IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

TOOLGEN, INC., Plaintiff, v. VERTEX PHARMACEUTICALS, INC., VERTEX PHARMACEUTICALS (CANADA) INCORPORATED, VERTEX PHARMACEUTICALS (EUROPE) LIMITED, VERTEX PHARMACEUTICALS (IRELAND) LIMITED, CRISPR THERAPEUTICS AG, CRISPR THERAPEUTICS INC., LONZA GROUP AG, LONZA NETHERLANDS B.V., ROSLIN CELL THERAPIES LIMITED, ROSLINCT US HOLDINGS, LLC, CHARLES RIVER LABORATORIES INC., AND BIOMAY AG Defendants.	)	Civ.A.No.: _____ **JURY TRIAL DEMANDED**

COMPLAINT

ToolGen, Inc. ("ToolGen"), by its attorneys, hereby alleges as follows:

NATURE OF THE ACTION

1. This is a patent infringement action arising under Title 35 of the United States Code and concerning infringement by Vertex Pharmaceuticals, Inc., Vertex Pharmaceuticals (Canada) Incorporated, Vertex Pharmaceuticals (Europe) Limited, Vertex Pharmaceuticals (Ireland) Limited, CRISPR Therapeutics AG, CRISPR Therapeutics Inc., Lonza Group AG, Lonza Netherlands B.V., Roslin Cell Therapies Limited, RoslinCT US Holdings, LLC, Charles River Laboratories Inc., and Biomay AG (collectively, "Defendants") under 35 U.S.C. §§ 271(a), 271(b), 271(c), and 271(g) of ToolGen's patent by engaging in the commercial manufacture, use,

sale, offer for sale, and/or importation of CASGEVY® ("Casgevy®") prior to the expiration of ToolGen's U.S. Patent No. 12,473,559 ("the '559 patent").

PARTIES

A. ToolGen

2. ToolGen is a corporation organized and existing under the laws of the Republic of Korea, having a principal place of business at 8F, 172, Magokjungang-ro, Gangseo-gu, Seoul, Republic of Korea.

3. ToolGen is a leading biotechnology company committed to developing more efficient and precise genome editing technologies. ToolGen was founded in 1999 by Dr. Jin-Soo Kim, a renowned scientist in the field of genome editing. ToolGen leads the genome editing industry having successfully developed zinc-finger nucleases ("ZFNs"), transcription activator-like effector nucleases ("TALENs"), and clustered regularly interspaced short palindromic repeats ("CRISPR")-CRISPR-associated protein 9 ("Cas9") platform technologies. ToolGen's genome editing technologies are employed across the globe for genome editing in human cells, model organisms, livestock, and plants.

4. In the genome editing community, ToolGen's work is recognized as the first successful demonstration of the direct introduction of the CRISPR Cas9 complex (also known as a ribonucleoprotein, or RNP) into cells, which includes Cas9 in its protein form. This approach avoids the cellular toxicity often associated with DNA- and mRNA-based systems and eliminates the risk of foreign DNA integration into the genome. With its significantly lower off-target effects providing superior safety profiles, the method developed by the inventors at ToolGen has become the standard protocol that is widely used today in therapeutic development as well as in

plant and animal genome editing. Defendants have also applied this method in the manufacture of Casgevy®.

B. Defendants

5. On information and belief, Vertex Pharmaceuticals, Inc. ("Vertex Inc.") is a corporation organized and existing under the laws of Massachusetts, having a registered agent for the service of process at Corporation Services Co., 84 State Street, Boston, Massachusetts 02109, and having a principal place of business at 50 Northern Avenue, Boston, Massachusetts 02210.

6. On information and belief, Vertex Pharmaceuticals (Canada), Incorporated ("Vertex Canada") is a corporation organized and existing under the laws of Canada having a registered office address at 20 Bay Street, Suite 1520, Toronto, Ontario M5J 2N8, Canada. On information and belief, Vertex Canada is a wholly owned subsidiary of Vertex Pharmaceuticals (Delaware), LLC. On information and belief, Vertex Pharmaceuticals (Delaware), LLC is a wholly owned subsidiary of Vertex Inc. On information and belief, Vertex Canada shares directors with Vertex Inc. including Charles Wagner Jr., Executive Vice President and Chief Operating & Financial Officer at Vertex Inc., and Jonathan Biller, Executive Vice President and Chief Legal Officer at Vertex Inc.

7. On information and belief, Vertex Pharmaceuticals (Europe), Limited ("Vertex Europe") is a corporation organized and existing under the laws of the United Kingdom having a registered office address at 2 Kingdom Street, London, England, W2 6BD. On information and belief, Vertex Europe is a wholly owned subsidiary of Vertex Pharmaceuticals (Cayman) Limited. On information and belief, Vertex Pharmaceuticals (Cayman) Limited is a wholly owned subsidiary of Vertex Pharmaceuticals UK Holdings Limited. On information and belief,

Vertex Pharmaceuticals UK Holdings Limited is a wholly owned subsidiary of Vertex Holdings, Inc. On information and belief, Vertex Holdings, Inc. is a wholly owned subsidiary of Vertex Inc.

