					
	Placebo (N=13)	R10933+R10987 2.4 g IV (N=14)	R10933+R10987 8.0 g IV (N=12)	R10933+R10987 Combined (N=26)	Total (N=39)
SARS-CoV-2 - NP Swab (log <sub>10</sub> copies/mL)					
n	13	11	10	21	34
Mean (SD)	4.52 (1.333)	5.90 (1.593)	5.66 (2.640)	5.79 (2.102)	5.30 (1.927)
Median	4.92	5.97	6.34	6.17	5.15
Min : Max	2.6 : 7.4	3.3 : 7.9	0.0 : 7.9	0.0 : 7.9	0.0 : 7.9

\*Seropositive is positive in one or more of the following SARS-COV-2 specific IgG Spike, IgA Spike, IgG Nucleocapsid

# VIRAL LOAD SIGNIFICANTLY HIGHER AT BASELINE IN THE SERONEGATIVE POPULATION

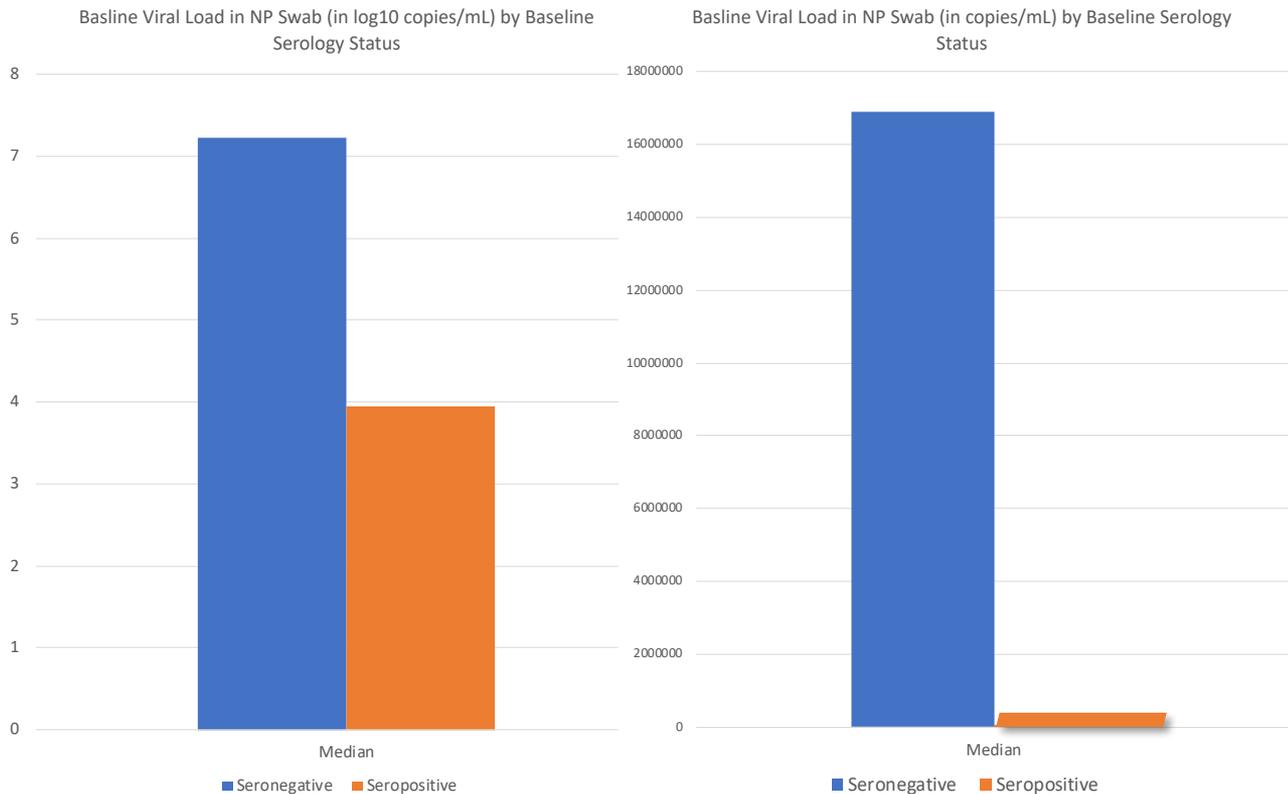
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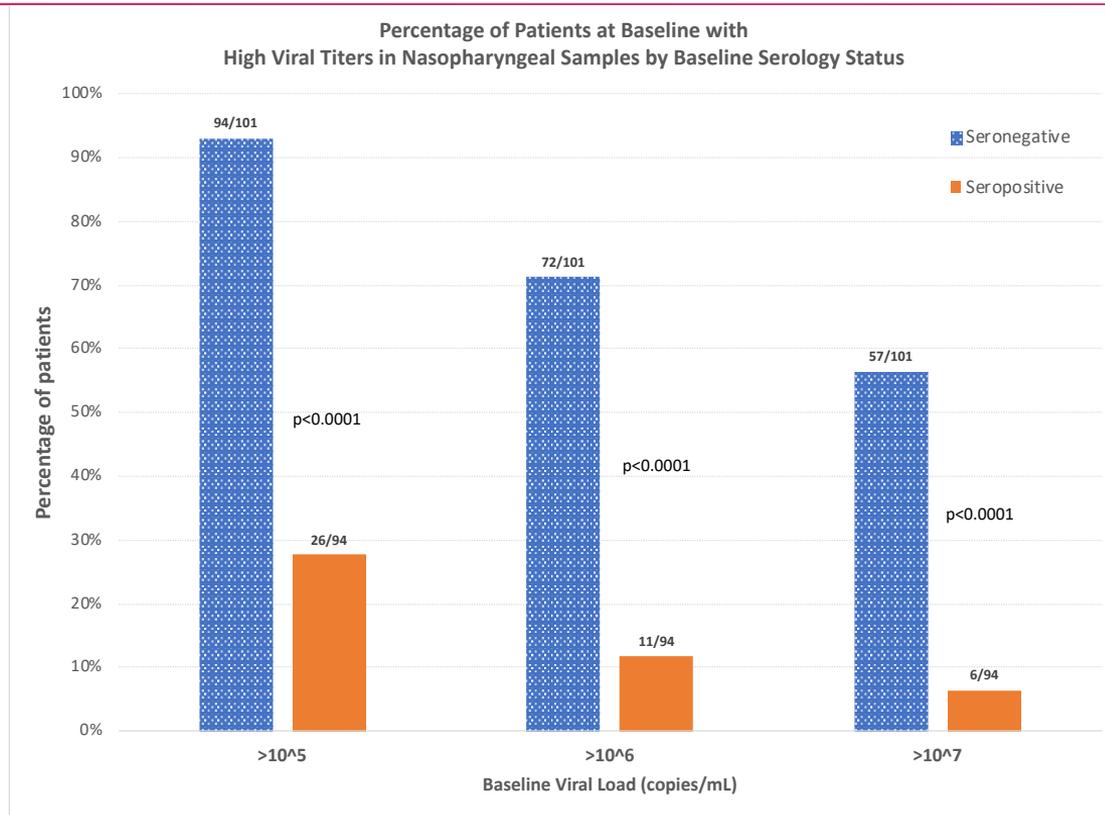
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Mean days of COVID-19  
symptoms before randomization:  
3.5 days



# PATIENTS WHO HAVE HIGHEST VIRAL LOADS CORRESPOND TO THOSE WHO HAVE NOT YET MOUNTED IMMUNE RESPONSE

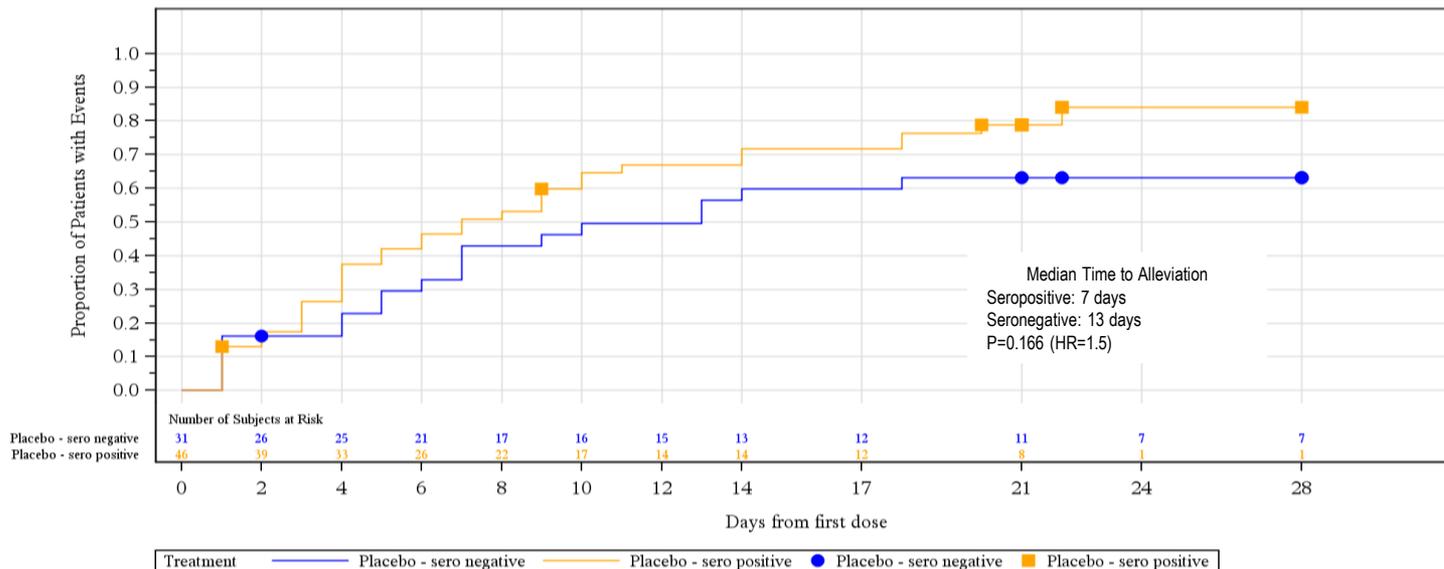


# IN PBO GROUP, “SEROAB-POSITIVE” PATIENTS ALSO HAD STRONG TREND FOR FASTER ALLEVIATION OF THEIR SYMPTOMS (~7 DAYS) THAN “SEROAB-NEGATIVE” PATIENTS (~13 DAYS)

