UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 16, 2022

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bluebird bio, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-35966**	**13-3680878**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

455 Grand Union Boulevard, Somerville, MA	**02145**
(Address of Principal Executive Offices)	**(Zip Code)**

(339) 499-9300
(Registrant's telephone number, including area code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instructions A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.01 par value per share	BLUE	The NASDAQ Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On September 16, 2022, bluebird bio, Inc. (the "Company") issued a press release regarding the Accelerated Approval of SKYSONA® (elivaldogene autotemcel), also known as eli-cel. A copy of the press release is attached as Exhibit 99.1.

The information contained in this item, including Exhibit 99.1 attached hereto, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On September 16, 2022, the Company announced that the U.S. Food and Drug Administration (the "FDA") has granted Accelerated Approval of SKYSONA to slow the progression of neurologic dysfunction in boys 4-17 years of age with early, active cerebral adrenoleukodystrophy ("CALD"). The Company has agreed to provide confirmatory long-term clinical data to the FDA as a condition of the SKYSONA Accelerated Approval, and continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

The Accelerated Approval of SKYSONA is based on data from the Company's Phase 2/3 study ALD-102 (Starbeam) (N=32) and Phase 3 study ALD-104 (N=35), and is based on 24-month Major Functional Disability ("MFD") free survival. A post-hoc enrichment analysis in symptomatic patients assessed MFD-free survival from onset of symptoms (neurologic function score ("NFS") $\geq$ 1) in SKYSONA treated (N=11) and untreated patients (N=7). SKYSONA treated patients had an estimated 72 percent likelihood of MFD-free survival at 24 months from time of first NFS $\geq$ 1, compared to untreated patients who had only an estimated 43 percent likelihood of MFD-free survival.

The SKYSONA Biologics License Application ("BLA") was reviewed by the FDA under priority review, and the Company received a rare pediatric priority review voucher upon approval. On September 15, 2022, prior to the completion of its review of the SKYSONA BLA, the FDA lifted the clinical hold on SKYSONA that was put in place in August 2021.

The Company anticipates that commercial product will be available by the end of 2022 through a limited number of Qualified Treatment Centers ("QTCs") in the United States, including Boston Children's Hospital and Children's Hospital of Philadelphia. The Company has set the wholesale acquisition cost of SKYSONA in the U.S. at $3.0 million.

Cautionary Statement Regarding Forward-Looking Statements

This Current Report on Form 8-K contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements, including statements regarding the availability of SKYSONA as a commercial product, including the availability at certain QTCs and the timing thereof. Such forward-looking statements are based on historical performance and current expectations and projections about the Company's future goals, plans and objectives and involve inherent risks, assumptions and uncertainties, including internal or external factors that could delay, divert or change any of them in the next several years, that are difficult to predict, may be beyond the Company's control and could cause its future goals, plans and objectives to differ materially from those expressed in, or implied by, the statements. No forward-looking statement can be guaranteed. Forward-looking statements in this Current Report on Form 8-K should be evaluated together with the many risks and uncertainties that affect the Company's business, particularly those identified in the risk factors discussion in the Company's Annual Report on Form 10-K for the year ended December 31, 2021, as updated by its subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. These risks and uncertainties include, but are not limited to: the risk that the efficacy and safety results from the Company's prior and ongoing clinical trials will not continue or be seen in the commercial treatment context; the risk that additional insertional oncogenic or other safety events associated with lentiviral vector, drug product, or myeloablation will be discovered or reported over time; the risk that the results of confirmatory studies may fail to support full approval of SKYSONA and, if not, additional studies may be required; the risk that the Company may not be able to obtain adequate price and reimbursement for any approved products, including the potential for delays or additional difficulties for SKYSONA in light of the FDA granting Accelerated Approval; the risk that the Company may encounter delays in the initiation of its commercial operations in the United States; the risk that the Company is not able to activate QTCs on the timeframe that we expect; the risk that the QTCs experience delays in their ability to enroll or treat patients; the risk that the Company experiences delays in establishing operational readiness across its supply chain following approval to support treatment in the commercial context; and the risk that any one or more of the Company's product candidates will not be successfully developed, approved by the FDA or commercialized. The forward-looking statements included in this Current Report on Form 8-K are made only as of the date

hereof and except as otherwise required by applicable law, the Company undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release of bluebird bio, Inc. dated September 16, 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: September 19, 2022

bluebird bio, Inc.