8. On information and belief, Vertex Pharmaceuticals (Ireland), Limited ("Vertex Ireland") is a corporation organized and existing under the laws of Ireland having a registered office address at Unit 49, Block 5, Northwood Court, Northwood Crescent, Dublin 9 D09 T665, Ireland. On information and belief, Vertex Ireland is a wholly owned subsidiary of Vertex Europe. On information and belief, Vertex Europe is a wholly owned subsidiary of Vertex Pharmaceuticals (Cayman) Limited. On information and belief, Vertex Pharmaceuticals (Cayman) Limited is a wholly owned subsidiary of Vertex Pharmaceuticals UK Holdings Limited. On information and belief, Vertex Pharmaceuticals UK Holdings Limited is a wholly owned subsidiary of Vertex Holdings, Inc. On information and belief, Vertex Holdings, Inc. is a wholly owned subsidiary of Vertex Inc.

9. On information and belief, CRISPR Therapeutics AG ("CRISPR AG") is a corporation organized and existing under the laws of Switzerland having a principal place of business at Baarerstrasse 14, Zug V8 CH-6300, Switzerland.

10. On information and belief, CRISPR Therapeutics Inc. ("CRISPR Inc.") is a corporation organized and existing under the laws of the State of Delaware, having a registered agent for the service of process at The Corporation Trust Company, Corporation Trust Center 1209 Orange Street, Wilmington, Delaware 19801, and having a principal place of business at 105 West First Street, South Boston, Massachusetts 02127. On information and belief, CRISPR Inc. is a wholly owned subsidiary of CRISPR AG.

11. On information and belief, Lonza Group AG ("Lonza AG") is a corporation organized and existing under the laws of Switzerland, having a principal place of business at Münchensteinerstrasse 38, Basel 4002, Switzerland.

12. On information and belief, Lonza Netherlands B.V. ("Lonza BV") is a corporation organized and existing under the laws of the Netherlands, having a principal place of business at Urmonderbaan 20-B, 6167 RD Geleen, Netherlands. On information and belief, Lonza BV is a wholly owned subsidiary of Lonza AG.

13. On information and belief, Roslin Cell Therapies Limited ("RoslinCT") is a corporation organized and existing under the laws of Scotland, having a principal place of business at Nine Edinburgh Bioquarter, 9 Little France Road, Edinburgh, Scotland EH16 4UX.

14. On information and belief, RoslinCT US Holdings, LLC ("RoslinCT US") is a corporation organized and existing under the laws of the State of Delaware, having a registered agent for the service of process at The Corporation Trust Company, Corporation Trust Center 1209 Orange Street, Wilmington, Delaware 19801, and having a principal place of business at 97 South Street, Hopkinton, Massachusetts 01748. On information and belief, RoslinCT US is a wholly owned subsidiary of RoslinCT.

15. On information and belief, Charles River Laboratories Inc. ("Charles River") is a corporation organized and existing under the laws of the State of Delaware, having a registered agent for the service of process at The Corporation Service Company, 251 Little Falls Drive, Wilmington, Delaware 19808, and a principal place of business at 251 Ballardvale Street, Wilmington, Massachusetts 01887.

16. On information and belief, Biomay AG ("Biomay") is a corporation organized and existing under the laws of Austria, having a principal place of business Ada-Lovelace-Straße 2, 1220 Wien, Austria.

JURISDICTION AND VENUE

17. This Court has jurisdiction over the subject matter of this action under 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

18. This Court has personal jurisdiction over Vertex Inc., Vertex Canada, Vertex Europe, Vertex Ireland, CRISPR AG, CRISPR Inc., Lonza AG, Lonza BV, Roslin CT, RoslinCT US, Charles River, and Biomay, because, on information and belief, each such Defendant has committed and will further commit or has aided, abetted, contributed to and participated in, and will further aid, abet, contribute to, or participate in, past and future tortious acts of patent infringement that are or will be purposefully directed at Massachusetts, including commercial activities for the infringing product in Massachusetts.

19. This Court also has personal jurisdiction over Vertex Inc., CRISPR Inc., RoslinCT US, and Charles River because each such Defendant's contacts with the State of Massachusetts, including Vertex Inc.'s incorporation in Massachusetts and CRISPR Inc., RoslinCT US, and Charles River's principal places of business in Massachusetts, are sufficiently continuous and systematic as to render each such Defendant essentially at home in this forum.

20. For these reasons, and for other reasons that will be presented to the Court if jurisdiction is challenged, this Court has personal jurisdiction over each Defendant.

21. Venue is proper for each Defendant in this Court because Vertex Inc. is incorporated in the Commonwealth of Massachusetts, and CRISPR Inc., RoslinCT US, and Charles River have principal places of business in the State of Massachusetts and have

committed infringing acts in Massachusetts and therefore reside in this judicial district, and because Vertex Canada, Vertex Europe, Vertex Ireland, CRISPR AG, Lonza AG, Lonza BV, RoslinCT, and Biomay are foreign entities who may be sued in any judicial district, including the District of Massachusetts. 28 U.S.C. § 1400(b); 28 U.S.C. §§ 1391(c)(2), 1391(c)(3).

THE PATENT-IN-SUIT

22. ToolGen Inc. is the owner of all right, title, and interest in the ’559 patent, titled “Cas9/RNA Complexes for Inducing Modifications of Target Endogenous Nucleic Acid Sequences in Nucleuses of Eukaryotic Cells.” The ’559 patent was duly and legally issued on November 18, 2025. A true and correct copy of the ’559 patent is attached hereto as Exhibit 1.

