

The Case for Federal Investment in Cell-Based Therapies for Patients with COVID-19

March 24, 2021



Advancing Regenerative Medicine and Cell Therapies for Patients in Need

Executive Summary

As the nation continues to face the unprecedented challenges of the coronavirus pandemic, the number of Americans that are continuing to contract COVID-19, become hospitalized, and in many cases—succumb to the disease—continues to be high. More than 30 million Americans have tested positive for COVID-19 and more than 540,000 Americans have died. While vaccines are making their way to eligible populations, and therapies are beginning to emerge, to date no approved therapy has shown significant benefit for the most severe cases, in which individuals are hospitalized.

Early evidence shows that cell-based therapies can play a key role in helping severely ill patients with COVID-19, given their immunomodulatory and anti-inflammatory characteristics.

There are now at least 114 clinical studies underway that explore the use of cell-based therapies for patients with COVID-19, 39 of which are being conducted in the United States. Eighty-three percent of the clinical trials being performed in the U.S. are either Phase 1 or Phase 2 studies. There is only one Phase 2/3 and one Phase 3 trial underway. At least 136 review articles have been published that describe the promise or potential of these therapies for treating COVID-19 patients, drawing from the results of earlier studies.

Early results from early-stage clinical studies are promising, but large-scale, randomized, placebo-controlled clinical trials are needed to confirm early results and help bring safe and effective treatments to patients in need.

The largest barrier to conducting clinical research related to cell-based therapies is the high cost of conducting these studies. The financial barriers associated with clinical trials is particularly problematic for academic and research institutions and small biotechnology companies, who are responsible for nearly all of the clinical trials being conducted for COVID-19 both in the United States and abroad.

The Administration recognizes the lack of reliable and accessible treatments for COVID-19 and the need for investment in the development and manufacturing of therapies, as outlined both within the January 21, 2021 [Executive Order](#) outlining policies to accelerate the development of novel therapies to treat COVID-19, and the [American Rescue Plan](#), which formed the basis for the COVID-19 relief package passed by Congress and signed into law by the President in early March 2021.

Congress has authorized nearly \$40 billion in funding for vaccines, therapeutics, and other medical supplies within three COVID-19 relief packages—two of which were passed and signed into law in 2020 and one of which was passed and signed into law earlier this year.

As the Administration establishes its priorities for the billions of dollars in funding authorized by Congress for COVID-19 vaccines and therapeutics and as Congress considers FY 2022 appropriations, both should assure that a portion of funds for research and development are directed towards cell-based therapies to help patients with COVID-19, as well as other serious and life-threatening conditions.

Therapies are Needed for Severely Ill Patients with COVID-19

More than 30 million Americans have tested positive for COVID-19 and more than 540,000 Americans have died. In its most severe form, COVID-19 leads to acute respiratory distress syndrome (ARDS) — a life-threatening lung injury that allows fluid to leak into the lungs and makes it difficult for patients to breathe. The number of [hospitalizations](#) in the U.S. has accelerated over the last several months, reaching more than 130,000 in early 2021.

According to multiple recent studies cited by the [Centers for Disease Control and Prevention](#) (CDC):

- 14 percent of patients in the U.S. are being hospitalized, and among all hospitalized patients, 26 to 32 percent are being admitted to the intensive care unit (ICU).
- Anywhere from 20 to 42 percent of hospitalized patients and 67 to 85 percent of patients admitted to the ICU develop ARDS.
- 39 to 72 percent of patients admitted to the ICU for COVID-19, die.
- Elderly patients and minorities are at greatest risk of serious complications and death.

While vaccines are making their way to eligible populations, and therapies are beginning to emerge, to date no approved therapy has shown significant benefit for the most severe cases. There is an urgent need for new modalities—that are broad-acting and safe—with the goal of preventing progression of COVID-19 in hospitalized patients to ICU-level care, but also importantly, to effectively treat those who are admitted to the ICU and to save lives.

To date, no approved therapy has shown significant benefit for severely ill COVID patients

30 million
COVID-19 Cases
in the U.S.