Regeneron Pharmaceuticals, Inc.  
 Protocol: R10933-10987-COV-2067 Phase 1/2

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Figure 14.1/1 Time to First Day of alleviation of All symptoms consistent with COVID-19 by Baseline Serology Status  
 Full Analysis Set (FAS) - Placebo only



# PROSPECTIVE HYPOTHESIS REGARDING PATIENTS MOUNTING THEIR OWN IMMUNE RESPONSE TO VIRUS

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- “SeroAb-Positive” patients also had strong trend for faster alleviation of their symptoms (in  $\sim 7$  days) than “SeroAb-Negative” patients (in  $\sim 13$  days)

# REGN-COV2 REDUCED VIRAL LOAD AND SYMPTOMS, WITH GREATEST BENEFIT IN PATIENTS WITH LOWER IMMUNE RESPONSES AND/OR HIGH VIRAL TITERS

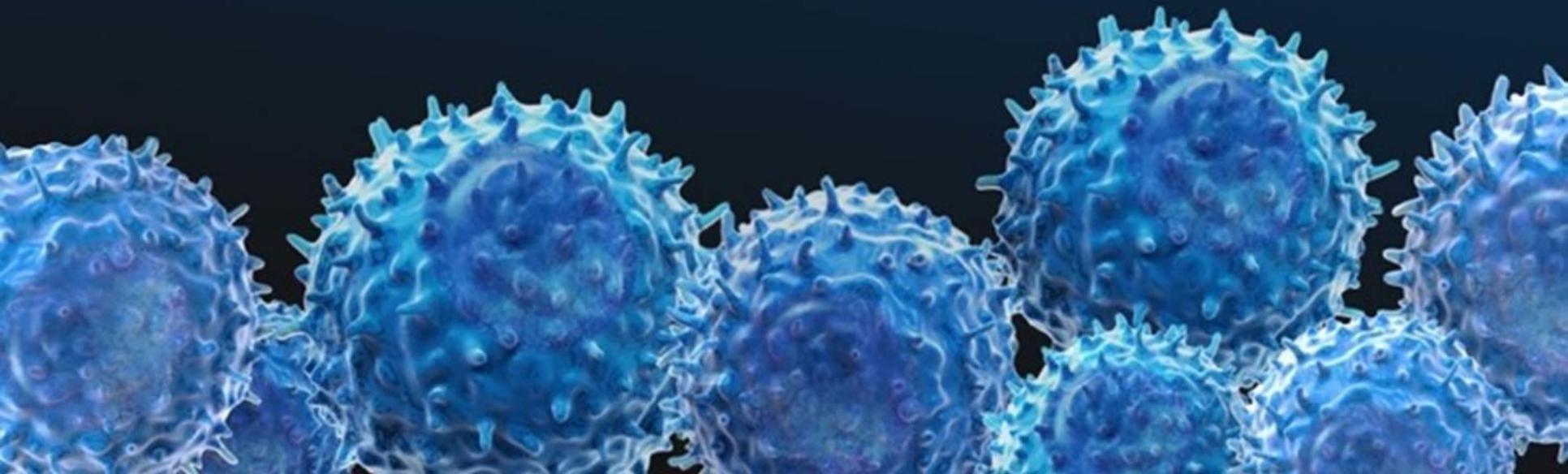
Goal of this descriptive analysis of first cohort of 275 patients from seamless Ph1/2/3 trial was to evaluate anti-viral activity and identify patients most likely to benefit from treatment, to be rapidly and prospectively confirmed in additional patients from ongoing trial

- **Prospective hypothesis regarding patients mounting their own immune response to virus: Focus on “SeroAb-Negative” patients**
  - **Key Virological Endpoints: Nominally significant activity in overall population, which was driven by “SeroAb-Negative” patients**
  - **Patients with higher baseline viral levels had increasingly larger benefits for viral reduction**
    - Nominally significant reduction in time weighted average change from baseline nasopharyngeal (NP) viral load through Day 7 in [seronegative population](#)
      - 0.60 log copies/mL greater reduction in viral load in 8.0 g (high dose) arm compared to PBO (P = 0.0297)
      - 0.51 log copies/mL greater reduction in viral load in 2.4 g (low dose) arm compared to PBO (P = 0.0630)
    - Nominally significant reduction in virus levels at Day 7 in patients with high viral loads at baseline ( $>10^7$ )
      - 1.79 log copies/mL reduction in viral load in 8.0 g (high dose) arm compared to PBO (P = 0.0015); 99% viral reduction compared to Pbo
      - 2.0 log copies/mL reduction in viral load in 2.4 g (low dose) arm compared to PBO (P = 0.001); 99% viral reduction compared to Pbo
  - **Similarly, patients with higher baseline viral levels also had increasingly larger benefits for symptom alleviation**
    - Among seronegative patients, time to symptom alleviation was reduced by a median of 5 days (Day 8 compared to Day 13 PBO) in the high dose group and a median of 7 days (Day 6 compared to Day 13 PBO) in the low dose group.
    - In patients with high viral loads as baseline ( $>10^6$ ), time to symptom alleviation was reduced by a median of 7 days (Day 6 compared to Day 13 PBO) in both dose groups.
  - **Both high and low dose showed similar activity in both viral reduction and symptom alleviation**
  - **Very small number of “medically-attended visits” (MAVs, e.g., ER visits and hospitalizations) – most outpatients do well**
    - >>>Of note, 10 of the 12 MAVs occurred in patients who were SeroAb-Negative at baseline, consistent with notion these are highest risk patients
    - >>>Positive trends related to treatment (15.2% in Pbo, 4.9% in low dose, and 7.7% in high dose)
- **PK of anti-spike monoclonals is linear and consistent with other Regeneron mAbs**
  - High antibody levels even one month after administration, consistent with high bioavailability and long half-life
- **Safety & Tolerability**
  - Both doses were well-tolerated
  - Infusion reactions, SAEs and AESIs were balanced across treatment and PBO groups (no deaths)



# STUDY DESIGN

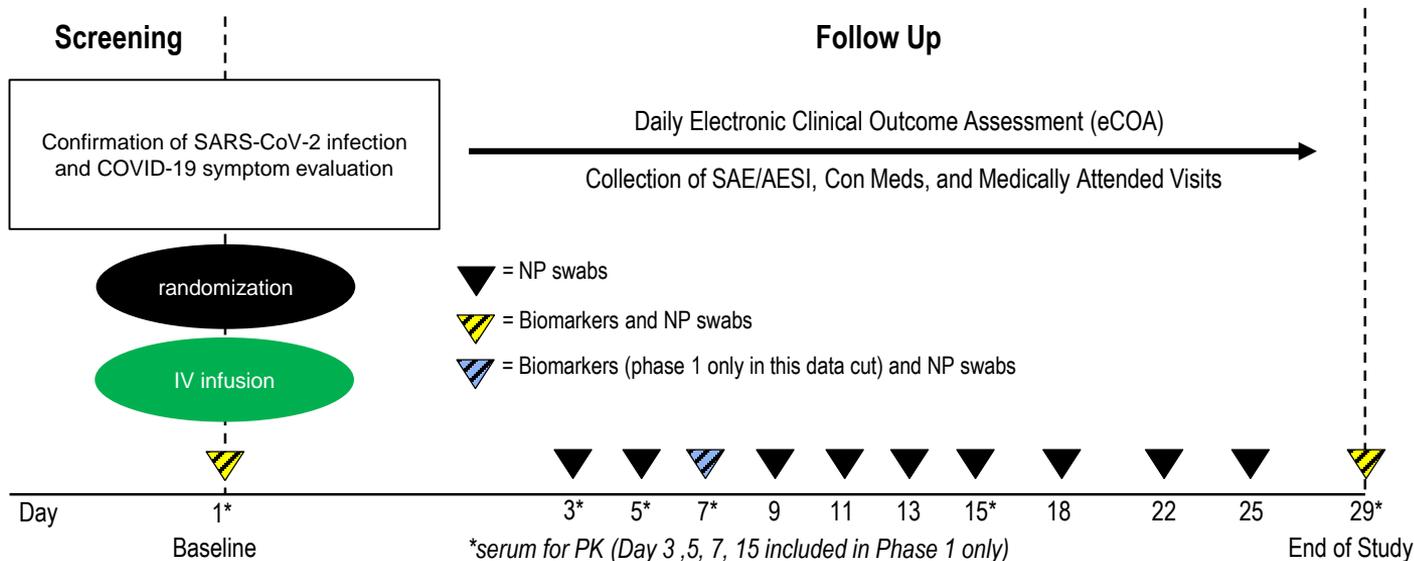
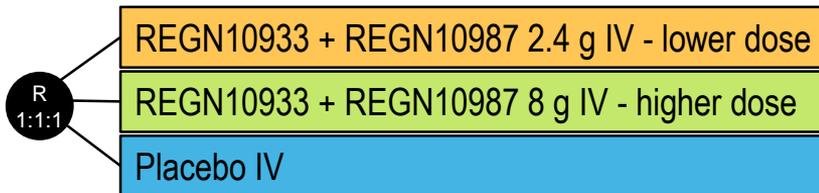
*REGENERON*



# STUDY DESIGN OVERVIEW FOR THIS DATA CUT (1<sup>ST</sup> 275 PATIENTS)

## Patient Population:

- Adult, *non-hospitalized* COVID-19 patients
- Symptom onset  $\leq 7$  days from randomization
- SARS-CoV-2 confirmed by molecular testing  $\leq 72$  hours from randomization
- Not on any putative COVID-19 therapies



# KEY DESCRIPTIVE VIROLOGIC AND CLINICAL ENDPOINTS OUTLINED IN SAP

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## Key Virologic Endpoints

- Time-weighted average change from baseline in viral load (log<sub>10</sub> copies/mL) from day 1 through day 7 in the Seronegative mFAS, as measured by quantitative reverse transcription quantitative polymerase chain reaction (RT-qPCR) in nasopharyngeal (NP) swab samples
- Additional landmark analyses on viral reduction

