SUPREME COURT OF THE STATE OF NEW YORK
COUNTY OF NEW YORK

ERRANT GENE THERAPEUTICS, LLC,

Plaintiff,

– against –

SLOAN KETTERING INSTITUTE FOR CANCER RESEARCH and BLUEBIRD BIO INC.,

Defendants.

Index No. 150856/2017
IAS Part 61
Hon. Barry R. Ostrager, J.S.C.

AFFIDAVIT OF MICHEL SADELAIN

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STATE OF OHIO)
) ss.:
COUNTY OF MONTGOMERY)

I, Michel Sadelain, MD, PhD, being duly sworn, state as follows:

1. I am the founding director of 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 and the immunology program of the Sloan Kettering Institute for Cancer Research ("Sloan Kettering").

2. 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 the transfer, regulation, and repair of genes in human cells. This unique physician-scientist partnership comprises 28 faculty members from both Memorial Hospital and the Sloan Kettering Institute who all 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 entities that are critical for the clinical implementation of cell therapies: (1) the Cell Therapy and Cell Engineering Facility led by Dr. Isabelle Rivière and (2) the Cell Therapy Center led by Dr. Renier Brentjens.

3. The Gene Transfer and Gene Expression Laboratory, under my leadership, investigates 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. The lab currently comprises 22 members who conduct research on T cell and stem cell engineering. I am responsible for the scientific direction, experimental planning, review and analysis of data, publication, and funding of those research activities.

I. Background and Experience

4. I earned an M.D. degree from the University of Paris, France, in 1984 and a Ph.D. 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"), before joining MSKCC in 1994 as an assistant member.

5. 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.

6. I have been working for almost three decades on a gene-therapy based treatment using stem cells for the blood disease beta-thalassemia. Beta-thalassemia is a genetic blood 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.

7. Whereas beta-thalassemia major affects only a few thousand people in the United States, beta-thalassemia (in all of its forms, not limited to major) is one of the two most common monogenic blood disorders worldwide (the other being sickle cell anemia). It is in particular found in people of Mediterranean origin. Worldwide, approximately 68,000 people are born with beta-thalassemia each year.

II. Discovery of the TNS9 Technology

8. My work on gene therapy began in 1989. During my postdoctoral fellowship at MIT, the head of the lab in which I was working suggested that I work on thalassemia (in addition to the work I was conducting on T-cells). My work on T-cells and thalassemia continued after I joined MSK in September 1994. From 1989 to 1994, I had conducted the work myself while at MIT; then, from 1994 to 2000, I pursued this research in my laboratory with my

graduate students and postdoctoral fellows, devoting approximately 50% of my time to thalassemia research and the other 50% to CAR-T cell research.

9. In July 2000, my lab published a landmark paper in *Nature* describing the technology I had developed to introduce beta-globin genes into hematopoietic stem cells.

10. As background, the body produces red blood cells through a complicated series of events that begins with cells called hematopoietic (i.e., "blood producing") stem cells, or HSCs. HSCs are normally found in the bone marrow. Our potentially curative treatment involves (1) extracting a patient's hematopoietic stem cells (HSCs), (2) utilizing a genetically-modified virus, known as a lentiviral vector, to stably insert a functional beta-globin gene into the extracted HSCs—this process is called transduction, and then (3) infusing the patient with the "genetically restored" HSCs that should now be capable of producing beta-globin in the derivative red blood cells.

11. At a high level, the research that I published in *Nature* was a proof of concept for using gene-therapy techniques to modify a patient's cells to produce therapeutic levels of hemoglobin. The work was the result of a complex series of experiments, which I generally describe in the following paragraphs.

12. The first step in this research—and the most innovative—was designing the genetic material that would be inserted into the patient's cells. The genetic material needed to include a functional beta-globin gene, but the beta-globin gene alone was not enough to cause the patient's cells to produce enough beta-globin. Genes are typically accompanied by other DNA sequences that allow the cell to control when the gene is turned on or off. These DNA sequences, called regulatory elements, are necessary for the cell to make beta-globin from the beta-globin gene. In 2000, scientists were just beginning to understand the role that these

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