As of March 24, 2021
Source: New York Times

543,000
COVID-19 Deaths
in the U.S.

As of March 24, 2021
Source: New York Times

Cell-Based Therapies Show Promising Results

Early evidence shows that cell-based therapies, including mesenchymal stromal cells (MSCs), can play a key role in helping severely ill patients with COVID-19, given their immunomodulatory and anti-inflammatory characteristics.

A [systematic review and meta-analysis](#) of clinical trials led by researchers at the Mayo Clinic and including researchers from the Duke University School of Medicine, Emory University, Case Western Reserve University, and the University of Miami Miller School of Medicine, showed a positive trend toward improved pulmonary function, reduced lung inflammation, and reduced mortality for patients with ARDS who were treated with MSCs. Several review articles published over the last year show similar results.

As summarized in Figure 1, at least 140 review articles have been published in peer-reviewed publications since March 2020 that offer insights on the potential or promise of cell-based therapies for patients with COVID-19. The vast majority (96 percent) describe the role of MSCs in treating COVID-19 patients. Review articles also describe the role of T-Reg cells, induced pluripotent stem cells (iPSCs), natural killer (NK) cells, and progenitor cells in addressing COVID-19.

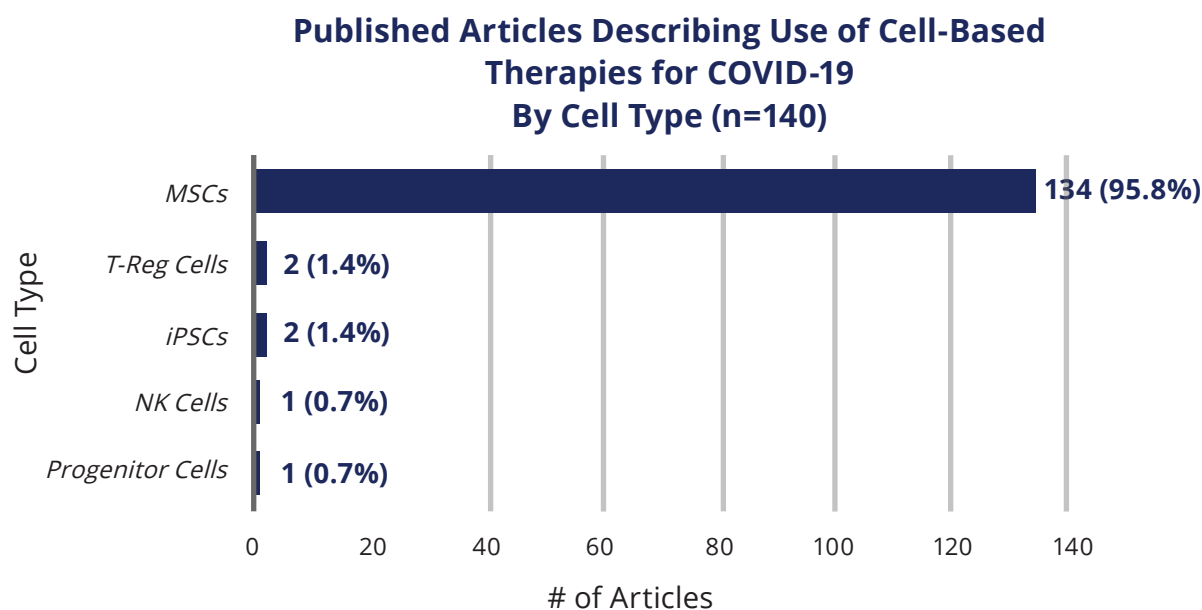


Figure 1. Number of Published Articles Related to the Use of Cell-Based Therapies for COVID-19, by Cell Type

A detailed list of published review articles—which is updated weekly—can be found at <https://allianceforcelltherapy.org/published-articles-describing-role-of-cell-therapies-for-covid-19/>.

Researchers involved in 27 clinical studies involving the use of cell-based therapies for seriously ill patients with COVID-19 have published their results, 25 of which were published or are to be published in peer-reviewed journals.

