Allogene Therapeutics Announces 2024 Platform Vision to Redefine the Future of CAR T Led by ALPHA3, the Industry's First Pivotal Trial for Frontline Consolidation in Large B-Cell Lymphoma

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- Four Core Programs Leverage Unique Attributes in Product Development and Trial Design to Demonstrate the Unmatched Potential of an Allogeneic CAR T
    1. **Large B-Cell Lymphoma (LBCL)**: Groundbreaking ALPHA3 Trial has Potential to Leapfrog Other CAR Ts and Embed Cemacabtagene Ansegedleucel (Cema-Cel, Previously ALLO-501A) in First Line (1L) Treatment in Community Cancer Centers Where Most Newly Diagnosed Patients Seek Care
    2. **Chronic Lymphocytic Leukemia (CLL):** New ALPHA2 Cohort Designed to Address a Limitation of Autologous Therapies in a Disease Where Poor T Cell Fitness is a Known Barrier to Efficacy
    3. **Autoimmune Disease (AID):** ALLO-329, Next-Generation CD19 Dagger™ Program will Focus on Scalability and Reduced or Chemotherapy-Free Lymphodepletion, Positioning Allogeneic CAR T to Transform Autoimmune Management and Meet the Demand of the Market
    4. **Renal Cell Carcinoma (RCC):** Ongoing TRAVERSE Trial Advances Scientific Innovation Underlying Dagger™ Biology to Optimize CAR T Cell Expansion and Persistence Thereby Maximizing the Potential of Allogeneic CAR T in Solid Tumors While Mitigating Treatment-Associated Inflammatory Response
- Differentiated Potential for Cema-Cel to Boost Cure Rates in the 1L Setting Expected to Decrease Demand for Later Line Treatment, Effectuating De-Prioritization of Third Line ALPHA2 and EXPAND Trials
- Company to Focus Manufacturing in Cell Forge 1 to Prepare and Scale for Future AlloCAR T™ Demand
- Prioritization Will Streamline Resources, Reduce Cash Burn and is Expected to Extend Financial Runway Into 2026
- Conference Call Scheduled for Today at 2:00 PM PT/5:00 PM ET

SOUTH SAN FRANCISCO, Calif., Jan. 04, 2024 (GLOBE NEWSWIRE) -- Allogene Therapeutics, Inc. (Nasdaq: ALLO), a clinical-stage biotechnology company pioneering the development of allogeneic CAR T (AlloCAR T™) products for cancer and autoimmune disease, today announced its 2024 Platform Vision that redefines the future of CAR T by leveraging the unique attributes of allogeneic CAR T products.

“Until now, CAR T development has been defined by how autologous CAR Ts are made and used. As a management team with extensive experience in both autologous and allogeneic CAR Ts, and the only Company with the breadth of data to demonstrate comparability between the two, we are uniquely positioned to potentially redefine development and trial design of allogeneic CAR T products that allows us to do what no autologous CAR T has done before,” said David Chang, M.D., Ph.D., President, Chief Executive Officer and Co-Founder of Allogene. “We believe this entirely new approach to development creates an advantage for our investigational AlloCAR T™ products now and in the future while providing a clinical framework to generate far more competitive CAR T products and dramatically expand market opportunity.”

The Foundation: Pivotal ALPHA3 1L Consolidation Trial in Large B Cell Lymphoma (LBCL)
In a commanding pivot for the CD19 program, the Company will focus development of its investigational product cemacabtagene ansegedleucel, or cema-cel (previously known as ALLO-501A) as part of the first line (1L) treatment plan for newly diagnosed and treated LBCL patients who are likely to relapse and need further therapy. The groundbreaking design of the ALPHA3 1L consolidation trial builds upon the results demonstrated in the Phase 1 ALPHA2 trial and leverages an investigational cutting-edge diagnostic test developed by Foresight Diagnostics to identify patients who have minimal residual disease (MRD) at the completion of 1L chemoimmunotherapy for treatment with cema-cel.