## Clinical Endpoint: Symptoms

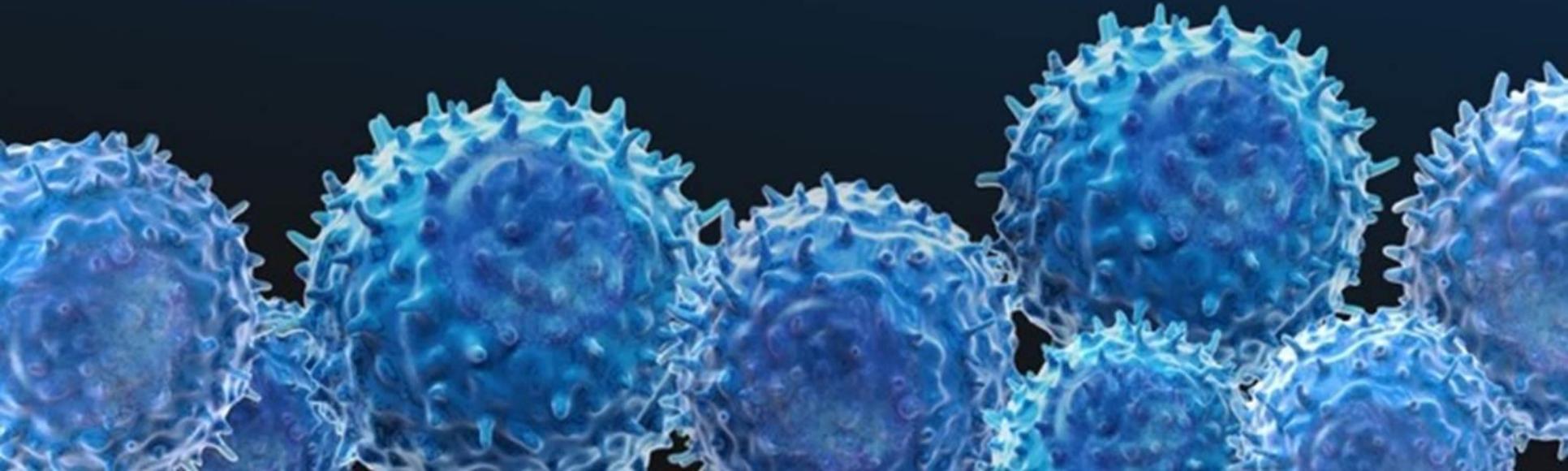
- Time to Alleviation of symptoms (going to mild or absent)

## Clinical Endpoint: Medically-attended visits

- Proportion of patients with  $\geq 1$  COVID-19-related medically-attended visit through day 29 for both seronegative FAS and FAS.

# BASELINE CHARACTERISTICS

*REGENERON*



# DEMOGRAPHICS

Table 14.1.1.1-1 Summary of Demographics and Baseline Characteristics  
Full Analysis Set (FAS)

	Placebo (N=93)	R10933+R10987 2.4 g IV (N=92)	R10933+R10987 8.0 g IV (N=90)	R10933+R10987 Combined (N=182)	Total (N=275)
<b>Age (Years)</b>					
n	93	92	90	182	275
Mean (SD)	45.2 (13.78)	43.1 (14.19)	44.3 (12.59)	43.7 (13.40)	44.2 (13.52)
<b>Age Group (Years), n (%)</b>					
18 - 44	43 (46.2%)	50 (54.3%)	48 (53.3%)	98 (53.8%)	141 (51.3%)
45 - 64	43 (46.2%)	35 (38.0%)	36 (40.0%)	71 (39.0%)	114 (41.5%)
65 - 84	7 (7.5%)	7 (7.6%)	6 (6.7%)	13 (7.1%)	20 (7.3%)
<b>Sex, n (%)</b>					
Male	50 (53.8%)	46 (50.0%)	38 (42.2%)	84 (46.2%)	134 (48.7%)
Female	43 (46.2%)	46 (50.0%)	52 (57.8%)	98 (53.8%)	141 (51.3%)
<b>Ethnicity, n (%)</b>					
Hispanic or Latino	46 (49.5%)	52 (56.5%)	55 (61.1%)	107 (58.8%)	153 (55.6%)
Not Hispanic or Latino	46 (49.5%)	39 (42.4%)	34 (37.8%)	73 (40.1%)	119 (43.3%)
Not Reported	1 (1.1%)	1 (1.1%)	1 (1.1%)	2 (1.1%)	3 (1.1%)
<b>Race, n (%)</b>					
White	72 (77.4%)	74 (80.4%)	78 (86.7%)	152 (83.5%)	224 (81.5%)
Black or African American	14 (15.1%)	15 (16.3%)	6 (6.7%)	21 (11.5%)	35 (12.7%)
Asian	2 (2.2%)	0	1 (1.1%)	1 (0.5%)	3 (1.1%)
American Indian or Alaska Native	2 (2.2%)	0	0	0	2 (0.7%)
Unknown	2 (2.2%)	0	1 (1.1%)	1 (0.5%)	3 (1.1%)
Not Reported	1 (1.1%)	3 (3.3%)	4 (4.4%)	7 (3.8%)	8 (2.9%)
<b>Obesity</b>					
BMI <= 30 kg/m <sup>2</sup>	51 (54.8%)	51 (55.4%)	42 (46.7%)	93 (51.1%)	144 (52.4%)
BMI > 30 kg/m <sup>2</sup>	34 (36.6%)	39 (42.4%)	42 (46.7%)	81 (44.5%)	115 (41.8%)
Missing	8	2	6	8	16

- Mean age: 44 years
- ~ 49% male
- ~55% Hispanic
- ~13% African American
- ~42% Obese

~65% with  $\geq 1$  risk factors for severe COVID-19

**Baseline characteristics well-balanced across treatment arms**

# BASELINE SEROLOGY STATUS CORRELATES WITH VIRAL LOAD (P<0.0001)

## Serostatus at baseline

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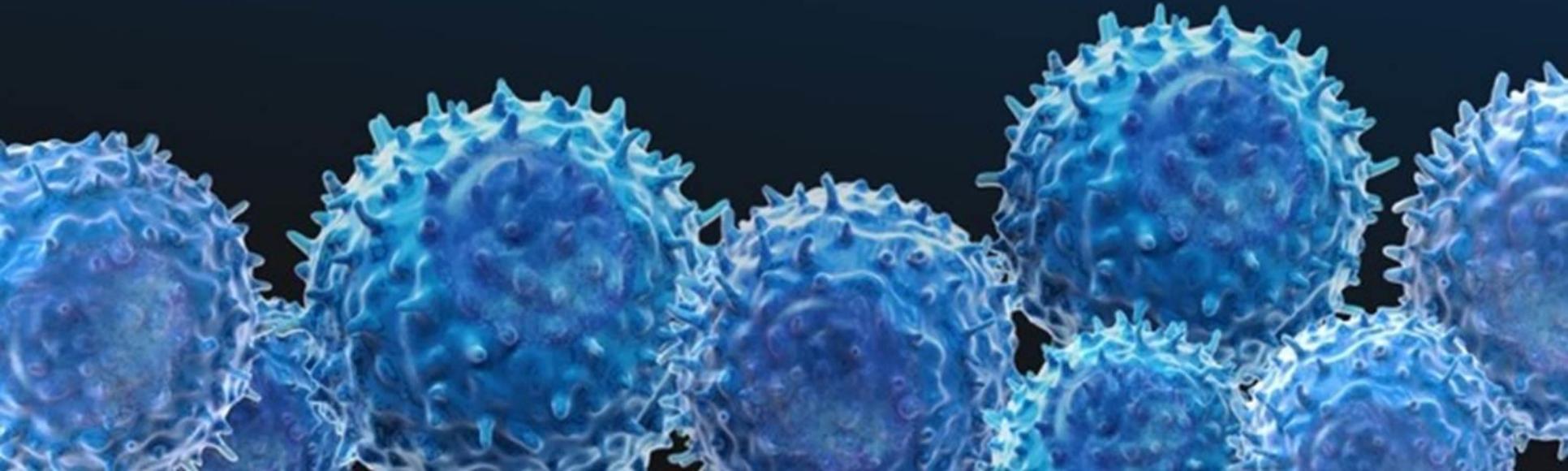
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n	13	11	10	21	34
Mean (SD)	4.52 (1.333)	5.90 (1.593)	5.66 (2.640)	5.79 (2.102)	5.30 (1.927)
Median	4.92	5.97	6.34	6.17	5.15
Min : Max	2.6 : 7.4	3.3 : 7.9	0.0 : 7.9	0.0 : 7.9	0.0 : 7.9

\*Seropositive is positive in one or more of the following SARS-COV-2 specific IgG Spike, IgA Spike, IgG Nucleocapsid

# VIROLOGIC OUTCOMES

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# NOMINALLY SIGNIFICANT 0.6 LOG REDUCTION IN VIRAL LOAD THROUGH DAY 7 (HIGH DOSE VS. PBO) IN SERONEGATIVE POPULATION

Regeneron Pharmaceuticals, Inc.  
Protocol: R10933-10987-COV-2067 Phase 1/2

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Table 14.2.1.1-3 Time-Weighted Average Change from Baseline in Viral Load from Day 1 at each visit in Nasopharyngeal (NP) Samples by Baseline Serology Status  
Modified Full Analysis Set (mFAS)

Baseline Serology Status: Negative

	Placebo (N=30)	R10933+R10987 2.4 g IV (N=35)	R10933+R10987 8.0 g IV (N=36)	R10933+R10987 Combined (N=71)
Time-weighted average change from baseline from Day 1 to Day 7 (log10 copies/mL)				
n	28	34	35	69
Mean (SD)	-1.32 (0.894)	-1.79 (0.802)	-1.86 (1.324)	-1.83 (1.091)
Median	-1.20	-1.86	-1.59	-1.72
Q1 : Q3	-1.96 : -0.58	-2.26 : -1.44	-2.52 : -0.97	-2.29 : -1.26
Min : Max	-3.0 : -0.1	-3.7 : 0.3	-6.5 : 0.6	-6.5 : 0.6
LS Mean (SE) [1]	-1.38 (0.20)	-1.89 (0.19)	-1.98 (0.19)	-1.93 (0.14)
95% CI [1]	(-1.78, -0.97)	(-2.26, -1.52)	(-2.35, -1.60)	(-2.20, -1.66)

Difference vs. Placebo by Day 7 (log10 copies/mL)

LS Mean (SE) [1]  
95% CI [1]  
p-value [1]

-0.51 (0.27)  
(-1.05, 0.03)  
0.0630

-0.60 (0.27)  
(-1.14, -0.06)  
0.0297

-0.56 (0.24)  
(-1.03, -0.08)  
0.0215

# NOMINALLY SIGNIFICANT 0.5 LOG REDUCTION IN VIRAL LOAD THROUGH DAY 7 (HIGH DOSE VS. PBO) IN OVERALL POPULATION - IRRESPECTIVE OF BASELINE SEROSTATUS

Regeneron Pharmaceuticals, Inc.