23. The ’559 patent claims, *inter alia*, a method of inducing a modification of a target endogenous nucleic acid sequence in a nucleus of a human cell, comprising: (i) preparing a Cas9 protein, wherein the Cas9 protein comprises a nuclear localization signal (NLS); (ii) preparing a single-guide RNA (sgRNA), wherein the sgRNA comprises a crRNA and a tracrRNA, wherein the sgRNA is transcribed *in vitro* or synthesized chemically, and wherein the target endogenous nucleic acid sequence includes a portion complementary to the crRNA of the sgRNA; (iii) providing a buffer in an *in vitro* environment; (iv) disposing the Cas9 protein into the buffer; (v) disposing the sgRNA into the buffer, wherein the sgRNA is disposed in at least a two-fold molar excess over the Cas9 protein in the buffer; (vi) allowing the Cas9 protein and the sgRNA to complex in the *in vitro* environment to form a Cas9/sgRNA complex; (vii) transfecting the Cas9/sgRNA complex into the human cell by electroporation, whereby the Cas9/sgRNA complex induces the modification of the target endogenous nucleic acid sequence in the nucleus of the human cell.

24. On information and belief, Defendants have knowledge of the ’559 patent and have had knowledge of the publication of the U.S. application for the ’559 patent (US 2024/0052356 (“the ’356 publication”)) on or about the date of its publication on February 15, 2024.[1] Plaintiff and certain of the Defendants are currently engaged in ongoing litigation in foreign jurisdictions regarding foreign patents related to the ’559 patent, including in the U.K., the Netherlands, and at the European Patent Office.

DEFENDANTS’ INFRINGEMENT OF THE PATENT-IN-SUIT

25. On information and belief, Vertex Inc. submitted to the U.S. Food & Drug Administration (“FDA”) BLA STN 125787 to manufacture exagamglogene autotemcel drug substance and drug product which is indicated for treatment of sickle cell disease (SCD) in patients 12 years of age or older with recurrent vaso-occlusive crises (VOCs) under the proprietary name Casgevy®. On information and belief, the FDA approved Vertex Inc.’s BLA STN 125787 on December 8, 2023.[2]

26. On information and belief, Vertex Inc. submitted to the FDA BLA STN 125785 to manufacture exagamglogene autotemcel drug substance and drug product which is indicated for treatment of patients aged 12 years and older with transfusion-dependent ß-thalassemia (TDT) under the proprietary name Casgevy®. On information and belief, the FDA approved Vertex Inc.’s BLA STN 125785 on January 16, 2024.

27. On information and belief, Vertex Inc. has acknowledged in its United States Securities and Exchange Commission (“SEC”) filings that it “enter[s] into exclusive and non-exclusive license agreements for proprietary third-party technology used in connection with [its]

[1] A corrected application was published on July 18, 2024.
[2] *FDA Approves First Gene Therapies to Treat Patients with Sickle Cell Disease, available at* https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease (December 8, 2023).

research activities" and that these "license agreements typically provide for the payment by [Vertex] of a license fee… milestone payments or royalties…." On information and belief, Vertex Inc. has entered into licenses to obtain access to patented technologies developed by others that Vertex Inc. has used in the development and manufacture of Casgevy®, including for example, entering into an agreement with Editas Medicine, Inc. for a non-exclusive sublicense to certain patents relating to CRISPR/Cas9 technology owned by the Broad Institute, Harvard University, and Massachusetts Institute of Technology.[3]

28. On information and belief, Vertex Inc. markets and sells Casgevy® in the United States.[4] On information and belief, Vertex Inc. has publicly identified at least four "Authorized Treatment Centers" located in Massachusetts at which Casgevy® is administered to patients.[5]

29. On information and belief, Vertex Inc., through its subsidiary Vertex Canada, has obtained regulatory approval to sell Casgevy® in Canada. On information and belief, the Casgevy® product sold in Canada is manufactured at two different manufacturing sites, including one in the United States.[6]

30. On information and belief, Vertex Inc., through its subsidiary Vertex Ireland, has obtained regulatory approval to sell Casgevy® in the European Union. On information and belief, the Casgevy® product sold in the European Union is manufactured at two different manufacturing sites, including one in the United States—Charles River's Memphis, Tennessee facility.[7]

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[3] *Vertex Pharmaceuticals, Inc. Form 10-K Annual Report* at 17, 55, F-22, *available at* https://investors.vrtx.com/static-files/09afd176-289e-4ad8-85c2-61431b647842.
[4] *Casgevy US Label*, *available at* https://pi.vrtx.com/files/uspi_exagamglogene_autotemcel.pdf (Revised September 2025); *Casgevy Website*, *available at* https://www.casgevy.com/.
[5] *Find an Authorized Treatment Center*, *available at* https://www.casgevyhcp.com/authorized-treatment-centers.
[6] *Summary Basis of Decision for Casgevy*, *available at* https://dhpp.hpfb-dgpsa.ca/review-documents/resource/SBD1739203842068 (February 8, 2025).
[7] *Casgevy Assessment Report* at 21, *available at* https://www.ema.europa.eu/en/documents/assessment-report/casgevy-epar-public-assessment-report_en.pdf (December 14, 2023).