By: /s/ Helen C. Fu

Name: Helen C. Fu

Title: Senior Vice President, General Counsel and Secretary

Exhibit 99.1

bluebird bio Receives FDA Accelerated Approval for SKYSONA® Gene Therapy for Early, Active Cerebral Adrenoleukodystrophy (CALD)

SKYSONA is the first FDA approved therapy shown to slow the progression of neurologic dysfunction in boys with this devastating and fatal neurodegenerative disease

Management team to host conference call Monday, September 19, at 8:00 a.m. ET

SOMERVILLE, Mass.-- Sept. 16, 2022-- bluebird bio, Inc. (Nasdaq: BLUE) today announced the U.S. Food and Drug Administration (FDA) has granted Accelerated Approval of SKYSONA® (elivaldogene autotemcel), also known as eli-cel, to slow the progression of neurologic dysfunction in boys 4-17 years of age with early, active cerebral adrenoleukodystrophy (CALD). The Company also confirmed that the previous clinical hold on the eli-cel clinical development program has been lifted.

CALD is a rare, progressive, neurodegenerative disease that primarily affects young boys and causes irreversible, devastating neurologic decline, including major functional disabilities such as loss of communication, cortical blindness, requirement for tube feeding, total incontinence, wheelchair dependence, or complete loss of voluntary movement. Nearly half of patients who do not receive treatment die within five years of symptom onset. Prior to the approval of SKYSONA treatment, effective options were limited to allogeneic hematopoietic stem cell transplant (allo-HSCT), which is associated with the risk of serious potential complications including death, that can increase dramatically in patients without a human leukocyte antigen (HLA) matched donor.

“Children with CALD and their families have been at the heart of bluebird’s mission since the company was founded more than a decade ago,” said Andrew Obenshain, chief executive officer, bluebird bio. “For the ALD community, this long-awaited approval represents significant hope and offers families a new option where, for many, there had been none. We are grateful to every individual who was involved in the development of SKYSONA and are committed to working with providers and payers to make this important treatment option available to patients and their families.”

“The agony of watching your child slip away is something no parent should have to bear,” said Elisa Seeger, co-founder, ALD Alliance. “We have made significant strides in providing children diagnosed with CALD the best chance at life with early identification of ALD through expanded newborn screening. Yet with limited treatment options, early diagnosis is still cause for despair instead of hope for many families. Today, parents whose boys receive a CALD diagnosis can have renewed hope for the future.”

“CALD strikes young boys in the prime of their development, robbing them of core neurologic functions necessary for survival. That is an unimaginable reality for any parent, and as a clinician, it is heartbreaking to have limited treatment options for these children and their families,” said David A. Williams, MD, Chief, Division of Hematology/Oncology, Boston Children’s Hospital[i]. “After supporting the clinical development of SKYSONA for nearly a decade as a study site, Boston Children’s Hospital is extremely pleased that an FDA-approved therapy is now available for children who urgently need new therapies.”

“As one of the largest and most experienced pediatric gene therapy and stem cell transplant programs in the world, the University of Minnesota is committed to expanding access and advancing care and research for patients with rare diseases like ALD,” said Paul Orchard, MD, a pediatric blood and marrow transplant physician at the University of Minnesota Medical School and M Health Fairview Masonic Children’s Hospital. “It’s crucial for these patients and families to have another therapeutic option for cerebral ALD beyond blood stem cell transplantation utilizing cells from another donor, and we’ve seen

firsthand the impact that gene therapy has on our patients. We are encouraged by progress we're making to treat these rare and devastating diseases."