Although 1L R-CHOP is curative for many with LBCL, approximately 30% of patients who initially respond will relapse[i]. The standard of care after 1L treatment has been simply to “watch and wait” for the disease to relapse. ALPHA3 takes advantage of cema-cel as a one-time, off-the-shelf treatment that can be administered immediately upon discovery of MRD following six cycles of R-CHOP, positioning it to become the standard “7 th cycle” of frontline treatment available to all eligible patients with MRD. ALPHA3 builds on the growing understanding that administration of CAR T therapies to patients with low disease burden improves both safety and efficacy outcomes. Cema-cel’s Phase 1 safety profile, with low rates of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), already permits its use in the outpatient setting in relapsed/refractory (r/r) patients and may further improve in patients with no radiological evidence of disease.

Start-up activities for the ALPHA3 trial have been initiated. The study will randomize approximately 230 patients who are MRD positive at the end of 1L therapy to either consolidation with cema-cel or the current standard of care (observation). The design, with a primary endpoint of event free survival (EFS), will initially include two lymphodepletion arms (one with standard fludarabine and cyclophosphamide plus ALLO-647 and one without ALLO-647).

The outcome of this pivotal trial could allow cema-cel to be embedded in the 1L setting to boost cure rates, potentially rendering later-line treatment obsolete, and making cema-cel available in community cancer centers where most earlier line patients seek care. As a result of this differentiated vision for cema-cel which competitively places its use ahead of other CAR T therapies, the Company will focus on quickly advancing this market-defining ALPHA3 trial and deprioritize the currently enrolling third line (3L) ALPHA2 and EXPAND trials.

The Higher Bar: ALPHA2 Cema-Cel Trial in Chronic Lymphocytic Leukemia (CLL)
There is a growing need for effective treatment in CLL post-Bruton tyrosine kinase inhibitors (BTKis) and B-cell lymphoma 2 inhibitor (BCL2i) therapies. While recent autologous CD19 CAR T data has been a positive step for patients with r/r CLL, these therapies are still not meeting the efficacy bar or expectations set in r/r LBCL. This is likely due in part to T cell dysfunction and high circulating tumor burden in CLL, making the isolation of functional T cells for autologous CAR T manufacturing difficult.

There is strong scientific rationale to believe that an AlloCAR T™ product derived from healthy donor cells could raise the bar and potentially create a clinically meaningful advance for these late-stage patients, with a one-time dose and simpler administration and logistics.

The new Phase 1 ALPHA2 cohort of 12 patients treated with the investigational product cema-cel provides the opportunity to set a higher bar where patients with CLL are not reliant on their own T cells' fitness to benefit from the curative potential of CAR T. This study, driven by investigator enthusiasm, will leverage currently active ALPHA2 trial sites in the U.S. which should allow it to advance quickly. It is expected to begin enrolling in Q1 2024 with initial data projected by YE 2024.

The Disruptor: ALLO-329 CD19 Dagger™ in Autoimmune Disease (AID)
The Company is applying its deep understanding of CAR Ts to design a next-generation allogeneic CAR T with reduced or chemotherapy-free conditioning that the Company believes can sustain the scale of the AID market while meeting the unique requirements for these patients where they seek care.

The risk tolerance of these patients is very different than those with cancer, in large part because of patient demographics, wide availability of effective therapies, and rheumatologists' general lack of experience with chemotherapy, leukapheresis procedures and cell therapies.

Incorporation of the Dagger technology into an off-the-shelf CD19 product for use in AID is designed to reduce or eliminate the need for standard chemotherapy while targeting CD19+ B-cells and CD70+ activated T-cells, both of which play a role in AID. Initiation of this Phase 1 trial with ALLO-329 is expected in early 2025.

The Key: TRAVERSE ALLO-316 in Renal Cell Carcinoma (RCC)
A fundamental discovery in early CAR T trials was the use of tocilizumab and steroids, the "safety key" needed to mitigate treatment-associated CRS without compromising CAR T function or efficacy. The Company believes it may have made the same cornerstone discovery in the TRAVERSE trial in renal cell carcinoma.

During the careful advancement of the TRAVERSE trial with ALLO-316, the Company has observed remarkable allogeneic CAR T cell expansion and persistence driven by its unique CD70 CAR that allows elimination of alloreactive host lymphocytes. This biology has brought the potential for clinical efficacy not often seen in patients with r/r RCC but has also resulted in a hyperinflammatory response in some patients as CD70 CAR T cells expand and persist.