31. On information and belief, Vertex Inc., through one or more of its subsidiaries, including Vertex Europe, has obtained regulatory approval to sell Casgevy® in additional jurisdictions, including the United Kingdom, the Kingdom of Saudi Arabia, the Kingdom of Bahrain, Switzerland, and the United Arab Emirates.[8]

32. On information and belief, Casgevy® is a cellular gene therapy consisting of autologous $CD34^+$ hematopoietic stem cells (HSCs) edited by CRISPR/Cas9-technology at the erythroid specific enhancer region of the *BCL11A* gene to reduce BCL11A expression in erythroid lineage cells, leading to increased fetal hemoglobin (HbF) protein production.[9]

33. On information and belief, Vertex Inc., Vertex Europe, CRISPR AG, and CRISPR Inc. "entered into a strategic research collaboration in 2015 focused on the use of CRISPR/Cas9 to discover and develop potential new treatments aimed at the underlying genetic causes of human disease …. Under an amended collaboration agreement, Vertex now leads global development, manufacturing and commercialization of [Casgevy®] and splits program costs and profits worldwide 60/40 with CRISPR Therapeutics."[10]

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[8] *Medicines & Healthcare Products Regulatory Agency, available at* https://products.mhra.gov.uk/search/?search=casgevy&page=1; *Casgevy Overview, European Medicines Agency, available at* https://www.ema.europa.eu/en/medicines/human/EPAR/casgevy (February 9, 2024); *European Commission Approves First CRISPR/Cas9 Gene-Edited Therapy, CASGEVY™ (exagamglogene autotemcel), for the Treatment of Sickle Cell Disease and Transfusion-Dependent Beta Thalassemia, available at* https://news.vrtx.com/news-releases/news-release-details/european-commission-approves-first-crisprcas9-gene-edited (February 13, 2024); *Vertex and CRISPR Therapeutics Announce Authorization of the First CRISPR/Cas9 Gene-Edited Therapy, CASGEVY™ (exagamglogene autotemcel), by the United Kingdom MHRA for the Treatment of Sickle Cell Disease and Transfusion-Dependent Beta Thalassemia, available at* https://news.vrtx.com/news-releases/news-release-details/vertex-and-crispr-therapeutics-announce-authorization-first (November 16, 2023); *CRISPR Therapeutics Provides Business Update and Reports Fourth Quarter and Full Year 2024 Financial Results, available at* https://ir.crisprtx.com/news-releases/news-release-details/crispr-therapeutics-provides-business-update-and-reports-12 (December 31, 2024).

[9] *Casgevy US Label* at Section 11, *available at* https://pi.vrtx.com/files/uspi_exagamglogene_autotemcel.pdf (Revised September 2025).

[10] *Vertex and CRISPR Therapeutics Announce Authorization of the First CRISPR/Cas9 Gene-Edited Therapy, CASGEVY™ (exagamglogene autotemcel), by the United Kingdom MHRA for the Treatment of Sickle Cell Disease and Transfusion-Dependent Beta Thalassemia, available at* https://investors.vrtx.com/news-releases/news-release-details/vertex-and-crispr-therapeutics-announce-authorization-first (November 16, 2023); *Strategic Collaboration, Option and License Agreement, available at*

34. On information and belief, Vertex Inc. engages and directs third parties, including the other Defendants, in the manufacture of Casgevy®.

35. On information and belief, Lonza AG entered into a commercial supply agreement with Vertex Inc. for the manufacture of Casgevy® on behalf of Vertex Inc. for the United States market. In particular, on information and belief, "[u]nder the terms of the agreement, Vertex will leverage Lonza's … experience in the commercial manufacture of cell therapy products. Lonza will manufacture CASGEVY® at the state-of-the-art cGMP cell therapy manufacturing facilities in Geleen (NL), with plans to expand to its Portsmouth (US) facility." On information and belief, Lonza AG received FDA approval for the commercial production of Casgevy® at its manufacturing site at Lonza BV in Geleen, Netherlands and manufactures Casgevy® at that location. On information and belief, Lonza AG plans to expand and/or has expanded its manufacture of Casgevy® to its Portsmouth, New Hampshire facility located in the United States.[11]

36. On information and belief, Charles River entered into a commercial supply agreement with Vertex Inc. for the manufacture of Casgevy® on behalf of Vertex Inc. for the

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https://www.sec.gov/Archives/edgar/data/875320/000087532016000067/vrtx10k_2015-exhibit106.htm; *Joint Development and Commercialization Agreement, available at* https://www.sec.gov/Archives/edgar/data/875320/000087532021000006/a10k_2020-exhibit106.htm; A*mendment No. 1 to the Amended and Restated Joint Development and Commercialization Agreement, available at* https://www.sec.gov/Archives/edgar/data/1674416/000095017023069892/crsp-ex10_1.htm; *Amended and Restated Joint Development and Commercialization Agreement, available at* https://www.sec.gov/Archives/edgar/data/875320/000087532021000027/a2021q210-qexhibit101.htm; *Non-Exclusive License Agreement, available at* https://www.sec.gov/Archives/edgar/data/1674416/000095017023009861/crsp-ex10_1.htm.

