**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): May 12, 2020**

# Stoke Therapeutics, Inc.

**(Exact Name of Registrant as Specified in its Charter)**

| **Delaware** | **001-38938** | **47-114582** |
|---|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(Commission File Number)** | **(I.R.S. Employer Identification No.)** |

| | |
|---|---|
| **45 Wiggins Ave**<br>**Bedford, Massachusetts** | **01730** |
| **(Address of principal executive offices)** | **(Zip Code)** |

**Registrant's telephone number, including area code: (781) 430-8200**

**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:

☐ 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, $0.0001 par value per share | STOK | Nasdaq Global Select Market |

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**

In connection with the 2020 Annual Meeting of the American Society of Gene & Cell Therapy ("ASGCT"), on May 12, 2020, Stoke Therapeutics, Inc. (the "Company") issued the press release attached as Exhibit 99.1. In addition, on May 12, 2020, the poster attached as Exhibit 99.2, which the Company will present at the ASGCT Annual Meeting, was posted to the ASGCT website.

The information furnished with this report, including Exhibit 99.1, 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 into any other filing under the Exchange Act or the Securities Act of 1933, as amended, except as expressly set forth by specific reference in such a filing.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

| Exhibit Number | Description |
|---|---|
| 99.1 | Press Release, dated May 12, 2020. |
| 99.2 | ASGCT Poster. |

**SIGNATURE**

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.

**STOKE THERAPEUTICS, INC.**

Date: May 12, 2020

By: /s/ Robin A. Walker
**Robin A. Walker**
**Senior Vice President, Chief Legal Officer and Chief Compliance Officer**

**Exhibit 99.1**

**Stoke Therapeutics Presents Preclinical Data That Demonstrate In-Vitro and In-Vivo Target Engagement and Protein Upregulation in *OPA1* Protein Deficiency, the Underlying Cause of the Most Common Inherited Optic Nerve Disorder**

*First in-vivo proof-of-concept for TANGO antisense oligonucleotides in an ocular disease*

*Results presented at the American Society of Gene and Cell Therapy Annual Meeting further validate the company's mutation-independent approach to amplifying protein expression to treat severe genetic diseases*

**BEDFORD, Mass., May 12, 2020** — Stoke Therapeutics, Inc., (Nasdaq: STOK), a biotechnology company pioneering a new way to treat the underlying cause of genetic diseases by precisely upregulating protein expression, today announced new preclinical data demonstrating in-vitro and in-vivo target engagement and protein upregulation in *OPA1* protein-deficient cells. *OPA1* protein deficiency is the underlying cause of autosomal dominant optic atrophy (ADOA), the most common inherited optic nerve disorder. This is the first proof-of-concept data for TANGO antisense oligonucleotides (ASOs) in an ocular disease. The results further validate the company's mutation-independent approach to amplifying protein expression to treat severe genetic diseases. These data will be presented today in a virtual poster session at the American Society of Gene and Cell Therapy (ASGCT) 2020 Annual Meeting.

"These data provide early evidence of the potential to address the underlying cause of autosomal dominant optic atrophy, an optic nerve disorder that causes progressive and irreversible vision loss starting in the first decade of a child's life. There are currently no approved treatments for ADOA," said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. "Our TANGO technology represents a unique, mutation-independent approach to treating the underlying cause of a variety of genetic diseases, particularly in the central nervous system and the eye. The ADOA program is one of several under consideration for future prioritization, and we look forward to nominating a second product candidate later this year."

ADOA affects approximately one in 30,000 people globally with a higher incidence in Denmark of one in 10,000 due to a founder effect. An estimated 65% to 90% of cases are caused by mutations in the *OPA1* gene.

The data presented today demonstrate in-vitro and in-vivo proof-of-concept for TANGO ASOs in an ocular disease. Highlights from today's presentation include:

- Dose-dependent decreases in non-productive *OPA1* mRNA and increases in *OPA1* protein expression were observed in-vitro and in-vivo.
- An increase in *OPA1* protein expression to approximately 75% of wild-type levels was observed in an *OPA1* haploinsufficient (*OPA1* +/-) cell line.
- In-vivo increases in *O*PA1 protein levels in the retina of wild-type rabbits were observed and the test ASO was well tolerated for up to 15 days after intravitreal injection.