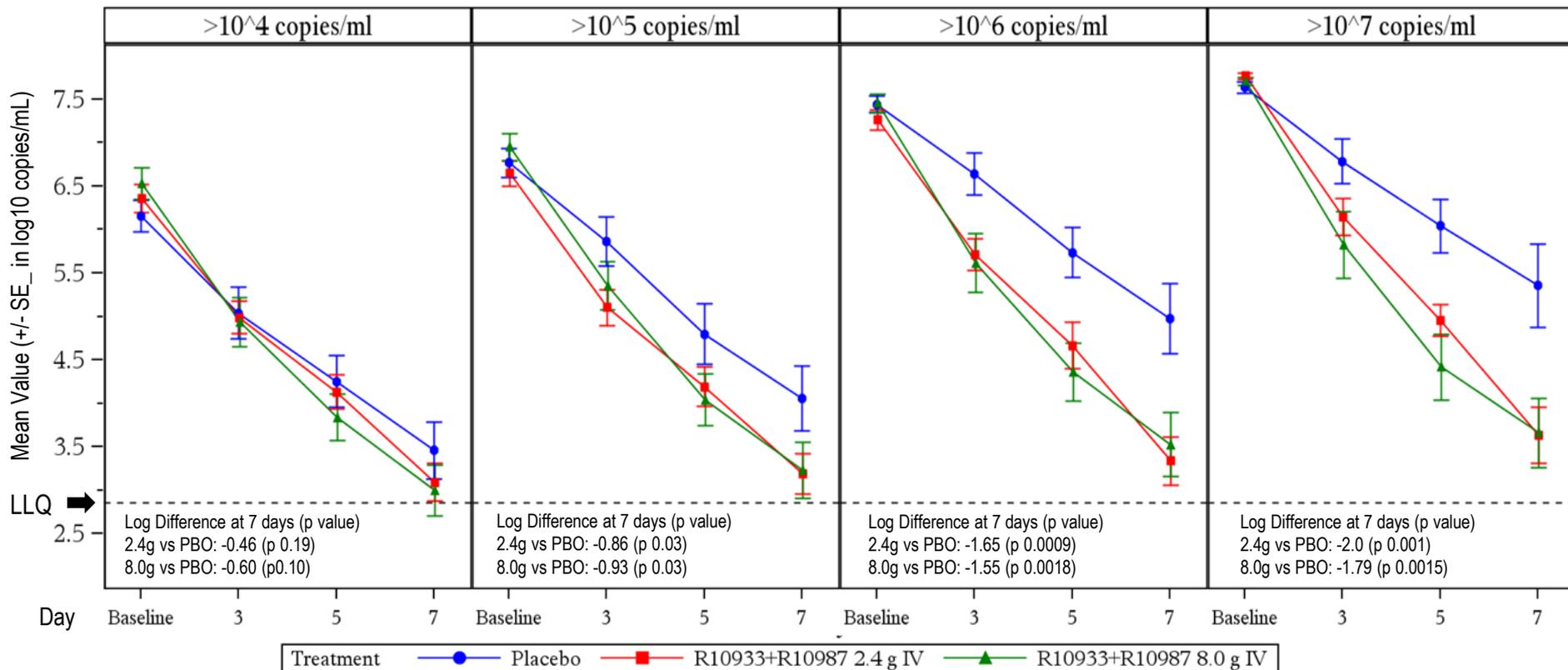
Protocol: R10933-10987-COV-2067 Phase 1/2

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Table 14.2.1.1-1 Time-Weighted Average Change from Baseline in Viral Load from Day 1 at each visit in Nasopharyngeal (NP) Samples  
Modified Full Analysis Set (mFAS)

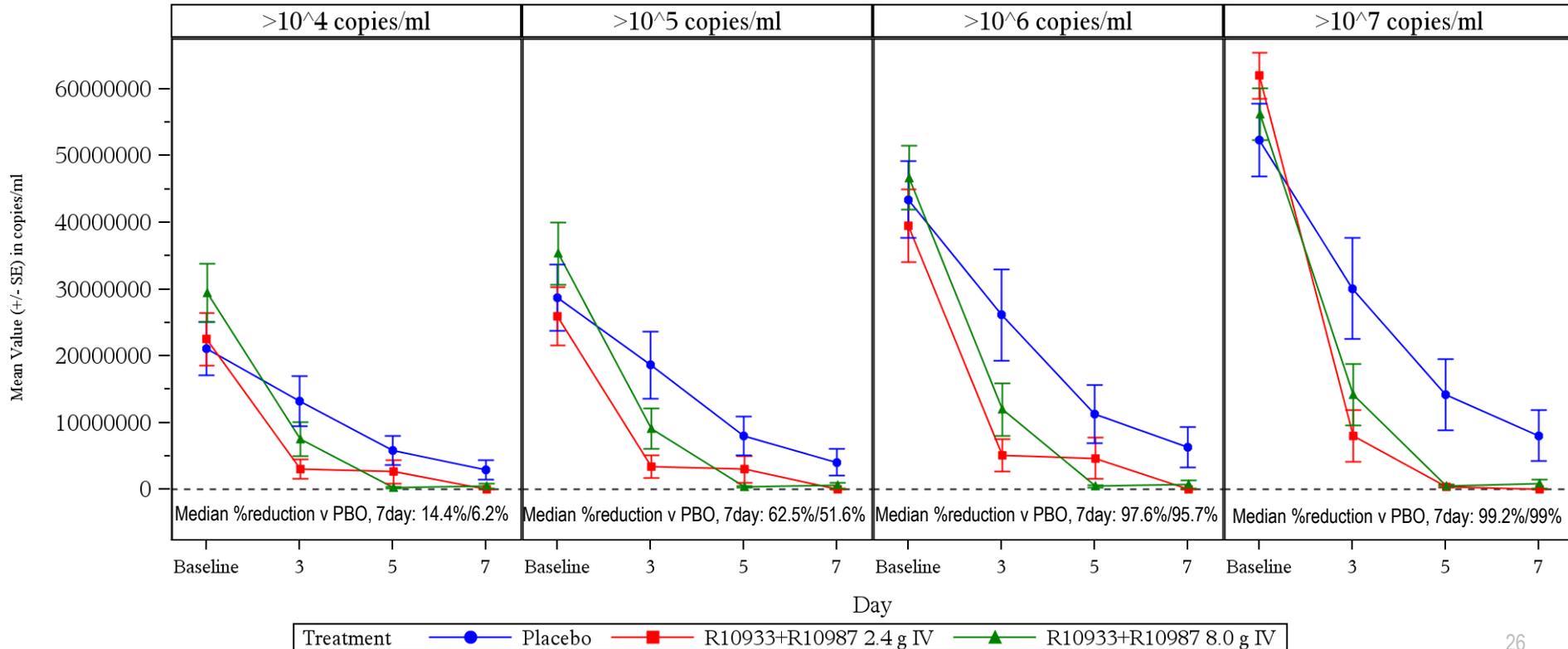
	Placebo (N=81)	R10933+R10987 2.4 g IV (N=73)	R10933+R10987 8.0 g IV (N=74)	R10933+R10987 Combined (N=147)
baseline from Day 1 to Day 7 (log <sub>10</sub> copies/mL)				
n	78	70	73	143
Mean (SD)	-1.27 (0.992)	-1.60 (0.939)	-1.74 (1.329)	-1.67 (1.153)
Median	-1.13	-1.73	-1.56	-1.68
Q1 : Q3	-2.10 : -0.60	-2.26 : -1.00	-2.43 : -0.86	-2.31 : -0.86
Min : Max	-3.2 : 1.4	-3.7 : 0.4	-6.5 : 0.6	-6.5 : 0.6
LS Mean (SE) [1]	-1.41 (0.13)	-1.64 (0.14)	-1.92 (0.14)	-1.77 (0.11)
95% CI [1]	(-1.67, -1.15)	(-1.91, -1.37)	(-2.21, -1.64)	(-1.99, -1.56)
Difference vs. Placebo by Day 7 (log <sub>10</sub> copies/mL)				
LS Mean (SE) [1]		-0.23 (0.18)	-0.51 (0.18)	-0.37 (0.15)
95% CI [1]		(-0.58, 0.12)	(-0.87, -0.16)	(-0.67, -0.06)
p-value [1]		0.2044	0.0049	0.0183