As a condition of the SKYSONA Accelerated Approval, bluebird has agreed to provide confirmatory long-term clinical data to the FDA. bluebird anticipates that this will include data from the ongoing long-term follow-up study (LTF-304), which follows patients treated in clinical trials for 15 years, and from commercially treated patients.

bluebird anticipates that commercial product will be available by the end of 2022 through a limited number of Qualified Treatment Centers (QTCs) in the United States, including Boston Children's Hospital and Children's Hospital of Philadelphia.

bluebird has set the wholesale acquisition cost of SKYSONA in the U.S. at $3.0M. Additional information is available through bluebird's patient support program, *my bluebird support*, which will provide personalized support for patients and their families related to all aspects of the gene therapy journey. Caregivers of patients with CALD can visit mybluebirdsupport.com or call 833-888-NEST (833-888-6378) Monday-Friday between 8 a.m. and 8 p.m. ET to ask questions and enroll.

The SKYSONA Biologics License Application (BLA) was reviewed by the U.S. FDA under Priority Review, and bluebird received a rare pediatric priority review voucher upon approval. SKYSONA was previously granted Orphan Drug designation, Rare Pediatric Disease designation, and Breakthrough Therapy designation.

SKYSONA Clinical Data
The approval of SKYSONA is based on data from bluebird bio's Phase 2/3 study ALD-102 (Starbeam) (N=32) and Phase 3 ALD-104 (N=35) study.

Both open-label, single-arm studies enrolled patients with early, active CALD who had elevated very long chain fatty acid (VLCFA) values, a Loes score between 0.5 and 9 (inclusive), and gadolinium enhancement on magnetic resonance imaging (MRI) of demyelinating lesions. Additionally, patients were required to have a neurologic function score (NFS) of ≤ 1, indicating limited changes in neurologic function. The efficacy of SKYSONA was compared to a natural history population.

Per protocol, patients treated with SKYSONA were assessed using the NFS and monitored for the emergence of six Major Functional Disabilities (MFDs) associated with CALD progression including loss of communication, cortical blindness, requirement for tube feeding, total incontinence, wheelchair dependence, or complete loss of voluntary movement.

The Accelerated Approval of SKYSONA is based on 24-month MFD-free survival. A post-hoc enrichment analysis in symptomatic patients assessed MFD-free survival from onset of symptoms (NFS ≥ 1) in SKYSONA treated (N=11) and untreated patients (N=7). SKYSONA treated patients had an estimated 72 percent likelihood of MFD-free survival at 24 months from time of first NFS ≥ 1, compared to untreated patients who had only an estimated 43 percent likelihood of MFD-free survival.

The most common non-laboratory adverse reactions (incidence ≥ 20%) are mucositis, nausea, vomiting, febrile neutropenia, alopecia, decreased appetite, abdominal pain, constipation, pyrexia, diarrhea, headache, and rash. The most common Grade 3 or 4 laboratory abnormalities (≥40%) include leukopenia, lymphopenia, thrombocytopenia, neutropenia, anemia, and hypokalemia. Please see SKYSONA Important Safety Information below, including a **Boxed Warning** for Hematologic Malignancy.

Enrollment is complete and all patients have been treated in both studies; follow-up in ALD-104 is ongoing. All patients who complete 24 months of follow-up in studies ALD-102 or ALD-104 are

encouraged to participate in a long-term follow-up study (LTF-304) to continue monitoring safety and efficacy outcomes in boys treated with SKYSONA through 15 years post-treatment. On September 15, 2022, the FDA lifted the clinical hold that was put in place August 2021, prior to the completion of its review of the SKYSONA Biologics License Application.