[11] *Lonza and Vertex Sign a Long-Term Commercial Supply Agreement for CASGEVY® (exagamglogene autotemcel), available at* https://www.lonza.com/news/2024-09-24-14-00 (September 24, 2024); *Vertex Presents Positive Long-Term Data On CASGEVY™ (exagamglogene autotemcel) at the American Society of Hematology (ASH) Annual Meeting and Exposition and Provides Program Update, available at* https://investors.vrtx.com/news-releases/news-release-details/vertex-presents-positive-long-term-data-casgevytm-0 (December 8, 2024); Lonza Group AG 2024 Annual Report at 53, *available at* https://www.lonza.com/investor-relations/-/media/EADB5E271BDC4B1A808DA9E80CB2C0B6.ashx; Lonza Group AG Earnings Call Transcript Q1 2025 (May 9, 2025) ("We see good progress in our collaboration with Vertex for CASGEVY, and we are ramping up production in our site in Geleen, the Netherlands, and expect our site in Portsmouth, U.S. to follow later this year."), *available at* https://www.roic.ai/quote/LZAGF/transcripts/2025/1.

United States market. On information and belief, Charles River has stated that it "receive[d] regulatory approval to manufacture CASGEVY" at its Memphis, Tennessee facility and is "working hand-in-hand with Vertex to manufacture [Casgevy®]" and "help bring this treatment to patients."[12]

37. On information and belief, RoslinCT entered into a commercial supply agreement with Vertex Inc. to "manufacture the first ever U.S. Food and Drug Administration (FDA) approved CRISPR-based gene therapy" for the United States market. In particular, on information and belief, "RoslinCT and Vertex have worked closely on an adaptive basis as Vertex progressed with its clinical and regulatory development to advance this world first therapeutic to patients …. Its state-of-the-art manufacturing facilities in Edinburgh, Scotland and Boston, US are purpose-built for cell therapy products."[13]

38. On information and belief, Biomay entered into a commercial supply agreement with Vertex Inc. for the preparation of recombinant nuclease Cas9 for use in gene editing therapies. In particular, on information and belief, Biomay has stated that it received "approval by the U.S. Food and Drug Administration (FDA) for the manufacturing, testing and release of recombinant Cas9 nuclease from its headquarters site. Cas9 is an essential component of CRISPR-based gene editing therapies, including CASGEVY® (exagamglogene autotemcel) developed and launched by Vertex Pharmaceuticals."[14]

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[12] *Charles River and Vertex Pharmaceuticals Reach Important Milestone in Cell Therapy Manufacturing Collaboration, available at* https://ir.criver.com/news-releases/news-release-details/charles-river-and-vertex-pharmaceuticals-reach-important (December 13, 2023).

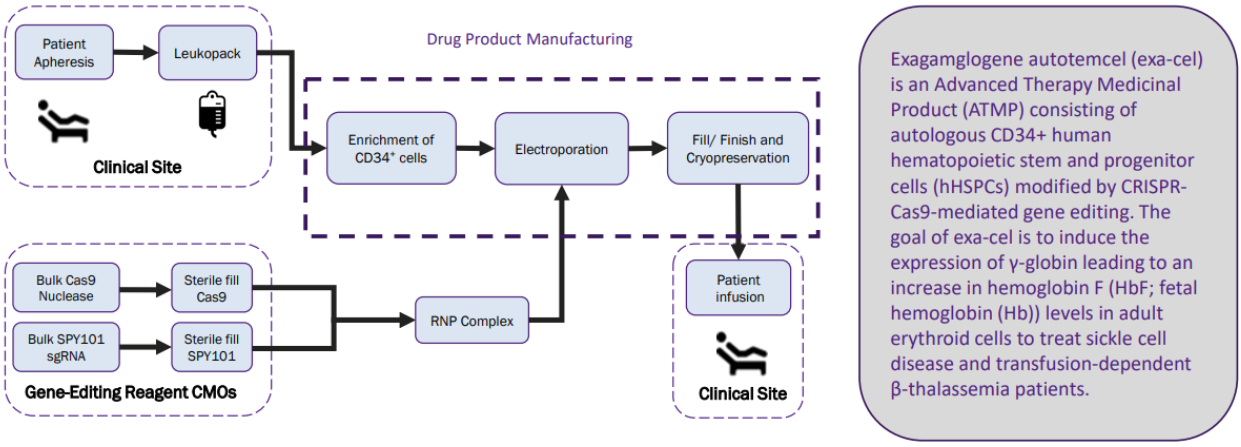
[13] *RoslinCT to manufacture first-ever US FDA approved CRISPR-based gene therapy CASGEVY™ (exagamglogene autotemcel), available at* https://www.roslinct.com/insights/roslinct-to-manufacture-first-ever-us-fda-approved-crispr-based-gene-therapy-casgevy-exagamglogene-autotemcel/ (December 11, 2023).

[14] *Biomay Obtains FDA Approval for Manufacturing of Cas9 Nuclease at Headquarters Site, available at* https://www.biomay.com/biomay-obtains-fda-approval-for-manufacturing-of-cas9-nuclease/ (April 28, 2025); *Biomay Announces its Successful Support of Approval of First CRISPR/Cas9-based Therapy, available at* https://www.biomay.com/biomay-successful-support-approval-crispr-cas9-therapy/ (January 25, 2024).