Leveraging recent advances in the management of hyperinflammation following autologous CAR T administration, the Company has developed a diagnostic and treatment algorithm similar to what the management team previously helped develop for CRS and ICANS. Like tocilizumab and steroids, this algorithm may mitigate the treatment-associated hyperinflammatory response without compromising the CAR T function needed to eradicate solid tumors. The Company has recently implemented a protocol amendment to further maximize the benefit-risk of ALLO-316 in patients with CD70+ RCC.

The next update from this trial is planned for a medical forum in Q2 2024 and will discuss the algorithm that is believed to be a critical advance for both the TRAVERSE trial as well as the industry at large. A more robust data update from the ongoing trial with the updated protocol is planned for later in 2024.

The Source: Proprietary Cell Forge 1 Allogeneic CAR T Manufacturing Facility
Cell Forge 1 (CF1), the Company's wholly owned and fully integrated manufacturing facility, serves as a crucial strategic asset given the potential outlook for allogeneic CAR T product demand. We believe the ability to scale and control manufacturing will allow the Company to deliver a consistently high-quality allogeneic CAR T product.

Financial Runway Extended into 2026
The refined approach of the 2024 Platform Vision results in a streamlined trial footprint as well as a focused pipeline prioritization, allowing the Company to implement a planned restructuring of resources in Q1 2024. The result will reduce cash burn and is expected to extend the Company's financial runway into 2026. Full 2024 guidance will be provided in the Company's Q4/YE 2023 quarterly call.

JP Morgan Preview Conference Call
The 2024 Platform Vision Conference Call will be hosted on Thursday, January 4, 2024, at 2:00 p.m. PT/5:00 p.m. ET and include presentations and/or commentary by:

- David Chang, M.D., Ph.D., President, Chief Executive Officer and Co-Founder
- Zachary Roberts, M.D., Ph.D., Executive Vice President, Research & Development and Chief Medical Officer
- Alex Herrera. M.D., Chief, Division of Lymphoma, Department of Hematology & Hematopoietic Cell Transplantation at The City of Hope

Dr. Chang will also present the 2024 Platform Vision at the 42nd Annual J.P. Morgan Healthcare Conference on Wednesday, January 10, 2024, at 8:15 a.m. Pacific Time. This event will be held in San Francisco at the Westin St. Francis.

Conference Call Details
Allogene will host a live conference call today at 2:00 p.m. Pacific Time / 5:00 p.m. Eastern Time to discuss the 2024 Vision for Allogene. If you would like the option to ask a question on the conference call, please use this link to register. Upon registering for the conference call, you will receive a personal PIN to access the call, which will identify you as the participant and allow you the option to ask a question.

JP Morgan Conference

A live audio webcast of the presentation will be made available on the Company's website at www.allogene.com under the Investors tab in the News and Events section.

Following these live audio webcasts, replays will be available on the Company's website for approximately 30 days. The materials presented will be available on the Allogene website.

About Cemacabtagene Ansegedleucel (Previously Known as ALLO-501A)
Cemacabtagene ansegedleucel, or cema-cel is a next generation anti-CD19 AlloCAR T™ investigational product for the treatment of large B cell lymphoma (LBCL). This product candidate is currently being studied in an ongoing potentially pivotal Phase 2 trial in relapsed/refractory (r/r) LBCL. The ALPHA3 pivotal Phase 2 trial in first line (1L) consolidation for the treatment of LBCL is expected to begin mid-2024. In June 2022, the U.S. Food and Drug Administration granted Regenerative Medicine Advanced Therapy (RMAT) designation to cema-cel in third line (3L) r/r LBCL.

About Allogene Therapeutics
Allogene Therapeutics, with headquarters in South San Francisco, is a clinical-stage biotechnology company pioneering the development of allogeneic chimeric antigen receptor T cell (AlloCAR T™) products for cancer and autoimmune disease. Led by a management team with significant experience in cell therapy, Allogene is developing a pipeline of “off-the-shelf” CAR T cell product candidates with the goal of delivering readily available cell therapy on-demand, more reliably, and at greater scale to more patients. For more information, please visit www.allogene.com, and follow @AllogeneTx on X (formerly Twitter) and LinkedIn.