Across all 25 studies with results published in peer-reviewed journals, mortality rates averaged 8 percent, which is less than the average mortality rate for severely ill patients with COVID-19 in the ICU, which range from [39 percent to 72 percent](#).

Nine of the 25 published studies were based on expanded access use of cell-based therapies for COVID patients. Only 5 of the 25 published findings were based on randomized, controlled trials, and the other 11 studies did not include randomization. Therefore the conclusions that can be drawn from published findings to date are limited.

Clinical Studies Exploring the Use of Cell-Based Therapies for COVID-19

At least 114 clinical studies are listed in www.clinicaltrials.gov that explore the use of cell-based therapies for patients with COVID-19.

As summarized in Figure 2, 36 percent of the 114 studies identified are being conducted in the United States.

**Clinical Studies Exploring Use of Cell-Based Therapies for COVID-19
By Location (n=114)**

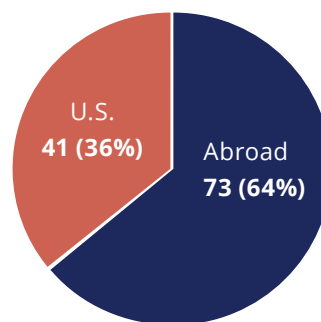


Figure 2. Number of Clinical Studies Exploring Use of Cell-Based Therapies for COVID-19, by Location

Some of the academic and medical institutions leading or participating in clinical trials or conducting related studies include Baptist Health, Baylor College of Medicine and Methodist Hospital System, Case Western Reserve University, Duke University School of Medicine, Emory University, Mayo Clinic, MD Anderson Cancer Center, Mount Sinai Icahn School of Medicine (in collaboration with Mesoblast), Sanford Health, University of California – San Francisco, University of Miami School of Medicine, University of Virginia School of Medicine, and Wake Forest Institute for Regenerative Medicine. There are also several biotechnology companies leading trials, including Athersys, Celularity, Longeveron, and Mesoblast, among others.

As indicated in Figure 3, the vast majority (74 percent) of clinical studies being conducted are focused on the use of MSCs for patients with COVID-19.

**Clinical Studies Exploring Use of Cell-Based Therapies for COVID-19
By Cell Type (n=114)**

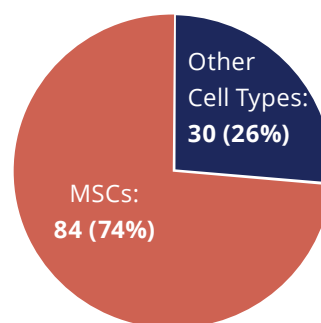


Figure 3. Number of Clinical Studies Exploring Use of Cell-Based Therapies for COVID-19, by Cell Type

At least 114 clinical trials are exploring the use of cell-based therapies for patients with COVID-19

Clinical Studies Exploring the Use of Cell-Based Therapies for COVID-19

As indicated in Figure 4 below, most (85 percent) of the clinical trials being performed worldwide are either Phase 1 (30 percent), Phase 1/2 (25 percent), or Phase 2 (30 percent) studies. Two of the studies are Phase 2/3 clinical trials and only one study is a Phase 3 trial.

All Clinical Studies Exploring Use of Cell-Based Therapies for COVID-19 By Phase (n=114)

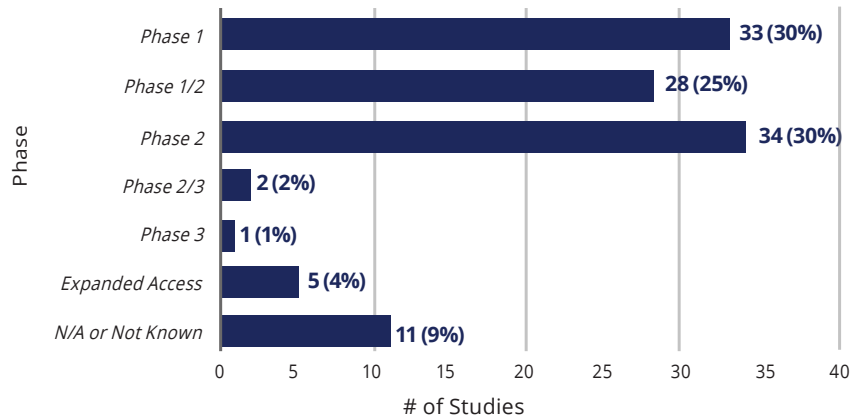


Figure 4. Number of Clinical Studies Exploring Use of Cell-Based Therapies for COVID-19, by Phase