About Cerebral Adrenoleukodystrophy (CALD)
CALD is a progressive and irreversible neurodegenerative disease that primarily affects young boys. The disorder is caused by mutations in the *ABCD1* gene that affect the production of adrenoleukodystrophy protein (ALDP) and subsequently leads to accumulation of very long-chain fatty acids (VLCFAs), primarily in the white matter of the brain and spinal cord. This accumulation leads to the breakdown of myelin, the protective sheath that nerve cells need to function effectively, especially for thinking and muscle control. The onset of symptoms of CALD typically occurs in childhood (median age 7). Early diagnosis and treatment of CALD is essential, as nearly half of patients who do not receive treatment die within five years of symptom onset.

Indication
SKYSONA is indicated to slow the progression of neurologic dysfunction in boys 4-17 years of age with early, active cerebral adrenoleukodystrophy (CALD). Early, active cerebral adrenoleukodystrophy refers to asymptomatic or mildly symptomatic (neurologic function score, NFS ≤ 1) boys who have gadolinium enhancement on brain magnetic resonance imaging (MRI) and Loes scores of 0.5-9.

This indication is approved under accelerated approval based on 24-month Major Functional Disability (MFD)- free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Limitations of Use

SKYSONA does not prevent the development of or treat adrenal insufficiency due to adrenoleukodystrophy.

An immune response to SKYSONA may limit the persistence of descendent cells of SKYSONA, causing rapid loss of efficacy of SKYSONA in patients with full deletions of the human adenosine triphosphate binding cassette, sub family D, member 1 (ABCD1) transgene.

SKYSONA has not been studied in patients with CALD secondary to head trauma.

Given the risk of hematologic malignancy with SKYSONA, and unclear long-term durability of SKYSONA and human adrenoleukodystrophy protein (ALDP) expression, careful consideration should be given to the appropriateness and timing of treatment for each boy, especially for boys with isolated pyramidal tract disease based on available treatment options since their clinical symptoms do not usually occur until adulthood.

Important Safety Information

BOXED WARNING: HEMATOLOGIC MALIGNANCY
Hematologic malignancy, including life-threatening cases of myelodysplastic syndrome, has occurred in patients treated with SKYSONA. Patients have been diagnosed between 14 months and 7.5 years after SKYSONA administration, and the cancers appear to be the result of the SKYSONA lentiviral vector, Lenti-D, integration in proto-oncogenes. Monitor patients closely for evidence of malignancy through complete blood counts at least every 6 months and through assessments for evidence for clonal expansion or predominance at least twice in the first year and annually thereafter; consider bone marrow evaluations as clinically indicated.

Hematologic Malignancy
Myelodysplastic syndrome (MDS), a hematologic malignancy, has developed in patients treated with SKYSONA in clinical studies. At the time of initial product approval, MDS had been diagnosed in three patients after administration of SKYSONA. The clinical presentation for the three patients varied. Two patients who were diagnosed at 14 months and 2 years after treatment with SKYSONA had preceding delayed platelet engraftment. The third patient had normal blood counts from 18 months to 5 years following treatment with SKYSONA and presented 7.5 years after SKYSONA administration with symptomatic anemia and thrombocytopenia and was subsequently diagnosed with MDS with increased blasts. All 3 patients underwent allogeneic hematopoietic stem cell transplant; 1 patient required pre-transplant chemotherapy and total body irradiation as treatment for excess blasts prior to transplant and 1 patient underwent total body irradiation as part of his conditioning regimen.

SKYSONA Lenti-D lentiviral vector integration into proto-oncogenes appears to have mediated the three cases of hematologic malignancy. The hematologic malignancies diagnosed at 14 months and 2 years involved integration into the *MECOM* proto-oncogene and increased expression of the oncoprotein EVI1. All patients treated with SKYSONA in clinical studies have integrations into *MECOM*; it is unknown which integrations into *MECOM* or other proto-oncogenes are likely to lead to malignancy.

Because of the risk of hematologic malignancy, carefully consider alternative therapies prior to the decision to treat a child with SKYSONA. Consider consultation with hematology experts prior to SKYSONA treatment to inform benefit-risk treatment decision and to ensure adequate monitoring for hematologic malignancy. Consider performing the following baseline hematologic assessments: complete blood count with differential, hematopathology review of peripheral blood smear, and bone marrow biopsy (core and aspirate) with flow cytometry, conventional karyotyping, and next generation sequencing (NGS) with a molecular panel appropriate for age and including coverage for gene mutations expected in myeloid and lymphoid malignancies; and testing for germline mutations that are associated with hematologic malignancy.