# REGN-COV2 PROVIDED GREATER REDUCTION IN VIRAL LOAD IN THOSE WITH HIGHER VIRAL LOAD AT BASELINE



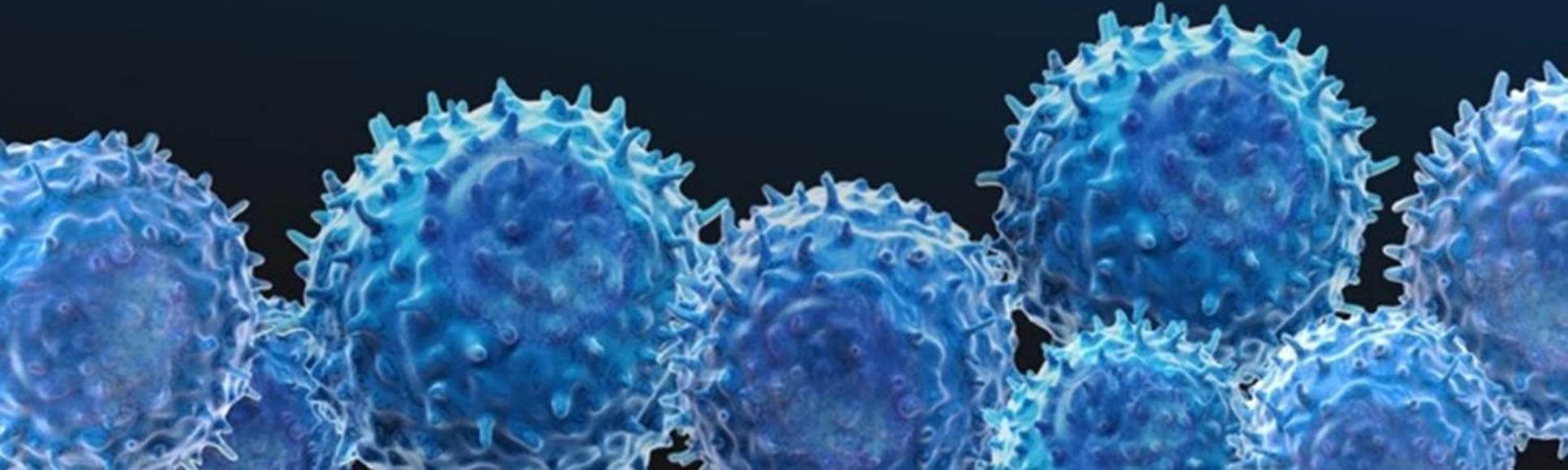
# REGN-COV2 PROVIDED GREATER REDUCTION IN VIRAL LOAD IN THOSE WITH HIGHER VIRAL LOAD AT BASELINE

Figure 9.1/2 Line Plot: Mean (+/-SE) Viral Load value in raw scale at Each Visit through Day 7 in Nasopharyngeal (NP) Samples  
Modified Full Analysis Set (mFAS)



CLINICAL OUTCOMES:  
SYMPTOM ALLEVIATION

*REGENERON*



# TIME TO FIRST ALLEVIATION OF SYMPTOMS (GOING TO MILD OR ABSENT) IS REDUCED IN TREATMENT GROUPS COMPARED TO PBO – AFFECTS MOST PRONOUNCED SERONEGATIVE POPULATION

## Day to alleviation, overall population (median)

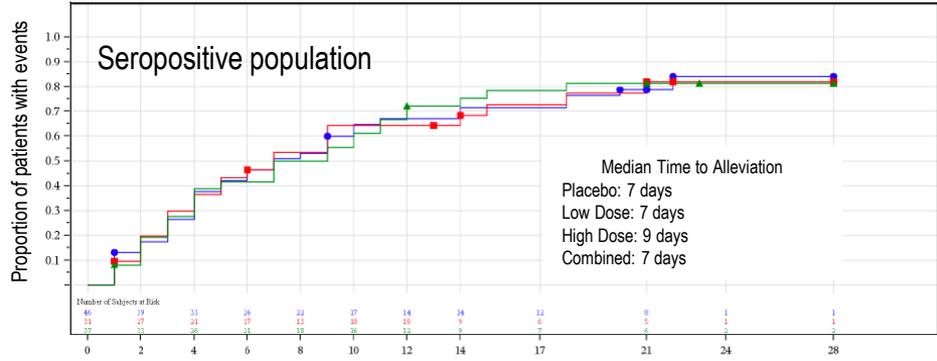
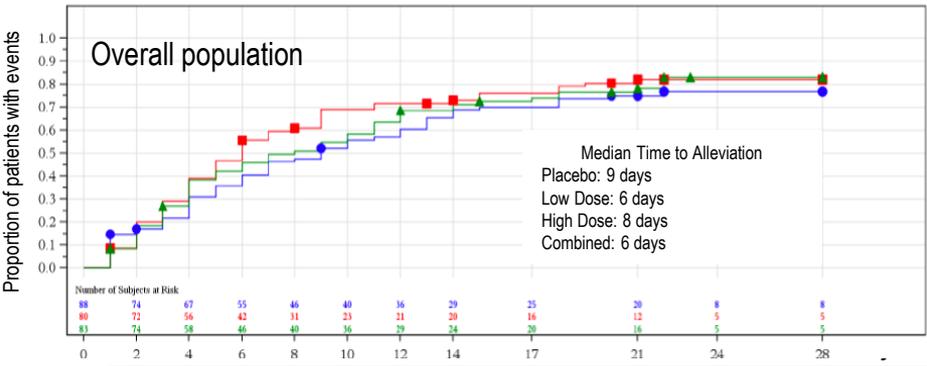
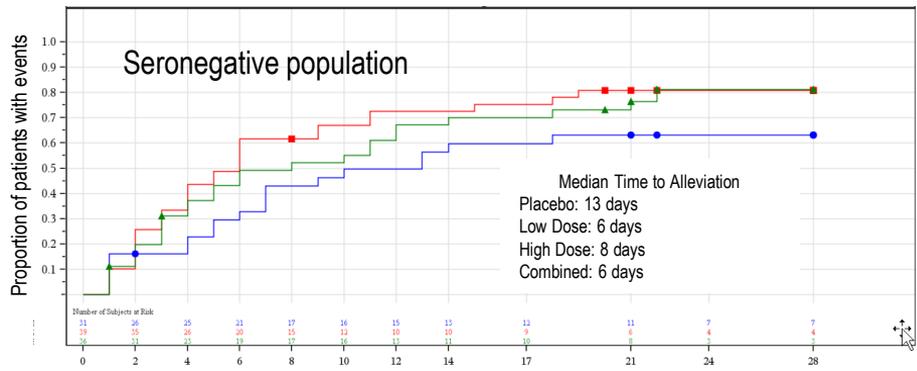
- PBO: 9 days
- Low dose: 6 day
- High dose: 8 days

## Seronegative

- PBO: 13 days
- Low dose: 6 day
- High dose: 8 days

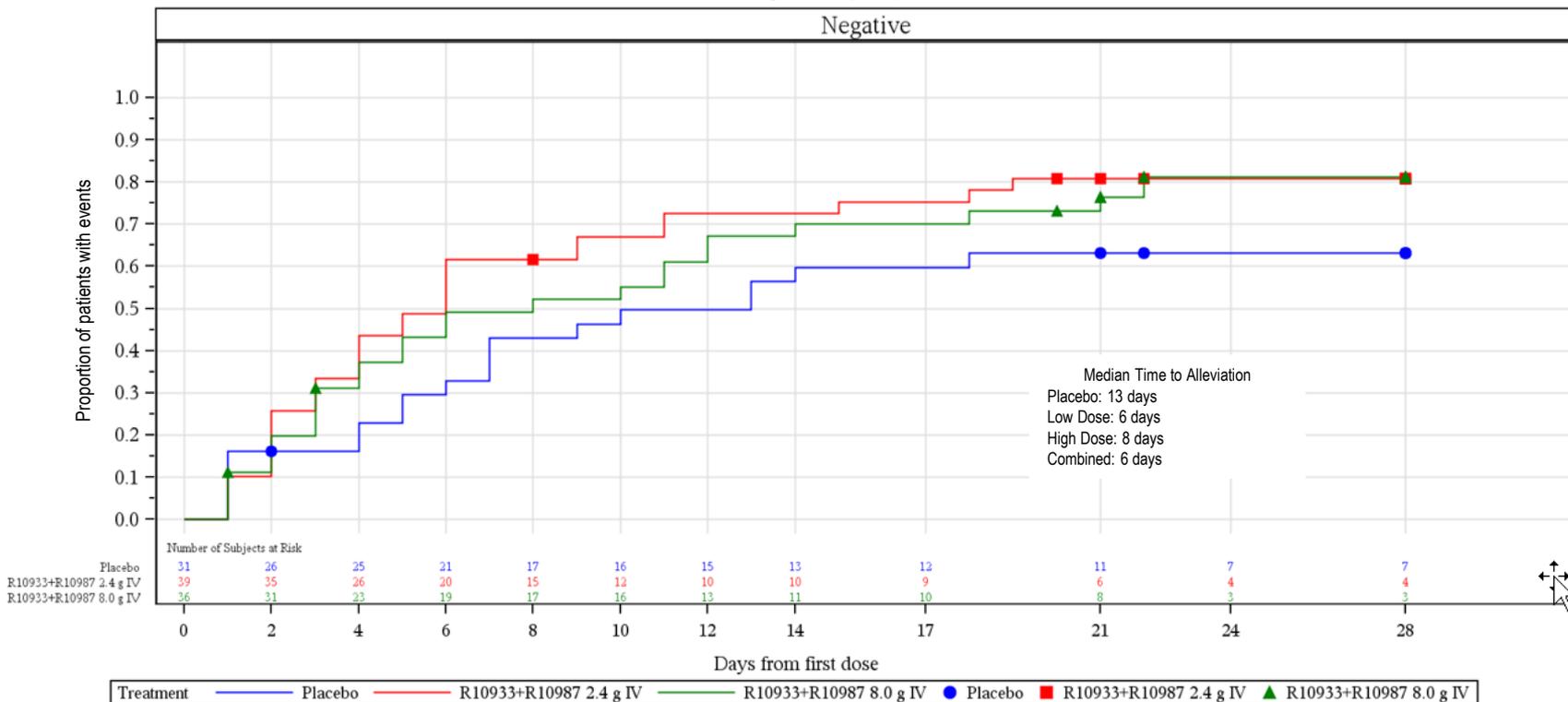
Overall	Placebo (N=93)	R10933+R10987 2.4 g IV (N=92)	R10933+R10987 8.0 g IV (N=90)	R10933+R10987 Combined (N=182)
Number of Patients assessed	88	80	83	163
Number of Patients with events [1]	65	63	64	127
Number of Patients censored [1]	23	17	19	36
<b>Median (95% CI) [2]</b>	<b>9.0(6.0, 12.0)</b>	<b>6.0(4.0, 8.0)</b>	<b>8.0(5.0, 11.0)</b>	<b>6.0(5.0, 9.0)</b>
<b>Min.: Max [3]</b>	<b>1: 28+</b>	<b>1: 28+</b>	<b>1: 28+</b>	<b>1: 28+</b>
Baseline Serology Status: Negative	Placebo (N=33)	R10933+R10987 2.4 g IV (N=41)	R10933+R10987 8.0 g IV (N=39)	R10933+R10987 Combined (N=80)
Number of Patients assessed	31	39	36	75
Number of Patients with events [1]	19	31	27	58
Number of Patients censored [1]	12	8	9	17
<b>Median (95% CI) [2]</b>	<b>13.0(6.0, .)</b>	<b>6.0(3.0, 9.0)</b>	<b>8.0(4.0, 12.0)</b>	<b>6.0(4.0, 10.0)</b>
<b>Min.: Max [3]</b>	<b>1: 28+</b>	<b>1: 28+</b>	<b>1: 28+</b>	<b>1: 28+</b>
Baseline Serology Status: Positive	Placebo (N=47)	R10933+R10987 2.4 g IV (N=37)	R10933+R10987 8.0 g IV (N=39)	R10933+R10987 Combined (N=76)
Number of Patients assessed	46	31	37	68
Number of Patients with events [1]	36	23	29	52
Number of Patients censored [1]	10	8	8	16
<b>Median (95% CI) [2]</b>	<b>7.0(4.0, 10.0)</b>	<b>7.0(4.0, 14.0)</b>	<b>9.0(4.0, 11.0)</b>	<b>7.0(4.0, 10.0)</b>
<b>Min.: Max [3]</b>	<b>1: 28+</b>	<b>1: 28+</b>	<b>1: 28+</b>	<b>1: 28+</b>
Baseline Serology Status: Other	Placebo (N=13)	R10933+R10987 2.4 g IV (N=14)	R10933+R10987 8.0 g IV (N=12)	R10933+R10987 Combined (N=26)
Number of Patients assessed	11	10	10	20
Number of Patients with events [1]	10	9	8	17
Number of Patients censored [1]	1	1	2	3
<b>Median (95% CI) [2]</b>	<b>12.0(1.0, 13.0)</b>	<b>5.5(3.0, 8.0)</b>	<b>7.5(2.0, 22.0)</b>	<b>6.0(4.0, 9.0)</b>
<b>Min.: Max [3]</b>	<b>1: 21+</b>	<b>3: 21+</b>	<b>2: 22</b>	<b>2: 22</b>