Details of today's presentation are as follows:

**Presentation Title:** Antisense oligonucleotide mediated increase of *OPA1* expression using TANGO technology for treatment of autosomal dominant optic atrophy

**Session Date & Time:** Tuesday, May 12, 2020; 5:30 p.m. – 6:30 p.m. E.T.

**Session Title:** Oligonucleotide Therapeutics

**Presenter:** Aditya Venkatesh, Ph.D., Senior Scientist, Stoke Therapeutics

The poster presented at ASGCT is now available online on the Events and Presentations section of Stoke's website at https://investor.stoketherapeutics.com/.

**About Autosomal Dominant Optic Atrophy**

Autosomal dominant optic atrophy (ADOA) is the most common inherited optic nerve disorder. It is a rare disease that causes progressive and irreversible vision loss in both eyes starting in the first decade of life. Symptoms typically begin between the ages of 4 and 6 years old, affecting males and females equally. The severity of the condition by adolescence reflects the overall level of visual function to be expected throughout most of the individual's adult life. Roughly half of people with ADOA fail driving standards and up to 46% are registered as legally blind. ADOA is considered a haploinsufficiency, as most people living with ADOA have genetic mutations in the *OPA1* gene that result in only half the necessary *OPA1* protein being produced. More than 400 *OPA1* mutations have been reported in people diagnosed with ADOA. Currently there is no approved treatment for people living with ADOA.

**About TANGO**

TANGO (Targeted Augmentation of Nuclear Gene Output) is Stoke's proprietary research platform. Stoke's initial application for this technology are diseases in which one copy of a gene functions normally and the other is mutated, also called haploinsufficiencies. In these cases, the mutated gene does not produce its share of protein, so the body does not function normally. Using the TANGO approach and a deep understanding of RNA science, Stoke researchers design antisense oligonucleotides (ASOs) that bind to pre-mRNA and help the target genes produce more protein. TANGO aims to restore missing proteins by increasing – or stoking – protein output from healthy genes, thus compensating for the non-functioning copy of the gene.

**About Stoke Therapeutics**

Stoke Therapeutics (Nasdaq: STOK), is a biotechnology company pioneering a new way to treat the underlying causes of severe genetic diseases by precisely upregulating protein expression to restore target proteins to near normal levels. Stoke aims to develop the first precision medicine platform to target the underlying cause of a broad spectrum of genetic diseases caused by haploinsufficiencies. Stoke is headquartered in Bedford, Massachusetts with offices in Cambridge, Massachusetts. For more information, visit https://www.stoketherapeutics.com/ or follow the company on Twitter at @StokeTx.

**Cautionary Note Regarding Forward-Looking Statements**

This press release contains "forward-looking" statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to: Stoke's ability to precisely upregulate protein expression in OPA1 protein-deficient cells; Stoke's ability to treat the underlying cause of ADOA; and Stoke's ability to use preclinical data to advance the development of TANGO ASOs to treat ocular disease. Statements including words such as "plan," "continue," "expect," "target," or "ongoing" and statements in the future tense are forward-looking statements. These

forward-looking statements involve risks and uncertainties, as well as assumptions, which, if they do not fully materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Forward-looking statements are subject to risks and uncertainties that may cause Stoke's actual activities or results to differ significantly from those expressed in any forward-looking statement, including without limitation risks and uncertainties related to Stoke's ability to develop, obtain regulatory approval for and commercialize TANGO ASOs to treat ocular disease; the impact of the COVID-19 pandemic on Stoke's operations and the U.S. and world economies; the timing and results of preclinical studies; the timing for nominating a second product candidate; risks associated with potential delays, work stoppages, or supply chain disruptions caused by the coronavirus pandemic; risks associated with current and potential future healthcare reforms; Stoke's ability to protect its intellectual property; and other risks set forth in our filings with the Securities and Exchange Commission, including the risks set forth in our quarterly report on Form 10-Q for the quarter ended March 31, 2020. These forward-looking statements are based on our current beliefs and expectations and speak only as of the date hereof and Stoke specifically disclaims any obligation to update these forward-looking statements or reasons why actual results might differ, whether as a result of new information, future events or otherwise, except as required by law.

