



## Two Science Publications Highlight Potential of REGN-COV2 Anti-Viral Antibody Cocktail to Protect Against SARS-CoV-2 Escape Mutants

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**Regeneron utilized 'rapid response' *VelociSuite*<sup>®</sup> technologies to identify pairs of potent and complementary antibodies that could be combined into antibody 'cocktails' for COVID-19**

**Cocktail approach protects against viral mutants by requiring simultaneous mutation at multiple genetic positions for viral escape**

[Regeneron Pharmaceuticals, Inc.](#) (NASDAQ: REGN) today announced that *Science* has accepted for publication two papers describing the creation of its novel two-antibody cocktail, REGN-COV2, and its potential to diminish risk of viral escape by effectively binding to the virus's critical spike protein in two separate, non-overlapping locations. The publications will be available online on Monday. Regeneron [also announced today](#) that REGN-COV2 has entered human clinical trials.

"Our work inventing novel antibodies has shown that individual antibodies, no matter how good, are likely not enough against the devastating virus that causes COVID-19 and the ways it seeks to 'escape' being neutralized," said George D. Yancopoulos, M.D., Ph.D., Co-Founder, President and Chief Scientific Officer at Regeneron. "The concept that drug cocktails can prevent viral escape has previously been demonstrated for traditional antiviral drugs used to treat HIV and other viruses. We now report the fundamental realization that this can also be true for antibody-based therapies, supporting our hope that our REGN-COV2 cocktail can be a potent weapon against COVID-19 while preventing the emergence of viral drug-resistance."

The first paper entitled "[Studies in humanized mice and convalescent humans yield a SARS-CoV-2 antibody cocktail](#)" describes Regeneron's parallel efforts using both humanized *VelocImmune*<sup>®</sup> mice and blood samples from recovered COVID-19 patients to generate a large and diverse collection of antibodies targeting multiple different regions of the critical receptor-binding domain (RBD) of the SARS-CoV-2 spike protein. The spike protein on the virus cell surface binds to the host cell and is required for infectivity. By blocking its interaction with the host cell, antibodies are able to neutralize the virus and block infection. Regeneron scientists selected pairs of highly potent individual antibodies that simultaneously and non-competitively bind to the RBD. Regeneron pursues a multi-antibody cocktail approach for infectious diseases in order to decrease the potential for the virus to escape.

Viral escape is when, under pressure from an anti-viral therapeutic, spontaneously arising mutant forms of the virus are able to 'escape' or evade the therapeutic's blocking action. These mutants are then 'selected' (i.e., are able to survive and proliferate despite the single therapeutic treatment) and may ultimately become the dominant strain of the virus.

The concept that drug cocktails can prevent viral escape has previously been demonstrated for traditional antiviral drugs used to treat HIV and other viruses. Regeneron now reports the fundamental realization that this can also be true for antibody-based therapies as reported in the second paper, entitled "[Antibody Cocktail to SARS-Cov-2 Spike Protein Prevents Rapid Mutational Escape Seen with Individual Antibodies.](#)" which further defines the protective value of the multiple-antibody approach against SARS-CoV-2 specifically. This research for the first time demonstrates that, under pressure from individual antibodies, mutant viruses were rapidly selected that evaded the blocking function of all individual antibodies tested, including antibodies that potently bind to highly-conserved regions on the spike protein. However, escape mutants could not be efficiently generated following exposure to the REGN-COV2 cocktail since it utilizes two antibodies that can simultaneously bind to distinct regions of the RBD.

"Our manuscripts describe the results of a cross-functional, comprehensive study, aiming to generate, isolate, select and functionally characterize human antibodies against SARS-CoV-2. We previously used the same technologies and cocktail approach to develop REGN-EB3, a novel triple antibody treatment for Ebola that demonstrated safety and efficacy versus the standard of care in a clinical trial in the Democratic Republic of Congo," said Christos Kyratsous, Ph.D., Vice President of Research, Infectious Diseases and Viral Vector Technologies at Regeneron. "We hope to see similar success with this program and help improve outcomes against this terrible disease."

REGN-COV2's preclinical development and preclinical/clinical manufacturing has been funded in part with federal funds from the Biomedical Advanced Research and Development Authority (BARDA), part of the office of the Assistant Secretary for Preparedness and Response at the U.S. Department of Health and Human Services, under OT number: HHSO100201700020C.

### About Regeneron

Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led for 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to seven FDA-approved treatments and numerous product candidates in development, all of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, infectious diseases, pain and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite*<sup>®</sup> technologies, such as *VelocImmune*<sup>®</sup>, which uses a unique genetically-humanized mouse to produce optimized fully-human antibodies and bispecific antibodies, and through ambitious research initiatives such as the Regeneron Genetics Center, which is conducting one of the largest genetics sequencing efforts in the world.

For additional information about the company, please visit [www.regeneron.com](http://www.regeneron.com) or follow @Regeneron on Twitter.

## **Regeneron Forward-Looking Statements and Use of Digital Media**

*This press release 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 business and its employees, collaborators, suppliers, and other third parties on which Regeneron relies, Regeneron's and its collaborators' ability to continue to conduct research and clinical programs (including those discussed in this press release), Regeneron's ability to manage its supply chain, net product sales of products marketed by Regeneron and/or its collaborators (collectively, "Regeneron's Products"), and the global economy; the nature, timing, and possible success and therapeutic applications of Regeneron's Products and product candidates and research and clinical programs now underway or planned, including without limitation REGN-COV2 (Regeneron's investigational dual antibody cocktail for the prevention and treatment of COVID-19) and REGN-EB3 (Regeneron's novel triple antibody treatment for Ebola); the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's product candidates (such as REGN-COV2 and REGN-EB3) and new indications for Regeneron's Products; unforeseen safety issues resulting from the administration of Regeneron's Products and product candidates (such as REGN-COV2 and REGN-EB3) in patients, including serious complications or side effects in connection with the use of Regeneron's Products and product candidates in clinical trials; 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, including without limitation REGN-COV2 and REGN-EB3; ongoing regulatory obligations and oversight impacting Regeneron's Products, research and clinical programs, and business, including those relating to patient privacy; 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; competing drugs and product candidates that may be superior to Regeneron's Products and product candidates; the extent to which the results from the research and development programs conducted by Regeneron or its collaborators may be replicated in other studies and lead to therapeutic applications; 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, labelling, 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; 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), to be cancelled or terminated without any further product success; and risks associated with intellectual property of other parties and pending or future litigation relating thereto (including without limitation the patent litigation and other related proceedings relating to Dupixent® (dupilumab) and Praluent® (alirocumab)), other litigation and other proceedings and government investigations relating to the Company and/or its operations, 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. 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-K for the year ended December 31, 2019 and its Form 10-Q for the quarterly period ended March 31, 2020. 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 any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.*

*Regeneron uses its media and investor relations website and social media outlets to publish important information about the Company, including information that may be deemed material to investors. Financial and other information about Regeneron is routinely posted and is accessible on Regeneron's media and investor relations website (<http://newsroom.regeneron.com>) and its Twitter feed (<http://twitter.com/regeneron>).*

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