# TIME TO ALLEVIATION OF SYMPTOMS (GOING TO MILD OR ABSENT) IS FASTER IN TREATMENT GROUPS COMPARED TO PBO; EFFECT MOST PRONOUNCED IN SERONEGATIVE POPULATION

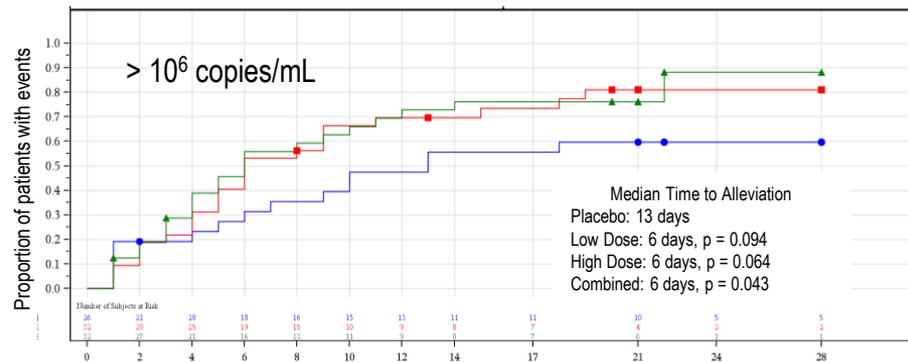
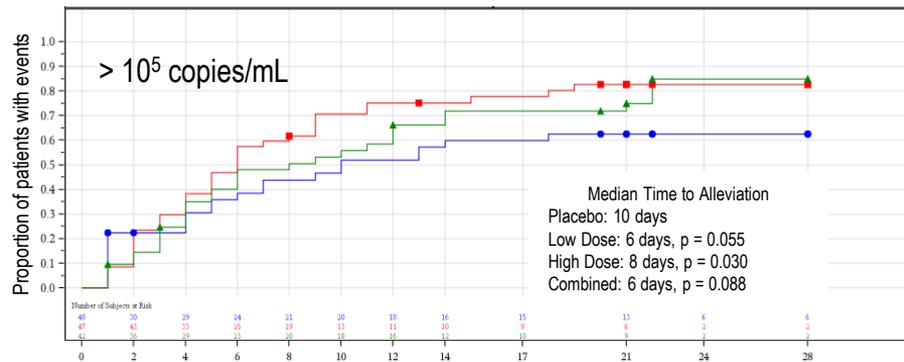
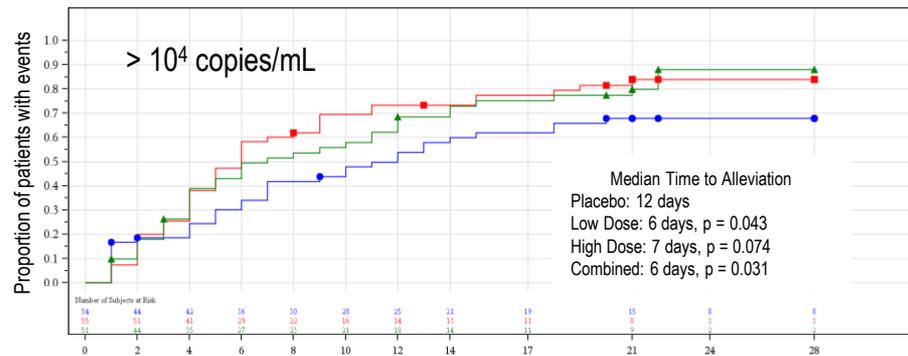
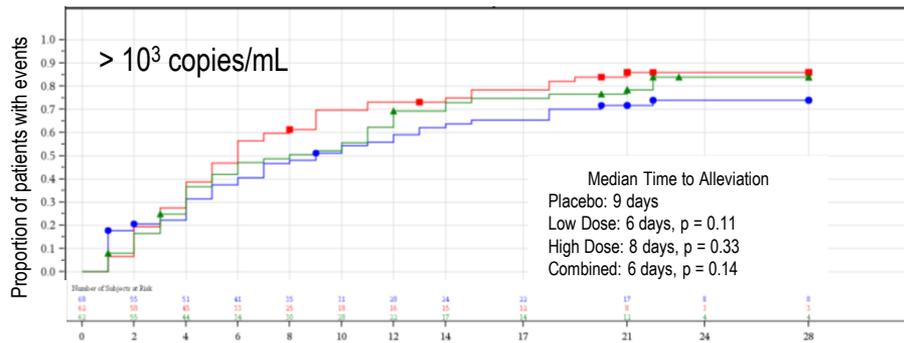


Treatment — Placebo — R10933+R10987 2.4 g IV — R10933+R10987 8.0 g IV ● Placebo ■ R10933+R10987 2.4 g IV ▲ R10933+R10987 8.0 g IV

# TIME TO ALLEVIATION OF SYMPTOMS (GOING TO MILD OR ABSENT) IS FASTER IN TREATMENT GROUPS COMPARED TO PBO; EFFECT MOST PRONOUNCED IN SERONEGATIVE POPULATION



# TIME TO ALLEVIATION OF SYMPTOMS (GOING TO MILD OR ABSENT) IS FASTER IN TREATMENT GROUPS COMPARED TO PBO; EFFECT MOST PRONOUNCED IN PATIENTS WITH HIGHER VIRAL LOAD

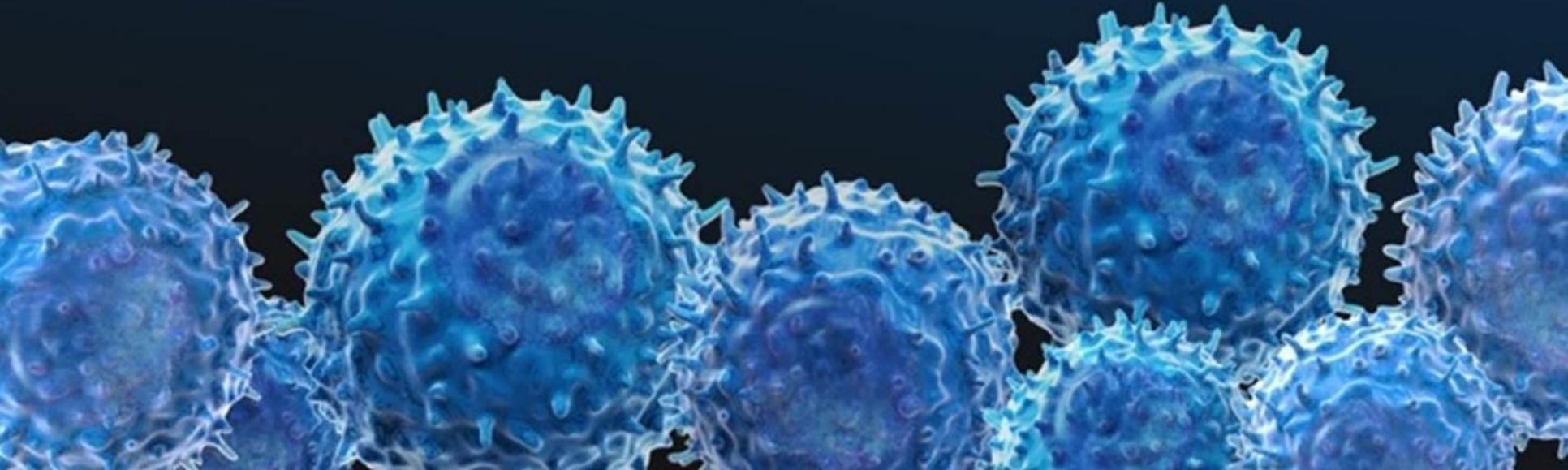


Days from first dose

Treatment — Placebo — R10933+R10987 2.4 g IV — R10933+R10987 8.0 g IV ● Placebo ■ R10933+R10987 2.4 g IV ▲ R10933+R10987 8.0 g IV