Early diagnosis of hematologic malignancy can be critically important, therefore, monitor patients treated with SKYSONA lifelong for hematologic malignancy. For the first fifteen years after treatment with SKYSONA, monitor via complete blood count (with differential) at least twice per year and via integration site analysis or other testing for evidence of clonal expansion and predominance at least twice in the first year and then annually. Consider appropriate expert consultation and additional testing such as more frequent complete blood count (with differential) and integration site analysis, bone marrow studies, and gene expression studies in the following settings after treatment with SKYSONA:

- Delayed or failed engraftment of platelets or other cell lines (patients who do not achieve unsupported platelet counts of $\geq 20 \times 10^9$/L on or after Day 60 appear to be at particularly high risk for developing malignancy); or
- New or prolonged cytopenias; or,
- Presence of clonal expansion or predominance (e.g., increasing relative frequency of an integration site, especially if ≥ 10% and present in *MECOM* or another proto-oncogene known to be involved in hematologic malignancy).

If hematologic malignancy is detected in a patient who received SKYSONA, contact bluebird bio at 1 833 999 6378 for reporting and to obtain instructions on collection of samples for further testing.

Serious Infections
Severe infections, including life-threatening or fatal infections, have occurred in patients after SKYSONA infusion. Important opportunistic infections that have been diagnosed within the first 3 months after treatment with SKYSONA include BK cystitis, cytomegalovirus reactivation, human herpesvirus-6 viremia,

candidiasis, and bacteremias. Opportunistic infections after the first 3 months include an atypical mycobacterium vascular device infection, pseudomonas bacteremia, and Epstein-Barr virus reactivations diagnosed as late as 18 months after treatment with SKYSONA. Serious infections involving adenovirus include a case of transverse myelitis at 6 months that was attributed to adenovirus and entero/rhinovirus infection, and a fatal adenovirus infection at 21 months in a patient with CALD progression who developed multisystem organ failure.

Grade 3 or higher infections occurred in 21% of all patients (12% bacterial, 3% viral, and 6% unspecified). The most common Grade 3 or higher infections were vascular device infections (7% of patients) diagnosed as late as 6 months after treatment with SKYSONA, and bacteremias (6% of patients) diagnosed as late as 8 months after treatment with SKYSONA.

Febrile neutropenia developed within two weeks after SKYSONA infusion in 72% of patients. In the event of febrile neutropenia, evaluate for infection and manage with broad-spectrum antibiotics, fluids, and other supportive care as medically indicated.

Monitor patients for signs and symptoms of infection before and after SKYSONA administration and treat appropriately. Administer prophylactic antimicrobials according to best clinical practices and clinical guidelines.

Avoid administration of SKYSONA in patients with active infections.

Prolonged Cytopenias
Patients may exhibit cytopenias, including pancytopenia, for > 1 year following conditioning and SKYSONA infusion.

Grade 3 or higher cytopenias on or after Day 60 following SKYSONA infusion occurred in 47% of patients and included low platelet count (14%), low neutrophil count (22%), low lymphocyte count (27%), and low hemoglobin (2%). Grade 3 cytopenias persisted beyond Day 100 in 15% of patients and included low platelet count (7%), low neutrophil count (9%), and low lymphocyte count (6%).

Serious adverse reactions of pancytopenia occurred in two patients who required support with blood and platelet transfusions as well as growth factors (G-CSF for up to 6 months and eltrombopag for up to 14 months) after SKYSONA administration. One patient had intercurrent parvovirus infection and his pancytopenia was ongoing at least two years after SKYSONA administration. Pancytopenia in the other patient was ongoing until he was diagnosed with myelodysplastic syndrome approximately two years after SKYSONA administration.