Similarly, Figure 5 indicates that 80 percent of the clinical trials being performed in the United States are either Phase 1 (29 percent), Phase 1/2 (22 percent), or Phase 2 (29 percent) studies. There is one Phase 2/3 clinical trial and one Phase 3 trial being conducted in the United States.

U.S. Clinical Studies Exploring Use of Cell-Based Therapies for COVID-19 By Phase (n=41)

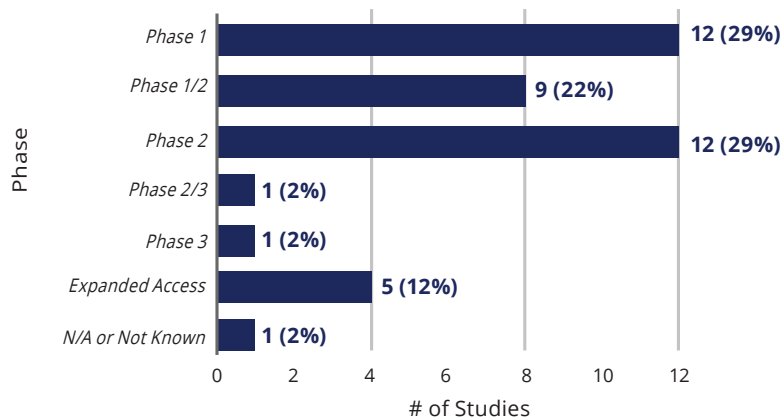


Figure 5. Number of U.S. Clinical Studies Exploring Use of Cell-Based Therapies for COVID-19, by Phase*

Results from early Phase 1 and Phase 2 clinical studies are promising, but large-scale, randomized, placebo-controlled clinical trials that take into account the evolving standard of care and current mortality rates are needed to confirm early results and help bring safe and effective treatments to patients in need.

A detailed analysis of clinical studies—updated weekly—can be found at <https://allianceforcelltherapynow.org/covid19-clinical-research-tracker/>.

*Percentages do not add up to 100 percent due to rounding

Large-scale, randomized, placebo-controlled clinical trials are needed to confirm early results and help bring safe and effective treatments to patients in need

Large-Scale, Randomized, Controlled Clinical Trials Likely Will Not Occur Without Federal Support

The [largest barrier](#) to conducting clinical research related to cell-based therapies is the high cost of conducting studies. The financial barriers associated with clinical trials is particularly problematic for academic and research institutions and small biotechnology companies, who are responsible for nearly all of the clinical studies both in the United States and abroad.

As summarized in Figure 6, 34 percent of U.S. clinical trials exploring the use of cell-based therapies for COVID-19 are being conducted by academic and research institutions. The remaining 66 percent are being conducted by industry—all small biotechnology companies—in some cases, in collaboration with health systems.