39. On information and belief, a third-party Contract Manufacturing Organization ("CMO") prepares the SPY101 sgRNA used in the manufacture of Casgevy®.[15]

A. Manufacture of Casgevy®

40. On information and belief, the general steps in the manufacturing process of Casgevy® are depicted below[16]:



41. Casgevy® is prepared from the patient's own HSCs, which are obtained via apheresis procedure(s). The autologous cells are enriched for CD34+ cells, and then genome edited *ex vivo* by introducing the CRISPR/Cas9 ribonucleoprotein (RNP) complex by electroporation. The guide RNA included in the RNP complex enables CRISPR/Cas9 to make a precise DNA double-strand break at a critical transcription factor binding site (GATA1) in the erythroid specific enhancer region of the *BCL11A* gene. As a result of the editing, GATA1 binding is disrupted and BCL11A expression is reduced. This reduction in BCL11A expression

[15] *Introduction to Casgevy, The First CRISPR-Cas9 Based Commercially Approved Therapy for SCD and TDT*, available at https://www.casss.org/docs/default-source/cgtp/2025-speaker-presentations/kadiyala-irina-vertex-pharmaceuticals-incorporated-2025.pdf; *FDA Analytical Method Review Memo for STN 125787, available at* https://www.fda.gov/media/175235/download?attachment; *January 16, 2024 Summary Basis for Regulatory Action, available at* https://www.fda.gov/media/175842/download; *December 8, 2023 Summary Basis for Regulatory Action, available at* https://www.fda.gov/media/175179/download.

[16] *Introduction to Casgevy, the First CRISPR-Cas9 Based Commercially Approved Therapy for SCD and TDT, available at* https://www.casss.org/docs/default-source/cgtp/2025-speaker-presentations/kadiyala-irina-vertex-pharmaceuticals-incorporated-2025.pdf.

conversely results in an increase in gamma-globin expression and downstream fetal hemoglobin formation. The edited CD34+ cells are formulated into a suspension in a sterile cryo-preservative medium and cryopreserved. Casgevy® is shipped as a frozen suspension in patient-specific vial(s). The product is thawed prior to infusion, and administered as a HSC transplant to the patient.[17]

42. On information and belief, the manufacture of Casgevy® involves the preparation of a *Streptococcus pyogenes*-derived Cas9 ("spCas9") protein containing a C and N-terminal sv40 large T antigen nuclear localization sequences (NLS).[18]

43. On information and belief, the manufacture of Casgevy® involves the preparation of SPY101 as a single-guide RNA (sgRNA) comprising a crRNA and a tracrRNA.[19]

44. On information and belief, the SPY101 sgRNA used in the manufacture of Casgevy® is synthesized chemically.[20]

45. On information and belief, the BCL11A target endogenous nucleic acid sequence includes a nucleic acid sequence that is complementary to the crRNA of SPY101.[21]

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[17] *Casgevy US Label* at Section 11, *available at* https://pi.vrtx.com/files/uspi_exagamglogene_autotemcel.pdf (Revised September 2025).

[18] *Casgevy Assessment Report* at 24, *available at* https://www.ema.europa.eu/en/documents/assessment-report/casgevy-epar-public-assessment-report_en.pdf (December 14, 2023); *Introduction to Casgevy, The First CRISPR-Cas9 Based Commercially Approved Therapy for SCD and TDT* at 9, available at https://www.casss.org/docs/default-source/cgtp/2025-speaker-presentations/kadiyala-irina-vertex-pharmaceuticals-incorporated-2025.pdf; Frangoul, *CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β-Thalassemia*, 384 NEW ENGLAND J. MED. 252, Suppl. Appx. at 7 (2020).

[19] *FDA Briefing Document BLA# 125787/0* at 17, *available at* https://www.fda.gov/media/173414/download; *Introduction to Casgevy, The First CRISPR-Cas9 Based Commercially Approved Therapy for SCD and TDT* at 9, available at https://www.casss.org/docs/default-source/cgtp/2025-speaker-presentations/kadiyala-irina-vertex-pharmaceuticals-incorporated-2025.pdf; Frangoul, *CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β-Thalassemia*, 384 NEW ENGLAND J. MED. 252, 254 Fig. 1B, Suppl. Appx. at 7-8 (2020).

[20] Frangoul, *CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β-Thalassemia*, 384 NEW ENGLAND J. MED. 252, Suppl. Appx. at 7 (2020); *Casgevy Assessment Report* at 17, *available at* https://www.ema.europa.eu/en/documents/assessment-report/casgevy-epar-public-assessment-report_en.pdf (December 14, 2023).

[21] *FDA Briefing Document BLA# 125787/0* at 17, *available at* https://www.fda.gov/media/173414/download; Frangoul, *CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β-Thalassemia*, 384 NEW ENGLAND J. MED. 252, 254 Fig. 1B, Suppl. Appx. at 7-8 (2020).

46. On information and belief, the manufacture of Casgevy® involves the use of a buffer in an *in vitro* environment into which the spCas9 protein and the SPY101 sgRNA (reconstituted from a lyophilized bulk powder) are added.[22]

47. On information and belief, the manufacture of Casgevy® involves the preparation of a SPY101/Cas9 protein complex (RNP) *in situ* just prior to electroporation by mixing the sgRNA and Cas9 protein at a 1:1 weight ratio.[23]

48. On information and belief, a 1:1 weight ratio of the SPY101 sgRNA and the spCas9 protein corresponds to about a 5:1 molar ratio of the sgRNA:Cas9 in the *in vitro* environment.