Monitor blood counts until normalization and assess patients for signs and symptoms of bleeding and/or infection prior to and after SKYSONA administration.

Delayed Platelet Engraftment
Delayed platelet engraftment has been observed with SKYSONA. Bleeding risk is increased prior to platelet engraftment and may continue after engraftment in patients with prolonged thrombocytopenia; 14% of patients had a platelet count ≤ 50×10^9/L beyond 60 days after treatment with SKYSONA.

Patients should be made aware of the risk of bleeding until platelet recovery has been achieved. Monitor patients for thrombocytopenia and bleeding according to standard guidelines. Conduct frequent platelet counts until platelet engraftment and platelet recovery are achieved. Perform blood cell count determination and other appropriate testing whenever clinical symptoms suggestive of bleeding arise.

Risk of Neutrophil Engraftment Failure
There is a potential risk of neutrophil engraftment failure after treatment with SKYSONA. Neutrophil engraftment failure was defined as failure to achieve 3 consecutive absolute neutrophil counts (ANC) ≥ 0.5×10^9 cells/L obtained on different days by Day 43 after infusion of SKYSONA. Monitor neutrophil counts until engraftment has been achieved. If neutrophil engraftment failure occurs in a patient treated with SKYSONA, provide rescue treatment with the back-up collection of CD34+ cells.

Hypersensitivity Reactions
Allergic reactions may occur with the infusion of SKYSONA. The dimethyl sulfoxide (DMSO) in SKYSONA may cause hypersensitivity reactions, including anaphylaxis which is potentially life-threatening and requires immediate intervention.

Anti-retroviral Use
Patients should not take anti-retroviral medications for at least one month prior to mobilization or the expected duration for elimination of the medications, and until all cycles of apheresis are completed. Anti-retroviral medications may interfere with manufacturing of the apheresed cells.

If a patient requires anti-retrovirals for HIV prophylaxis, mobilization and apheresis of CD34+ cells should be delayed until HIV infection is adequately ruled out.

Laboratory Test Interference
SKYSONA affects polymerase chain reaction (PCR) assays for HIV due to LVV provirus insertion. A PCR based assay should not be used to screen for HIV infection in patients treated with SKYSONA as a false positive test result is likely.

Adverse Reactions
Most common non-laboratory adverse reactions (≥ 20%): mucositis, nausea, vomiting, febrile neutropenia, alopecia, decreased appetite, abdominal pain, constipation, pyrexia, diarrhea, headache, rash.

Most common Grade 3 or 4 laboratory abnormalities (≥40%): leukopenia, lymphopenia, thrombocytopenia, neutropenia, anemia, hypokalemia.

Vaccines
Vaccination is not recommended during the 6 weeks preceding the start of myeloablative conditioning, and until hematological recovery following treatment with SKYSONA. Where feasible, administer childhood vaccinations prior to myeloablative conditioning for SKYSONA.

Males of Reproductive Potential
Advise patients of the risks associated with mobilization and conditioning agents.
Males capable of fathering a child and their female partners of childbearing potential should use an effective method of contraception (intra uterine device or combination of hormonal and barrier contraception) from start of mobilization through at least 6 months after administration of SKYSONA.

Data are available on the risk of infertility with myeloablative conditioning. Advise patients of the option to cryopreserve semen before treatment if appropriate.

Please see full Prescribing Information for SKYSONA, including **BOXED WARNING** and Medication Guide.

Investor Conference Call Information
bluebird bio will host a call for analysts and investors on Monday, September 19, 2022, at 8:00 a.m. ET. Please note that there is a new process to access the call via telephone. To register online and receive a

dial in number and unique PIN to access the live conference call, please follow this link https://register.vevent.com/register/BI6661b71df881495eb2148380462a257c.

The live webcast of the call may be accessed by visiting the "Events & Presentations" page within the Investors & Media section of the bluebird website at http://investor.bluebirdbio.com. A replay of the webcast will be available on the bluebird website for 90 days following the event.

