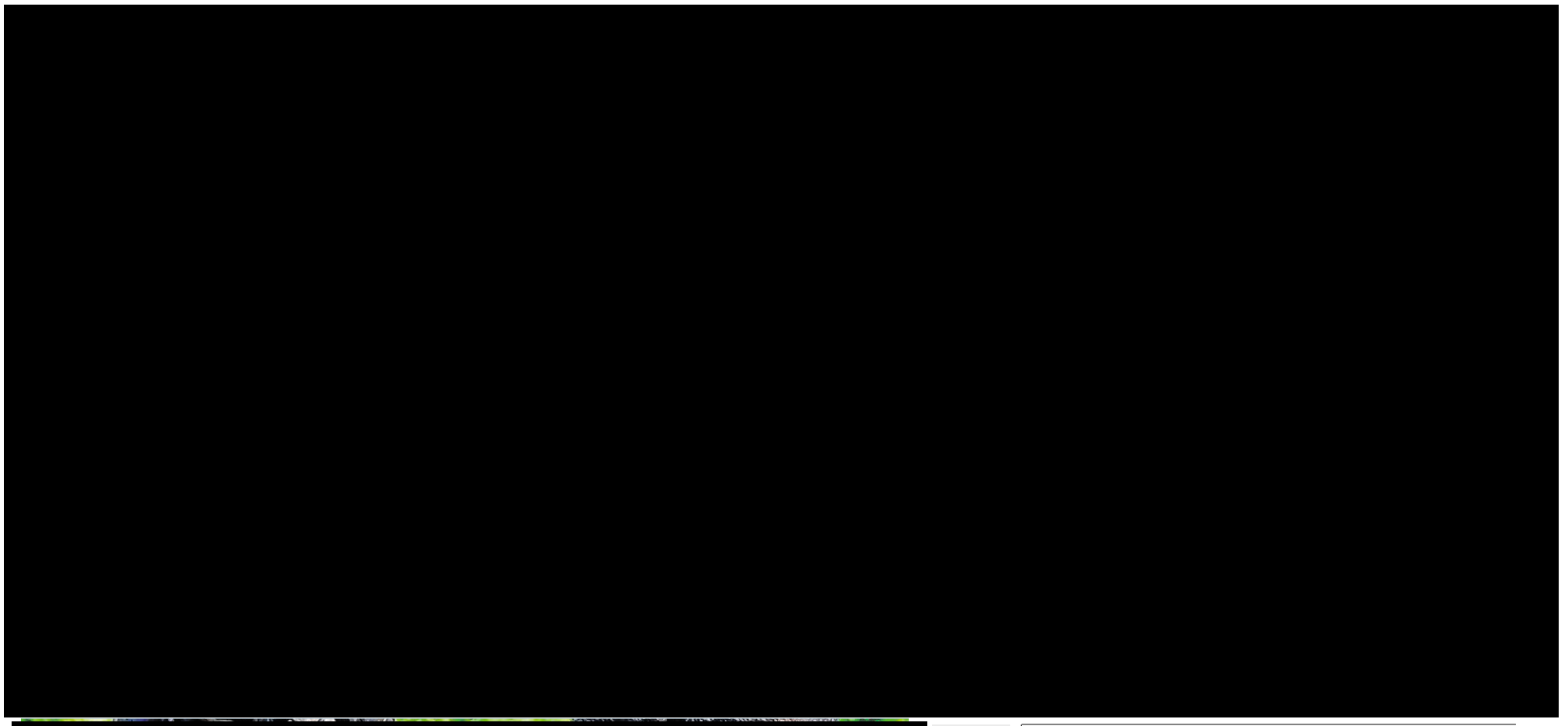

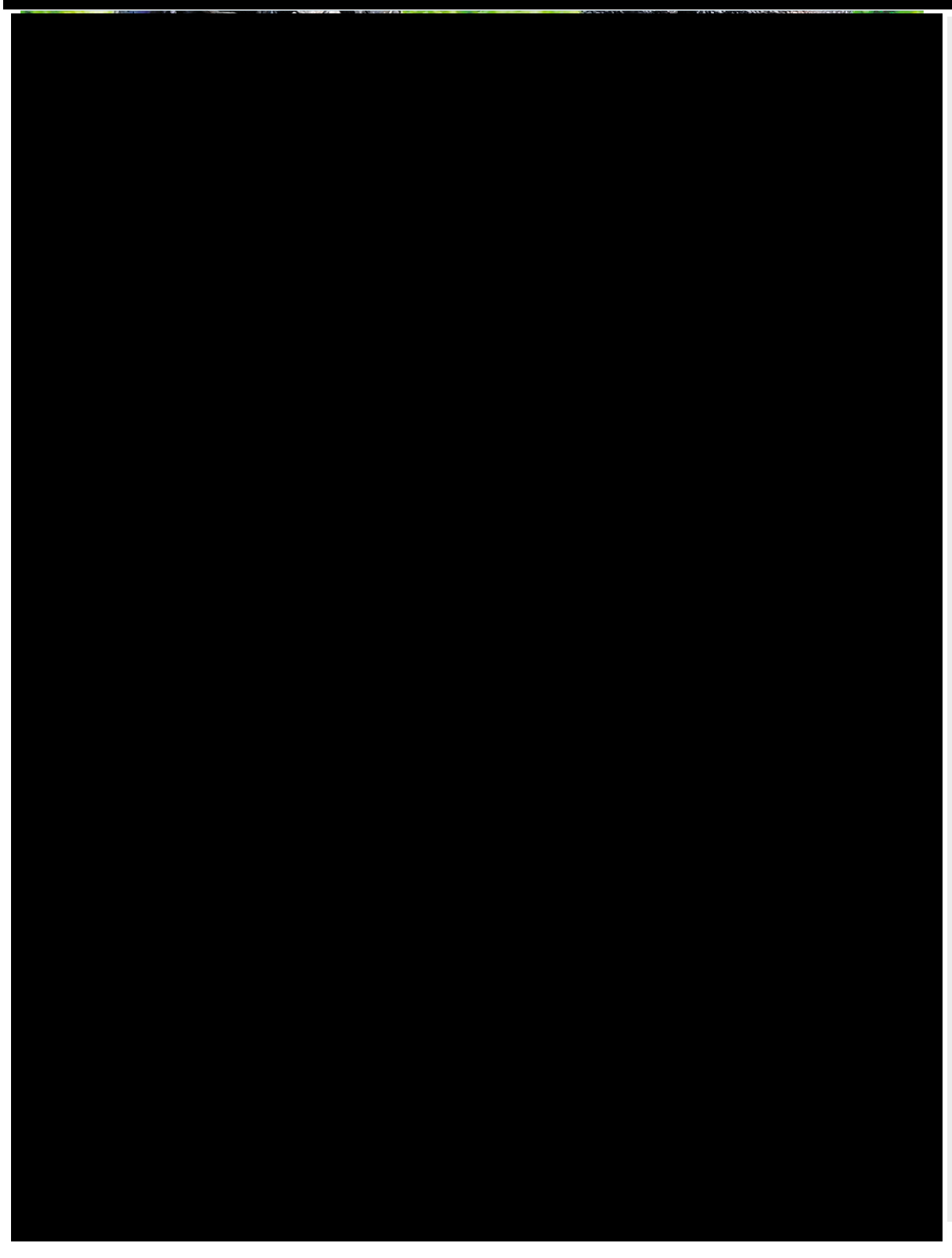

Environmental Protection Agency Acts, 1992 to 2007
Genetically Modified Organisms (Deliberate Release) Regulations, S.I. No 500 of 2003
PROPOSED DELIBERATE RELEASE OF A GENETICALLY MODIFIED ORGANISM

Intellia Therapeutics, Inc. (Intellia), of Cambridge, Massachusetts, 02139, USA, in accordance with the above legislation has given notification to the Environmental Protection Agency (EPA) of a proposal to conduct a clinical trial in Ireland using a Genetically Modified Organism (GMO). If the proposal is approved by the EPA, the clinical trial would also be governed by the Health Products Regulatory Authority under the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations, 2004 S.I. No 190 of 2004 and amendments.

Description of the GMO proposed for use in the clinical trials

Intellia is developing NTLA-3001 for the treatment of adults with Alpha-1 Antitrypsin Deficiency (AATD)-associated lung disease. NTLA-3001 ("study intervention") is an investigational product that utilizes an adeno-associated virus (AAV) vector (the GMO) and CRISPR/Cas9 genome editing technology to deliver a therapeutic transgene, in this case *SERPINA1,* to the target tissue.

The GMO is a non-replicating, bioengineered AAV viral vector capable of transducing liver hepatocytes when delivered systemically. In contrast to conventional recombinant AAV gene therapies, NTLA-3001 harnesses a CRISPR-mediated double-stranded DNA break to facilitate insertion of the transgene into a safe harbour locus to leverage an endogenous genomic promoter for transcription and protein expression.

Purpose of the clinical trials