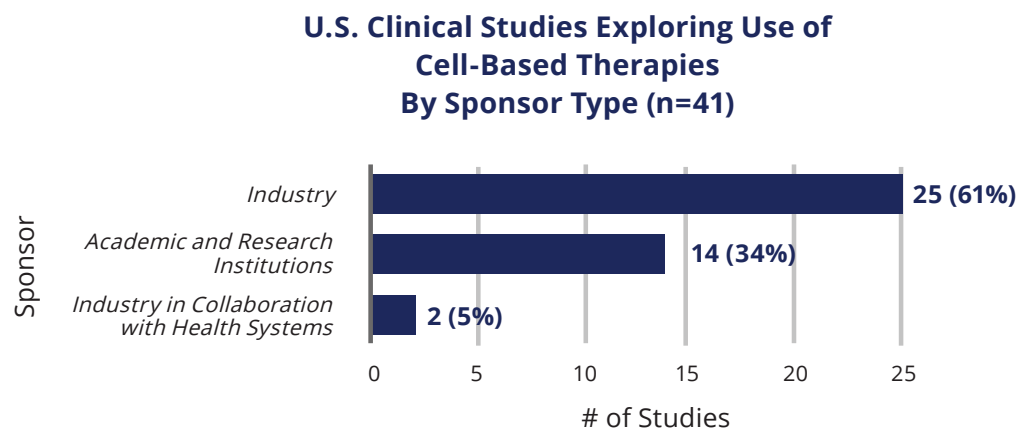


Figure 6. Number of U.S. Clinical Studies Exploring Use of Cell-Based Therapies for COVID-19, by Sponsor Type

While results from early phase clinical trials and meta-analyses and systematic reviews show promise, the large-scale, randomized, placebo-controlled clinical trials that are needed to confirm early results and ultimately bring safe and effective treatments to severely ill COVID-19 patients will not occur without federal funding and support.

The Biden Administration has recognized the lack of reliable and accessible treatments for COVID-19 and the need for investment in the development and manufacturing of therapies both within the January 21, 2021 [Executive Order](#) and the [American Rescue Plan](#), which formed the basis for the COVID-19 relief package passed by Congress and signed into law by the President in early March 2021.

Congress has also authorized nearly \$40 billion in funding for vaccines, therapeutics, and other medical supplies within three COVID-19 relief packages—two of which were passed and signed into law in 2020 and one of which was signed into law earlier this year.

However to date, little or no federal funding provided through COVID-19 relief legislation has been used to support clinical trials exploring the use of cell-based therapies for patients with COVID-19, despite the more than 100 clinical studies that have been initiated and the 140 published articles that describe the promise or potential of these therapies for this deadly disease.

While early results show promise, the large-scale, randomized, controlled clinical trials that are needed to confirm early results and ultimately bring safe and effective treatments to COVID-19 patients in need *will not occur without federal funding and support*

The Administration and Congress Should Direct Funding to Cell-Based Therapies for Patients with COVID-19

Federal funding should be directed toward clinical trials exploring use of regenerative medicine and cell therapies for COVID-19 and other serious conditions

As COVID-19 and related hospitalizations continue to surge across the U.S., there are still no approved therapies for seriously ill, hospitalized patients.

While vaccines are making their way to eligible populations, it will take months for Americans to get vaccinated, and—as the research shows—many may choose to forgo vaccination. Millions of Americans will continue to contract COVID-19 and thousands more will die. There is an urgent need for new modalities—that are broad-acting and safe—to help severely ill, hospitalized patients with COVID-19.

Cell-based therapies show promise for treating seriously ill patients with COVID-19, but large-scale, randomized, placebo-controlled trials—which are needed to confirm efficacy—cannot move forward without federal partnership and support.

As the Administration establishes its priorities for the billions of dollars in funding authorized by Congress for COVID-19 vaccines and therapeutics, and as Congress considers fiscal year 2022 appropriations, both should assure that a portion of funds for research and development are directed towards cell-based therapies to help patients with COVID-19, as well as other serious and life-threatening conditions.

“To enhance the Nation’s ability to quickly develop the most promising COVID-19 interventions, the Secretary of Health and Human Services (HHS), in consultation with the Director of the National Institutes of Health, shall ... develop a plan for supporting a range of studies, including large-scale randomized trials, for identifying optimal clinical management strategies, and for supporting the most promising treatments for COVID-19 and future high-consequence public health threats...”

The White House. Executive Order on Improving and Expanding Access to Care and Treatments for COVID-19. January 21, 2021.