Cautionary Note on Forward-Looking Statements for Allogene
This press release contains forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. The press release may, in some cases, use terms such as “predicts,” “projects,” “believes,” “potential,” “proposed," “continue,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “may,” “could,” “might,” “will,” “should” or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements include statements regarding intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things: ALPHA3 being a pivotal trial; the pace, timing and extent to which we may enroll patients in our clinical trials or release data from such trials; the timing and ability to progress the ALPHA2, EXPAND, ALPHA3 and TRAVERSE trials; the timing of filing Investigational New Drug applications relating to ALLO-329 and the progress and success of such clinical program; clinical outcomes, which may materially change as more patient data become available; the design and potential benefits of our Dagger™ technology including the ability to enhance engraftment, expansion and persistence of AlloCAR T cells, the ability to resist rejection of AlloCAR T cells by the host immune cells and the expected benefits therefrom, or the ability to reduce or eliminate the need for standard chemotherapy while targeting CD19+ B-cells and CD70+ activated T-cells in autoimmune disease, and our plans to deploy the Dagger™ technology; the potential for our product candidates to be approved; the potential benefits of AlloCAR T products; the ability of our product candidates to treat various stages and types of cancers including hematological and solid tumors or to treat autoimmune disease; our level of operating expenses and the extent of our cash runway; our ability to expand indications or therapeutic fields for our allogeneic CAR T product candidates; our ability to broaden patient access to CAR T therapy; the modes of action or the biologic impacts of our product candidates including the engraftment, expansion, persistence and efficacy of allogeneic CAR T cells, the ability of AlloCAR T cells from being recognized by host T cells without triggering an immune response, and the ability to selectively eliminate CD70 positive alloreactive host immune cells; the incidence, severity and manageability of side effects of allogeneic CAR T therapies; the extent to which our clinical trials will support regulatory approval of our product candidates; the extent to which and type of lymphodepletion strategies that may be required in conjunction with our product candidates; the potential for off-the-shelf CAR T products; our ability to deliver cell therapy on-demand, more reliably, and at greater scale to more patients. Various factors may cause material differences between Allogene’s expectations and actual results, including, risks and uncertainties related to: our product candidates are based on novel technologies, which makes it difficult to predict the time and cost of product candidate development and obtaining regulatory approval; the limited nature of our Phase 1 data from our clinical trials and the extent to which such data may or may not be validated in any future clinical trial; our product candidates may cause undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval or limit their commercial potential; the extent to which the Food and Drug Administration disagrees with our clinical or regulatory plans or the import of our clinical results, which could cause future delays to our clinical trials, including initiation of clinical trials, or require additional clinical trials; we may encounter difficulties enrolling patients in our clinical trials; we may not be able to demonstrate the safety and efficacy of our product candidates in our clinical trials, which could prevent or delay regulatory approval and commercialization; challenges with manufacturing or optimizing manufacturing of our product candidates; and our ability to obtain additional financing to develop our products and implement our operating plans. These and other risks are discussed in greater detail in Allogene’s filings with the SEC, including without limitation under the “Risk Factors” heading in its Annual Report on Form 10-K for the year ended December 31, 2022, and in its Quarterly Report on Form 10-Q for the quarter ended September 30, 2023. Any forward-looking statements that are made in this press release speak only as of the date of this press release. Allogene assumes no obligation to update the forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

AlloCAR T™ and Dagger™ are trademarks of Allogene Therapeutics, Inc.

Allogene’s investigational oncology products utilize TALEN ® gene-editing technology pioneered and owned by Cellectis. ALLO-501 and cemacabtagene ansegedleucel (previously known as ALLO-501A) are anti-CD19 AlloCAR T™ investigational products being developed under a collaboration agreement between Servier and Allogene based on an exclusive license granted by Cellectis to Servier. Servier grants to Allogene exclusive rights to ALLO-501 and cemacabtagene ansegedleucel in the U.S.

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[i] Tilly H, Morschhauser F, Sehn LH, Friedberg JW, et al. Polatuzumab Vedotin in Previously Untreated Diffuse Large B-Cell Lymphoma. N Engl J Med. 2022;386(4):351-363

Source: Allogene Therapeutics, Inc.