About SKYSONA® (elivaldogene autotemcel), also known as eli-cel
SKYSONA is a one-time gene therapy custom-designed to treat the underlying cause of cerebral adrenoleukodystrophy (CALD). SKYSONA uses *ex-vivo* transduction with the Lenti-D lentiviral vector (LVV) to add functional copies of the *ABCD1* gene into a patient's own hematopoietic stem cells (HSCs). The addition of the functional *ABCD1* gene allows patients to produce the ALD protein (ALDP), which can then participate in the local degradation of very long-chain fatty acids (VLCFAs). This degradation of VLCFAs is believed to slow or possibly prevent further inflammation and demyelination.

About bluebird bio, Inc.
bluebird bio is pursuing curative gene therapies to give patients and their families more bluebird days. With a dedicated focus on severe genetic diseases, bluebird has industry-leading clinical and research programs for sickle cell disease, beta-thalassemia and cerebral adrenoleukodystrophy and is advancing research to apply new technologies to these and other diseases. We custom design each of our therapies to address the underlying cause of disease and have developed in-depth and effective analytical methods to understand the safety of our lentiviral vector technologies and drive the field of gene therapy forward.

Founded in 2010, bluebird has the largest and deepest *ex-vivo* gene therapy data set in the world—setting the standard for industry. Today, bluebird continues to forge new paths, combining our real-world experience with a deep commitment to patient communities and a people-centric culture that attracts and grows a diverse flock of dedicated birds.

For more information, visit **bluebirdbio.com** or follow us on social media at **@bluebirdbio**, **LinkedIn**, **Instagram** and **YouTube**.

SKYSONA and bluebird bio are trademarks of bluebird bio, Inc.

bluebird bio Cautionary Statement Regarding Forward-Looking Statements
This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements, including statements regarding the satisfaction of the post-marketing requirement to provide confirmatory data on SKYSONA, the timing of availability of SKYSONA as a commercial product, including the availability at certain QTCs, and the availability of services offered by the *my bluebird support* program to support patient treatment. Such forward-looking statements are based on historical performance and current expectations and projections about our future goals, plans and objectives and involve inherent risks, assumptions and uncertainties, including internal or external factors that could delay, divert or change any of them in the next several years, that are difficult to predict, may be beyond our control and could cause our future goals, plans and objectives to differ materially from those expressed in, or implied by, the statements. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many risks and uncertainties that affect bluebird bio's business, particularly those identified in the risk factors discussion in bluebird bio's Annual Report on Form 10-K for the year ended December 31, 2021, as updated by our subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. These risks and uncertainties include, but are not limited to: the risk that the efficacy and safety results from our prior and ongoing clinical trials will not continue or be seen in the commercial treatment context; the risk that additional

insertional oncogenic or other safety events associated with lentiviral vector, drug product, or myeloablation will be discovered or reported over time; the risk that the results of ongoing or future studies, including LTF-304, may fail to support full approval of SKYSONA and, if not, additional studies may be required; the risk that we may not be able to obtain adequate price and reimbursement for any approved products; the risk that we may encounter delays in the initiation of our commercial operations in the United States; the risk that we are not able to activate QTCs on the timeframe that we expect; the risk that the QTCs experience delays in their ability to enroll or treat patients; the risk that we experience delays in establishing operational readiness across our supply chain following approval to support treatment in the commercial context; and the risk that any one or more of our product candidates will not be successfully developed, approved by the FDA or commercialized. The forward-looking statements included in this press release are made only as of the date of this press release and except as otherwise required by applicable law, bluebird bio undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise.

Investors:
Courtney O'Leary, 978-621-7347
coleary@bluebirdbio.com

Media:
Jess Rowlands, 857-299-6103
jess.rowlands@bluebirdbio.com

# # #

[i] Dr. David Williams, Chief of Hematology/Oncology at Boston Children's Hospital served as a Principal Investigator for SKYSONA clinical studies. He has consulted for bluebird bio but has not consulted for the SKYSONA (also known as eli-cel) technology.