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Julie Allickson, PhD
Chief, Manufacturing Development Center Officer, Wake Forest Institute for Regenerative Medicine

Arnold Caplan, PhD
Professor of Biology, Director of the Skeletal Research Center, Case Western Reserve University

George Christ, PhD
Professor of Biomedical Engineering and Orthopaedic Surgery, Director of Basic and Translational Research in Orthopaedic Surgery; University of Virginia School of Engineering and Applied Sciences

Colleen Delaney, MD, MSc
Founder, Chief Scientific Officer and Executive Vice President of Research and Development, Deverra Therapeutics and Professor, Department of Pediatrics, Division of Pediatric Hematology/Oncology, University of Washington

Joe GN "Skip" Garcia, MD
Dr. Merlin K. DuVal Professor of Medicine, University of Arizona Health Sciences

Geoffrey Green
Chief Executive Officer, Longeveron

Joshua M. Hare, MD, FACC, FAHA
Louis Lemberg Professor of Medicine, Founding Director, Interdisciplinary Stem Cell Institute, University of Miami, Miller School of Medicine

Joanne Kurtzberg, MD
Jerome Harris Distinguished Professor of Pediatrics; Professor of Pathology; Director, Marcus Center for Cellular Cures; Director, Pediatric Blood and Marrow Transplant Program; Director, Carolinas Cord Blood Bank; Co-Director, Stem Cell Transplant Laboratory; Duke University Medical Center

Brian Lindberg
Chief Legal Officer, General Counsel, Chief Policy Officer, National Marrow Donor Program and Be The Match

Keith L. March, MD, PhD
Director, University of Florida Center for Regenerative Medicine; Vice Chief, Cardiology Research; Professor, Cardiovascular Medicine and Department of Medicine, University of Florida

Janet M. Marchibroda
President, Alliance for Cell Therapy Now; Executive Director, NFL Alumni Health; Fellow, Bipartisan Policy Center

Maria T. Millan, MD
President and CEO, California Institute for Regenerative Medicine

J. Marc Overhage, MD, PhD
Principal Investigator, Alliance for Cell Therapy Research Evidence Development Collaboration, Alliance for Cell Therapy Now

David A. Pearce, PhD
President of Innovation, Research, and World Clinic, Sanford Health; Senior Scientist, Sanford Children's Health Research Center; Professor of Pediatrics, University of South Dakota Sanford School of Medicine

Wenchun Qu, MD, PhD
Associate Professor of Anesthesiology; Associate Professor of Physical Medicine and Rehabilitation; Physiatrist and Pain Specialist, Mayo Clinic

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Board Member, President of Chapters, Co-Director of Healthcare Initiatives, NFL Alumni

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Robert A. Milton Chair; Director, NSF Engineering Research Center for Cell Manufacturing Technologies; Director, Marcus Center for Cell-Therapy Characterization and Manufacturing; Technical Lead, National Cell Manufacturing Consortium; Director, Center for ImmunoEngineering, Georgia Institute of Technology

Fred Sanfilippo, MD, PhD
Professor, Health Policy and Management, Rollins School of Public Health, Emory University; Director, Emory-Georgia Tech Healthcare Innovation Program; Medical Director, The Marcus Foundation

Beth Shaz, MD
Professor in Pathology, Deputy Director of the Marcus Center for Cellular Cures, Duke University School of Medicine; Former Chief Medical and Scientific Officer and Senior Vice President, New York Blood Center

Bernard Siegel, JD
Executive Director, Regenerative Medicine Foundation; Founder and Chair, World Stem Cell Summit

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President and Chair, Stem for Life and Cura Foundation

Piotr P. Witkowski, MD, PhD
Associate Professor of Surgery, Biological Sciences Division, University of Chicago

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About Alliance for Cell Therapy Now

Alliance for Cell Therapy Now (Alliance) is an independent, non-profit organization guided by leaders representing academic and medical institutions, industry innovators, and patients, that is working to advance safe and effective regenerative medicine and cell therapies for patients in need. For more information, go to <http://allianceforcelltherapynow.org/>

For More Information

For more information, contact Alliance for Cell Therapy Now via email at communications@allianceforcelltherapynow.org or via phone at 202.922.9077.