49. On information and belief, the manufacture of Casgevy® involves the transfection of CD34+ cells with the SPY101/spCas9 RNP by electroporation.[24]

50. On information and belief, the manufacture of Casgevy® involves the SPY101/spCas9 RNP inducing a double-strand break in GATA1 site of *BCL11A* gene in the nucleus of the CD34+ cells.[25]

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[22] *Casgevy Assessment Report* at 19, 23, *available at* https://www.ema.europa.eu/en/documents/assessment-report/casgevy-epar-public-assessment-report_en.pdf (December 14, 2023); Frangoul, *CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β-Thalassemia*, 384 NEW ENGLAND J. MED. 252, Suppl. Appx. at 7 (2020).

[23] S. Mahajan Declaration Under 37 C.F.R. § 1.132 in Support of U.S. Pat. Appl. No. 18/612,729 dated November 6, 2024 at ¶ 5; *Casgevy Assessment Report* at 23, *available at* https://www.ema.europa.eu/en/documents/assessment-report/casgevy-epar-public-assessment-report_en.pdf (December 14, 2023); Frangoul, *CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β-Thalassemia*, 384 NEW ENGLAND J. MED. 252, Suppl. Appx. at 7 (2020).

[24] S. Mahajan Declaration Under 37 C.F.R. § 1.132 in Support of U.S. Pat. Appl. No. 18/612,729 dated November 6, 2024 at ¶ 5; *Casgevy Assessment Report* at 19, *available at* https://www.ema.europa.eu/en/documents/assessment-report/casgevy-epar-public-assessment-report_en.pdf (December 14, 2023); *FDA Briefing Document BLA# 125787/0* at 18, *available at* https://www.fda.gov/media/173414/download.

[25] *Casgevy US Label* at Section 11, *available at* https://pi.vrtx.com/files/uspi_exagamglogene_autotemcel.pdf (Revised September 2025).

B. Defendants' Infringement of the '559 Patent

51. ToolGen incorporates each of the above paragraphs 1-50 as though fully set forth herein.

52. On information and belief, the manufacture of Casgevy® directly infringes, either literally or under the doctrine of equivalents, one or more claims of the '559 patent, including but not limited to at least claim 1 of the '559 patent.

53. On information and belief, Defendants have manufactured and will manufacture Casgevy® in the United States for sale in the United States or abroad. The acts of Defendants in the manufacture of Casgevy® in the United States constitute acts that directly infringe and/or induce infringement of the '559 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(a) and/or (b), respectively, because Casgevy® is manufactured using a method of inducing a modification of a target endogenous nucleic acid sequence in a nucleus of a human cell, comprising: (i) preparing a Cas9 protein, wherein the Cas9 protein comprises a nuclear localization signal (NLS); (ii) preparing a single-guide RNA (sgRNA), wherein the sgRNA comprises a crRNA and a tracrRNA, wherein the sgRNA is transcribed *in vitro* or synthesized chemically, and wherein the target endogenous nucleic acid sequence includes a portion complementary to the crRNA of the sgRNA; (iii) providing a buffer in an *in vitro* environment; (iv) disposing the Cas9 protein into the buffer; (v) disposing the sgRNA into the buffer, wherein the sgRNA is disposed in at least a two-fold molar excess over the Cas9 protein in the buffer; (vi) allowing the Cas9 protein and the sgRNA to complex in the *in vitro* environment to form a Cas9/sgRNA complex; (vii) transfecting the Cas9/sgRNA complex into the human cell by electroporation, whereby the Cas9/sgRNA complex induces the modification of the target endogenous nucleic acid sequence in the nucleus of the human cell, as claimed in the '559

patent. On information and belief, Defendants have manufactured and will manufacture Casgevy® with knowledge that such manufacture infringes the ’559 patent.

54. On information and belief, one or more Defendants sold and/or offered for sale and will sell and/or offer to sell Casgevy® in the United States. The sale of Casgevy® in the United States constitutes an act that directly infringes the ’559 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(a) or under 35 U.S.C. § 271(g), respectively, because Casgevy® is a product manufactured in the U.S. or is manufactured outside the U.S. using a process patented in the United States, in particular, a method of inducing a modification of a target endogenous nucleic acid sequence in a nucleus of a human cell, comprising: (i) preparing a Cas9 protein, wherein the Cas9 protein comprises a nuclear localization signal (NLS); (ii) preparing a single-guide RNA (sgRNA), wherein the sgRNA comprises a crRNA and a tracrRNA, wherein the sgRNA is transcribed *in vitro* or synthesized chemically, and wherein the target endogenous nucleic acid sequence includes a portion complementary to the crRNA of the sgRNA; (iii) providing a buffer in an *in vitro* environment; (iv) disposing the Cas9 protein into the buffer; (v) disposing the sgRNA into the buffer, wherein the sgRNA is disposed in at least a two-fold molar excess over the Cas9 protein in the buffer; (vi) allowing the Cas9 protein and the sgRNA to complex in the *in vitro* environment to form a Cas9/sgRNA complex; (vii) transfecting the Cas9/sgRNA complex into the human cell by electroporation, whereby the Cas9/sgRNA complex induces the modification of the target endogenous nucleic acid sequence in the nucleus of the human cell, as claimed in the ’559 patent. On information and belief, one or more Defendants has sold and/or offered for sale and will sell and/or offer to sell Casgevy® in the United States with knowledge that such sale and/or offer for sale infringes the ’559 patent.