COVID-19-RELATED  
MEDICALLY ATTENDED VISITS

*REGENERON*



# COVID-19-RELATED MEDICALLY ATTENDED VISITS ARE NUMERICALLY LOWER IN TREATMENT GROUPS OVERALL POPULATION

Regeneron Pharmaceuticals, Inc.  
Protocol: R10933-10987-COV-2067 Phase 1/2

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Table 14.2.2.10-1 Proportion of Patients with  $\geq 1$  COVID-19 Related Medically-attended Visit through Day 29  
Full Analysis Set (FAS)

	Placebo (N=93) n/N1 (%)	R10933+R10987 2.4 g IV (N=92) n/N1 (%)	R10933+R10987 8.0 g IV (N=90) n/N1 (%)	R10933+R10987 Combined (N=182) n/N1 (%)
Patients with $\geq 1$ COVID-19 Related Medically-attended Visit through Day 29	6/93 (6.5%)	3/92 (3.3%)	3/90 (3.3%)	6/182 (3.3%)
95% CI [1]	( 2.4%, 13.5%)	( 0.7%, 9.2%)	( 0.7%, 9.4%)	( 1.2%, 7.0%)
Proportion Difference vs Placebo		-3.2%	-3.1%	-3.2%
95% CI [1]		(-17.5%, 11.1%)	(-17.7%, 11.2%)	(-15.5%, 9.4%)
P-Value		0.2293	0.1763	0.1343

By Patient (n=12)	PBO	Low Dose	High Doses
Outpt/Phys Off/TM	2	1	0
Urgent Care	0	0	1
ER	3	2	2
Hospitalization	1	0	0
<b>Totals:</b>	<b>6</b>	<b>3</b>	<b>3</b>

# COVID-19-RELATED MEDICALLY ATTENDED VISITS ARE NUMERICALLY LOWER IN BOTH TREATMENT GROUPS (SERONEGATIVE POPULATION)

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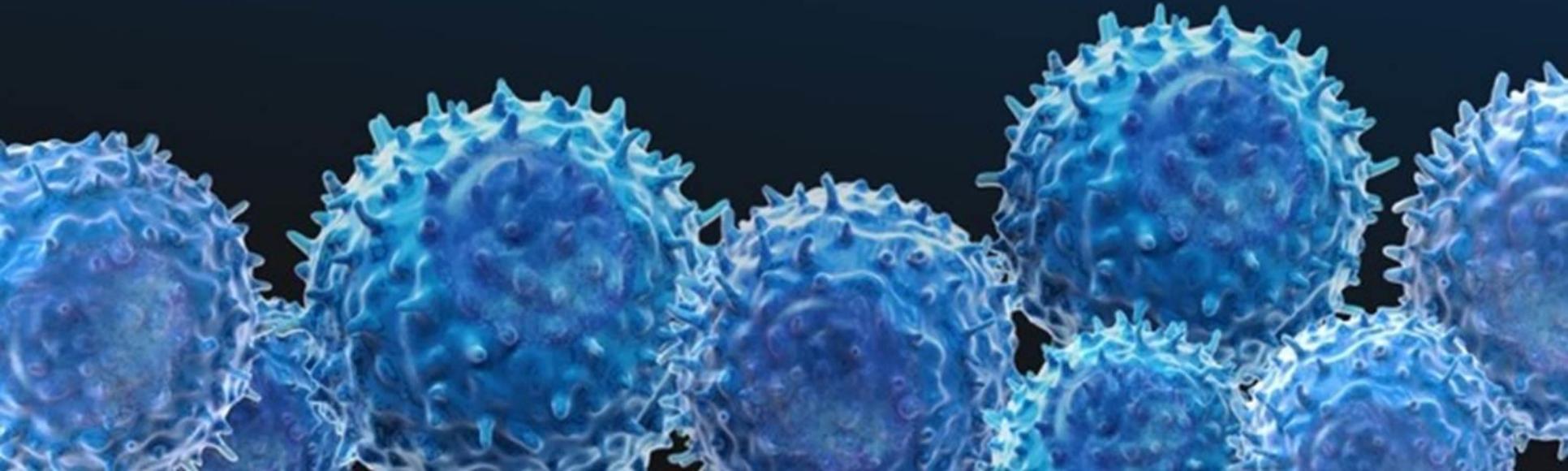
Table 14.2.2.10-2 Proportion of Patients with  $\geq 1$  COVID-19 Related Medically-attended Visit through Day 29 by Baseline Serology Status  
Full Analysis Set (FAS)

Baseline Serology Status: Negative

	Placebo (N=33) n/N1 (%)	R10933+R10987 2.4 g IV (N=41) n/N1 (%)	R10933+R10987 8.0 g IV (N=39) n/N1 (%)	R10933+R10987 Combined (N=80) n/N1 (%)
Patients with $\geq 1$ COVID-19 Related Medically-attended Visit through Day 29	5/33 (15.2%)	2/41 (4.9%)	3/39 (7.7%)	5/80 (6.3%)
95% CI [1]	( 5.1%, 31.9%)	( 0.6%, 16.5%)	( 1.6%, 20.9%)	( 2.1%, 14.0%)
Proportion Difference vs Placebo		-10.3%	-7.5%	-8.9%
95% CI [1]		(-32.4%, 12.6%)	(-30.2%, 15.9%)	(-28.7%, 11.3%)
P-Value		0.1370	0.2723	0.1324

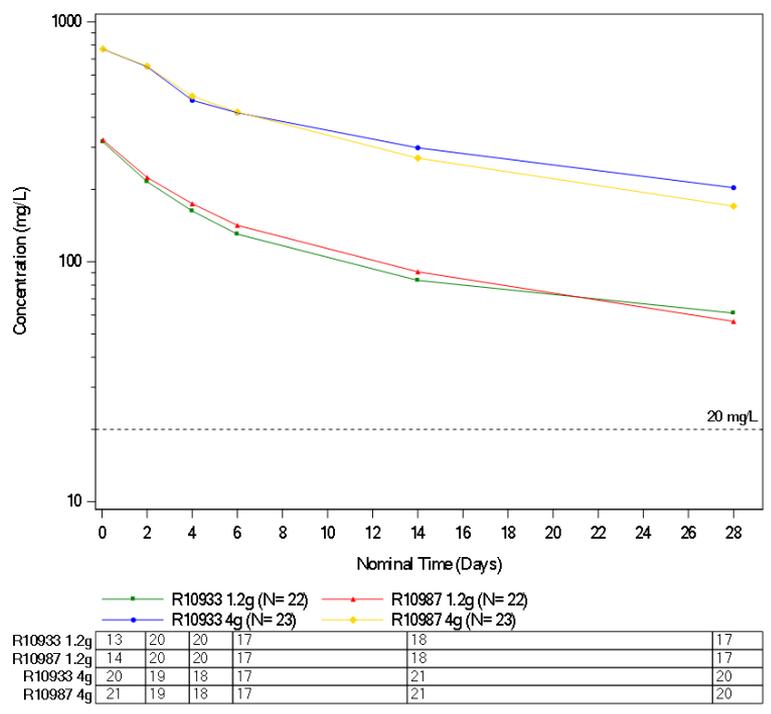
# PHARMACOKINETICS

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# CONCENTRATION-TIME PROFILES OF REGN10933 AND REGN10987 IN SERUM CONSISTENT WITH LINEAR PK FOR SINGLE IV 2.4G AND 8G DOSES (PHASE 1)

Median Concentrations of REGN10933 and REGN10987 in Serum Over Time by Dose in Phase 1 (Log Scale)

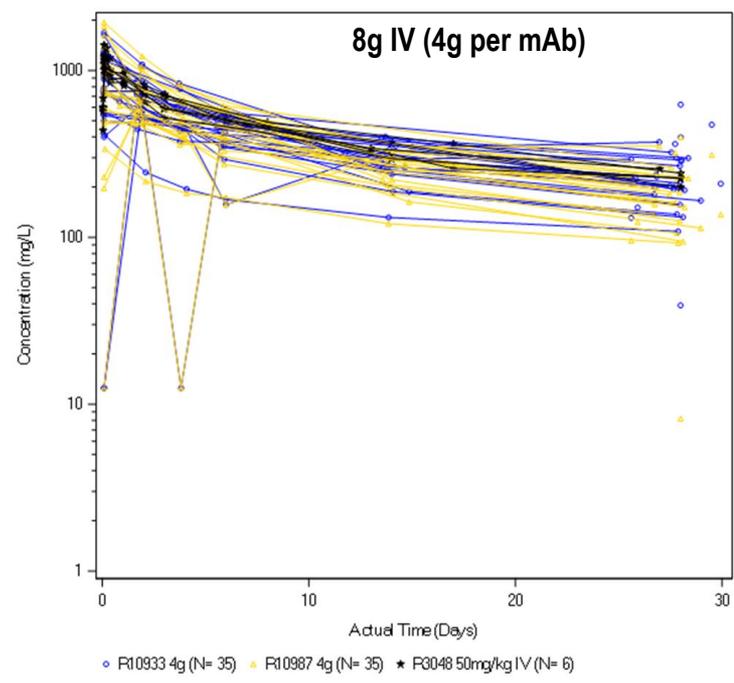
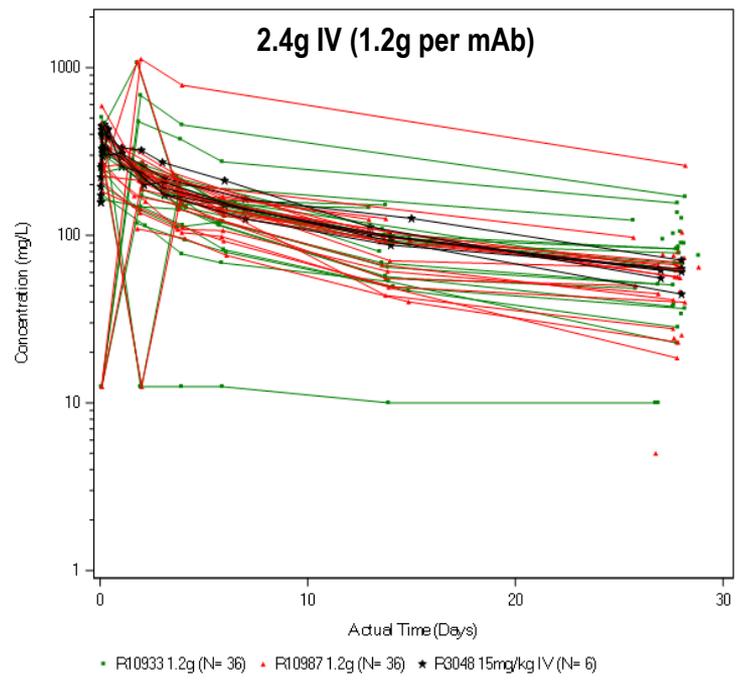