Alpha-1 antitrypsin deficiency (AATD) is a rare, debilitating, inherited autosomal codominant disorder arising from mutations in the *SERPINA1* gene, which encodes the alpha-1 antitrypsin protein, a protease inhibitor of the proteolytic enzyme neutrophil elastase. The approach being used for NTLA-3001 involves using CRISPR/Cas9 technology to site-specifically introduce a copy of *SERPINA1* into the albumin locus in the hepatocyte genome for durable, non-dilutive transgene persistence.

The primary objective of the study is to evaluate the safety and tolerability of NTLA-3001 following a single treatment infusion in adult participants with AATD-associated lung disease.

Proposed location of the clinical trials

Two Irish sites, Beaumont Hospital, Beaumont Rd, Dublin 9, and St James´ Hospital, James Street, Dublin 8, will participate in the clinical trial. However, administration of NTLA-3001 will only occur at St James´ Hospital.

Date of the proposed clinical trials

The notification covers the treatment of clinical trial patients at the named locations between December 2024 and March 2030. The clinical trial aims to enroll around 30 patients worldwide and 4 patients in Ireland.

In accordance with article 16(1) of the Genetically Modified Organisms (Deliberate Release) Regulations, S.I. No 500 of 2003, any person or body may make representations in writing, which will be no later than 28 days from the date of publication of this notice. Representations will be to the Environmental Protection Agency, Office of Environmental Sustainability, P.O. Box 3000, Johnstown Castle Estate, Co Wexford, IRELAND and will be subject to a fee of €10 (guidance on fee payment may be obtained by writing to licensing@epa.ie). Further information on the proposed deliberate release may be obtained from the Environmental Protection Agency.