UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

BLUEBIRD BIO, INC.,
Petitioner,

v.

SLOAN KETTERING INSTITUTE FOR CANCER RESEARCH,
Patent Owner.

Case No. IPR2023-00070
Patent No. 7,541,179

DECLARATION OF MICHEL SADELAIN
IN SUPPORT OF PATENT OWNER'S PRELIMINARY RESPONSE

I, Michel Sadelain, declare as follows:

1. I am over the age of twenty-one years and am fully competent to make this Declaration. I make the following statements based on personal knowledge and, if called to testify to them, could and would do so.

Education

2. I am the founding director for the Center for Cell Engineering and head of the Gene Transfer and Gene Expression Laboratory at Memorial Sloan-Kettering Cancer Center ("MSKCC"), where I hold the Stephen and Barbara Friedman Chair. I am also a member of the departments of medicine at Memorial Hospital for Cancer and Allied Diseases ("Memorial Hospital") and the immunology program of the Sloan-Kettering Institute for Cancer Research ("Sloan-Kettering Institute").

3. The Center for Cell Engineering at MSKCC was established to foster research on cellular therapies. The Center brings together researchers who investigate adoptive T-cell therapies, bone marrow and cord blood transplantation, human stem cell biology, and transfer regulation and repair of genes in human cells. This unique physician-scientist partnership comprises over twenty faculty members from both Memorial Hospital and Sloan-Kettering Institute, all of whom have scientific or clinical interests in cancer or monogenic blood disorders and strive to devise and implement breakthrough therapies for those diseases. As the director of the Center, I provide scientific advice and organize meetings, annual retreats, and

peer reviews of scientific data. The Center has led to the establishment of two other MSKCC facilities that are critical for the clinical implementation of cell therapies: (1) the Michael G. Harris Cell Therapy and Cell Engineering Facility led by Dr. Isabelle Rivière; and (2) the Cellular Therapeutics Center led until recently by Dr. Renier Brentjens.

4. My laboratory, the Gene Transfer and Gene Expression Laboratory investigates, under my leadership, ways to insert genes into hematopoietic stem cells using viral vectors and to control how those genes are expressed, as well as ways to improve immune responses against tumor cells. My laboratory currently comprises about twenty-five members who conduct research on T cells and stem cell engineering. I am responsible for the scientific direction, experimental planning, review and analysis of data from, publication, and funding of those research activities.

5. I earned Doctor of Medicine (M.D.) degree and Master of Science (M.S.) degree in physiology from the University of Paris, France, in 1984, and a Doctor of Philosophy (Ph.D.) degree in immunology from the University of Alberta, Canada, in 1989. Following a clinical residency at the Centre Hospitalier Universitaire Saint-Antoine in Paris, I completed a postdoctoral fellowship at the Whitehead Institute for Biomedical Research, Massachusetts Institute of

Technology ("MIT"), Cambridge, Massachusetts, before joining MSKCC in 1994 as an Assistant Member in the Sloan-Kettering Immunology Program.

6. I am a member of the American Society of Hematology, the American Association for Cancer Research, and the American Society of Cell and Gene Therapy, where I served on the board of directors from 2004 to 2007, and as president from 2015 to 2016. I am an elected member of the American Society for Clinical Investigation. I have authored more than 200 scientific papers and book chapters. Among other awards, I received the 2012 William B. Coley Award for Distinguished Research in Tumor Immunology, the 2013 Sultan Bin Khalifa International Thalassemia Award, the 2017 Passano Laureate and Physician Scientist Award, the 2018 Pasteur-Weizmann/Servier International Prize, the 2019 Jacob and Louise Gabbay Award in Biotechnology and Medicine, the 2019 INSERM International Prize, and the 2020 Leopold Griffuel Award.

7. I have been working for approximately three decades on a gene therapy-based treatment for hemoglobinopathies, which are blood disorders caused by mutations in or near globin genes. My focus has been on using stem cells for the blood disease beta-thalassemia. Beta-thalassemia is a genetic disorder caused by mutations in or near the beta-globin gene, which provides instructions for making the beta-chain of hemoglobin (also referred to as beta-globin), that is produced in red blood cells and carries oxygen to cells throughout the body. In people with beta-

thalassemia, low levels of hemoglobin lead to a lack of oxygen in parts of the body. Patients with two deficient beta-globin genes have a more severe form of the disease called beta-thalassemia major. Persons with beta-thalassemia major require regular blood transfusions. For most patients, the disease is incurable because they lack matched donors for bone marrow or stem cell transplants to restore the production of red blood cells with a normal hemoglobin content. In addition to the logistical difficulties associated with lifelong blood transfusions, a side-effect of blood transfusions is a build-up of iron in the body of the transfusion recipient. Patients with beta-thalassemia major experience this condition, known as iron-overload, as a result of requiring regular blood transfusions. This side effect can lead to other health problems requiring additional therapies.

8. Whereas beta-thalassemia major affects only a few thousand people in the United States, beta-thalassemia (in all of its forms) is one of the two most common monogenic blood disorders worldwide, with the other being sickle cell anemia. Beta-thalassemia is commonly found in people of Mediterranean origin. Worldwide, approximately 68,000 people are born with beta-thalassemia each year.

9. A copy of my current curriculum vitae is attached as Appendix A.

The TNS9 Vector's Conception and Reduction to Practice

10. In the late 1990s and into the 2000s, which was the time I was doing the work described below, gene therapy was regarded as a nascent, cutting-edge, but

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