## Half-life estimates for REGN10933 and REGN10987

- Conc vs Time profiles of REGN10933 and REGN10987 are highly consistent with those for MERS and EBOLA mAbs that are also IgG mAbs directed against exogenous targets and produced from the REGN Velocigene technology
- As such, terminal  $t_{1/2}$  for the anti-Spike mAbs is expected to fall within the range of those for the MERS and Ebola mAbs
  - MERS  $t_{1/2}$  18 to 24 days
  - EBOLA  $t_{1/2}$  20 to 32 days
- Estimated half-life for anti-Spike mAbs using last 3 mean concentrations
  - 24 and 25 days for 1.2g and 4g REGN10933, resp
  - 21 and 18 days for 1.2g and 4g REGN10987, resp
- $t_{1/2}$  values in this range are sufficient to support monthly dosing

**INDIVIDUAL CONCENTRATIONS OF REGN10933 AND REGN10987 IN SERUM (COMBINED PHASE 1 & 2 DATA):  
WITH EXCEPTION OF 1 LOW-DOSE PATIENT, ALL HAD DAY 29 TARGET CONCENTRATION  $\geq 20$ MG/L  
WITH EXCEPTION OF 1 HI-DOSE PATIENT, ALL HAD DAY 29 TARGET CONCENTRATION  $\geq 100$ MG/L**

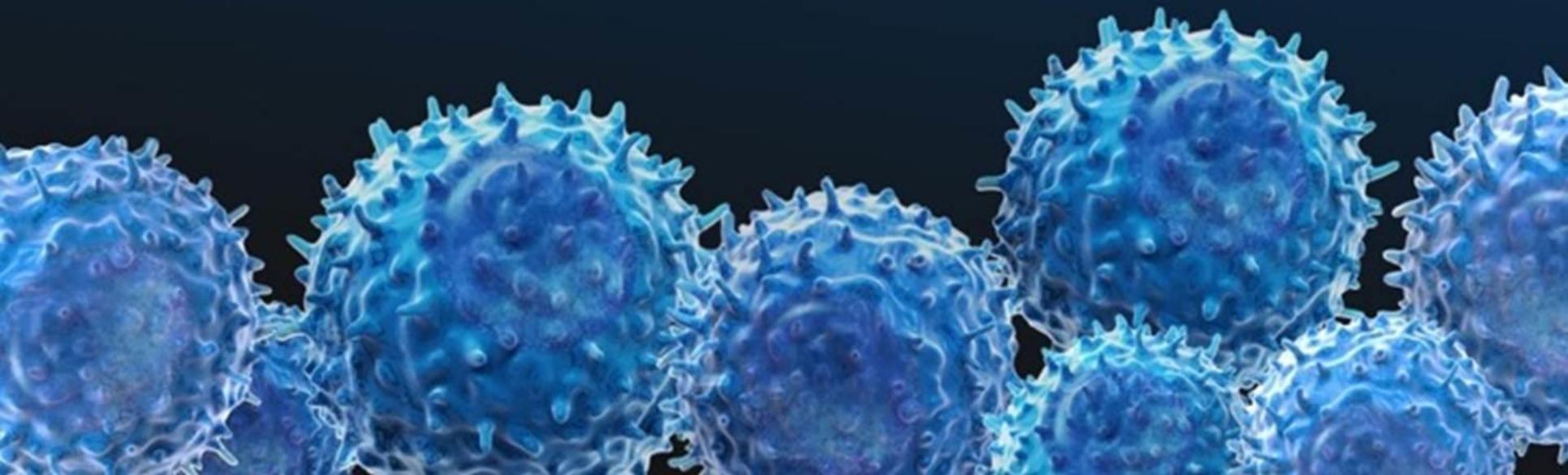
Individual Concentrations of REGN10933 and REGN10987 in Serum Over Time for 1.2g IV (Left Panel) and 4g IV (Right Panel) per mAb  
Overlaid with Individual Concentrations for REGN3048\* in Serum Over Time at 15mg/kg IV (Left Panel) and 50mg/kg IV (Right Panel)





# SAFETY

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# SUMMARY OF SAFETY

Patients with:	PBO (N=93)	Low Dose (2.4g IV) (N=88)	High Dose (8.0g IV) (N=88)
TEAE	4 (4.3%)	1 (1.1%)	2 (2.3%)
SAE	2 (2.2%)	1 (1.1%)	0
Infusion-related reactions Grade $\geq$ 2 thru Day 4	1 (1.1%)	0	2 (2.3%)
Hypersensitivity reactions Grade $\geq$ 2 thru Day 29	2 (2.2%)	0	1 (1.1%)
Deaths	0	0	0
TEAE leading to study infusion interruption	1 (1.1%)	0	1 (1.1%)

TEAE: Treatment Emergent Adverse Event  
(TEAE = SAE + AESI)

SAE: Serious Adverse Event

AESI: Adverse Events of Special Interest  
(AESI = Grade  $\geq$ 2 infusion related reactions or hypersensitivity reactions)

# PROSPECTIVE HYPOTHESIS REGARDING PATIENTS MOUNTING THEIR OWN IMMUNE RESPONSE TO VIRUS

**Before treatment, serology was used to divide patients into those who were “SeroAb-Positive” (had measurable endogenous Abs to COVID19) vs those “SeroAb-Negative” (no measurable Abs)**

- As expected, “SeroAb-Positive” patients had much lower viral levels at baseline compared to “SeroAb-Negative” patients ( $p < 0.0001$ ), and rapidly achieved viral loads approaching “LLQ” even without treatment
- In contrast, “SeroAb-Negative” patients had significantly higher viral levels at baseline, and cleared virus more slowly in the absence of treatment
  - The median viral load in SeroAb-negative patients was  $17 \times 10^6$  copies/mL, whereas in the SeroAb-positive patients it was only  $8.9 \times 10^3$  copies/mL.
  - 93% of the SeroAb-Negative population had viral titers  $> 10^5$  copies/mL, compared to only 28% in the SeroAb-Positive group
- “SeroAb-Positive” patients also had strong trend for faster alleviation of their symptoms (in ~7 days) than “SeroAb-Negative” patients (in ~13 days)

# REGN-COV2 REDUCED VIRAL LOAD AND SYMPTOMS, WITH GREATEST BENEFIT IN PATIENTS WITH LOWER IMMUNE RESPONSES AND/OR HIGH VIRAL TITERS

Goal of this descriptive analysis of first cohort of 275 patients from seamless Ph1/2/3 trial was to evaluate anti-viral activity and identify patients most likely to benefit from treatment, to be rapidly and prospectively confirmed in additional patients from ongoing trial

- **Prospective hypothesis regarding patients mounting their own immune response to virus: Focus on “SeroAb-Negative” patients**
  - **Key Virological Endpoints: Nominally significant activity in overall population, which was driven by “SeroAb-Negative” patients**
  - **Patients with higher baseline viral levels had increasingly larger benefits for viral reduction**
    - Nominally significant reduction in time weighted average change from baseline nasopharyngeal (NP) viral load through Day 7 in [seronegative population](#)**
      - 0.60 log copies/mL greater reduction in viral load in 8.0 g (high dose) arm compared to PBO (P = 0.0297)
      - 0.51 log copies/mL greater reduction in viral load in 2.4 g (low dose) arm compared to PBO (P = 0.0630)
    - Nominally significant reduction in virus levels at Day 7 in patients with high viral loads at baseline ( $>10^6$ )**
      - 1.79 log copies/mL reduction in viral load in 8.0 g (high dose) arm compared to PBO (P = 0.0015); 99% viral reduction compared to Pbo
      - 2.0 log copies/mL reduction in viral load in 2.4 g (low dose) arm compared to PBO (P = 0.001); 99% viral reduction compared to Pbo
  - **Similarly, patients with higher baseline viral levels also had increasingly larger benefits for symptom alleviation**
    - Among seronegative patients, time to symptom alleviation was reduced by a median of 5 days (Day 8 compared to Day 13 PBO) in the high dose group and a median of 7 days (Day 6 compared to Day 13 PBO) in the low dose group.
    - In patients with high viral loads as baseline ( $>10^6$ ), time to symptom alleviation was reduced by a median of 7 days (Day 6 compared to Day 13 PBO) in both dose groups.
  - **Both high and low dose showed similar activity in both viral reduction and symptom alleviation**
  - **Very small number of “medically-attended visits” (MAVs, e.g., ER visits and hospitalizations) – most outpatients do well**
    - >>>Of note, 10 of the 12 MAVs occurred in patients who were SeroAb-Negative at baseline, consistent with notion these are highest risk patients
    - >>>Positive trends related to treatment (15.2% in Pbo, 4.9% in low dose, and 7.7% in high dose)
- **PK of anti-spike monoclonals is linear and consistent with other Regeneron mAbs**
  - High antibody levels even one month after administration, consistent with high bioavailability and long half-life
- **Safety & Tolerability**
  - Both doses were well-tolerated
  - Infusion reactions, SAEs and AESIs were balanced across treatment and PBO groups (no deaths)

## KEY TAKEAWAYS FROM TODAY'S UPDATE

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- The REGN-COV2 antibody cocktail reduces viral loads and symptoms vs. placebo in non-hospitalized patients who are infected with SARS-COV2
- Greatest improvements were observed in patients who had not mounted their own effective immune response prior to treatment (antibody seronegative and/or high viral loads at baseline)
- Results are being shared with regulators and will be used to inform next steps