55. On information and belief, one or more Defendants has caused and will cause the importation into the United States of Casgevy®. The importation of Casgevy® in the United States constitutes an act that directly infringes and/or induces infringement of the '559 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(g) and/or (b), respectively, because Casgevy® is manufactured using a method of inducing a modification of a target endogenous nucleic acid sequence in a nucleus of a human cell, comprising: (i) preparing a Cas9 protein, wherein the Cas9 protein comprises a nuclear localization signal (NLS); (ii) preparing a single-guide RNA (sgRNA), wherein the sgRNA comprises a crRNA and a tracrRNA, wherein the sgRNA is transcribed *in vitro* or synthesized chemically, and wherein the target endogenous nucleic acid sequence includes a portion complementary to the crRNA of the sgRNA; (iii) providing a buffer in an *in vitro* environment; (iv) disposing the Cas9 protein into the buffer; (v) disposing the sgRNA into the buffer, wherein the sgRNA is disposed in at least a two-fold molar excess over the Cas9 protein in the buffer; (vi) allowing the Cas9 protein and the sgRNA to complex in the *in vitro* environment to form a Cas9/sgRNA complex; (vii) transfecting the Cas9/sgRNA complex into the human cell by electroporation, whereby the Cas9/sgRNA complex induces the modification of the target endogenous nucleic acid sequence in the nucleus of the human cell, as claimed in the '559 patent. On information and belief, Defendants have caused and will cause the importation into the United States of Casgevy® with knowledge that such importation infringes the '559 patent.

56. On information and belief, one or more Defendants caused and will cause the importation of a single-chain guide RNA (sgRNA), wherein the sgRNA comprises a crRNA and a tracrRNA, and of a Cas9 protein comprising a C and N-terminal sequence, components of a patented machine, manufacture, combination or composition, or a material or apparatus for use

in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use, for use in the manufacture of Casgevy®. The importation of a component of a patented machine, manufacture, combination or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use in an infringement of such patent, and not a staple article or commodity of commerce suitable for substantial non-infringing use in the United States constitutes an act of contributory infringement, either literally or under the doctrine of equivalents, under 35 U.S.C. § 271(c). On information and belief, one or more Defendants caused and will cause the importation of a single-chain guide RNA (sgRNA), wherein the sgRNA comprises a crRNA and a tracrRNA, and of a Cas9 protein comprising a C and N-terminal sequence, with knowledge that such importation infringes the ’559 patent.

57. On information and belief, Defendants have formed a joint enterprise in the manufacture, sale, offer for sale, and/or importation of Casgevy® in the United States and/or the manufacture, sale, offer for sale, and/or importation of Casgevy® in the United States has been performed under the direction and/or control of Vertex Inc.

58. Defendants have directly infringed, induced the infringement of, and contributorily infringed one or more claims of the ’559 patent, either literally or under the doctrine of equivalents, under 35 U.S.C. §§ 271(a), 271(b), 271(c), and/or 271(g) by engaging in the manufacture, sale, and/or offer for sale of Casgevy® in the United States, importation of Casgevy® into the United States, and/or importation into the United States of materials or

apparatus for use in the manufacture of Casgevy® in the United States with the knowledge that such use infringes the ’559 patent.

59. ToolGen has been substantially and irreparably damaged by Defendants’ infringement of the ’559 patent.

60. ToolGen is entitled to the relief provided by 35 U.S.C. §§ 271(a), 271(b), 271(c), 271(g), and 284, including an award of damages adequate to compensate ToolGen for the infringing acts committed by Defendants with respect to the subject matter claimed in the ’559 patent.

PRAYER FOR RELIEF

WHEREFORE, ToolGen prays that this Court grant the following relief:

a) Judgment that Defendants have infringed one or more claims of the ’559 patent by engaging in the manufacture of Casgevy® in the United States, importation of Casgevy® into the United States, and/or importation into the United States of materials or apparatus for use in the manufacture of Casgevy® in the United States with the knowledge that such use infringes the ’559 patent prior to the expiration of the ’559 patent, inclusive of any extensions and additional periods of exclusivity;

b) Damages or other monetary relief from Defendants adequate to compensate ToolGen for Defendants’ infringement of the ’559 patent, together with pre-judgment and post-judgment interest;

c) Judgment that Defendants’ infringement of the ’559 patent is and has been willful and that the damages awarded be trebled pursuant to 35 U.S.C. § 284;

d) A judgment that this case is an exceptional case pursuant to 35 U.S.C. § 285 and an award of attorney’s fees; and

e) Such other and further relief, whether monetary or equitable, as the Court may deem just and proper.

DEMAND FOR JURY TRIAL

61. Pursuant to Federal Rule of Civil Procedure 38(b), ToolGen demands a trial by jury on all issues so triable.

Dated: November 18, 2025	/s/ Benjamin M. Stern Benjamin M. Stern (BBO# 646778) NUTTER, MCCLENNEN & FISH, LLP 155 Seaport Blvd. Boston, MA 02210 Tel: (617) 439-2000 Fax: (617) 310-9542 bstern@nutter.com *Attorneys for ToolGen, Inc.*
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