**Stoke Media & Investor Contact:**
Dawn Kalmar
Vice President, Head of Corporate Affairs
dkalmar@stoketherapeutics.com
781-303-8302

# Antisense oligonucleotide mediated incr
# for treatment of autc

Aditya Venkatesh[1], Zhiyu Li[2], Syed Ali[1], Anne Christiansen[1], Kian Huat L
[1]Stoke Therapeutics, Bedford, MA, [2]Medical Genetics and Ophthalmic

## Background

Autosomal dominant optic atrophy (ADOA) is one of the most commonly diagnosed optic neuropathies. This optic nerve disease is associated with structural and functional mitochondrial deficits that lead to degeneration of the retinal ganglion cells and progressive, irreversible loss of vision. A majority of ADOA patients carry mutations in *OPA1* and most mutations lead to haploinsufficiency (Lenaers G. et al. Orphanet J Rare Dis 2012). *OPA1* encodes a mitochondrial GTPase with a critical role in mitochondrial fusion, ATP synthesis and apoptosis. Currently, there is no approved disease-modifying treatment for ADOA patients. Here, we employ TANGO (Targeted Augmentation of Nuclear Gene Output), a novel therapeutic approach, that uses antisense oligonucleotides (ASOs), to increase the endogenous expression of *OPA1*.

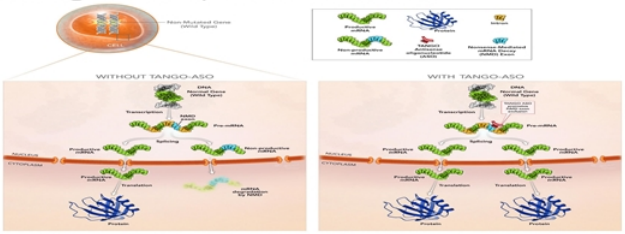



**Figure 1: Mechanism of TANGO:** TANGO reduces non-productive messenger RNAs (mRNA), which are normally targeted for degradation by nonsense-mediated mRNA decay (NMD) as shown in **Figure 1**. In turn, TANGO increases productive mRNA and protein. TANGO specifically increases expression of canonical target mRNA and full-length protein, only in tissues with endogenous gene expression. As these events are naturally-occurring, TANGO can upregulate the wild-type alleles in the context of autosomal dominant haploinsufficiency diseases such as ADOA.

Additionally, TANGO offers the following advantages for treating ocular diseases:

- ✓ Intravitreal injection of ASOs permits diffusion throughout the eye, including retinal neurons
- ✓ Long-term efficacy (>1 year in mouse retina) after single intravitreal injection (Kach et al, ARVO Poster Presentation May 2019)
- ✓ No specialized formulation or encapsulation required for ASO therapy
- ✓ Potential to target large genes not amenable to AAV-based gene therapy

## *OPA1* non-productive splicing event identification and validation

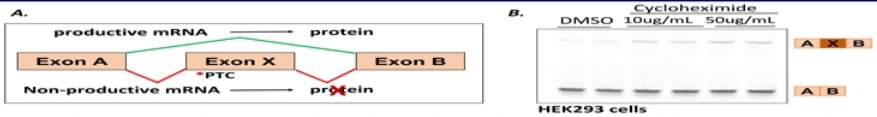



**Figure 2.** Novel NMD exon inclusion event (Exon X) identified in the *OPA1* gene which leads to the introduction of a premature termination codon (PTC) resulting in a non-productive mRNA transcript degraded by non-sense mediated decay (NMD) (Panel A). As NMD is a translation-dependent process, the protein synthesis inhibitor cycloheximide (CHX) was used to evaluate the true abundance of the event. Panel B shows an increase in *OPA1* transcripts containing the NMD exon in HEK293 cells with increasing CHX dose. Other ocular cell lines also validated for the presence of the NMD exon (ARPE-19, Y79).

## *OPA1* NMD event is conserved in the primate and rabbit eye

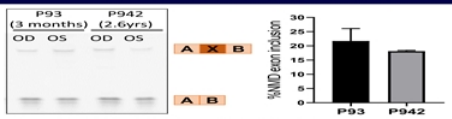



**Figure 3**: RT-PCR data from posterior segment of eye of *Chlorocebus sabaeus* (green monkey) with accompanying quantification of NMD exon abundance at 3 months and 2.6 years of age (N=1/age). Data represents average of OD and OS values for each animal. OD: oculus dextrus (right eye); OS: oculus sinister (left eye); P: post-natal day

NMD event also conserved in the rabbit retina (See Figure 7, Panels B and C).

**Abundance of event is likely to be higher *in vivo*, given that NMD is presumed active in the tissue**

## Specific ASOs r
## and increase prod

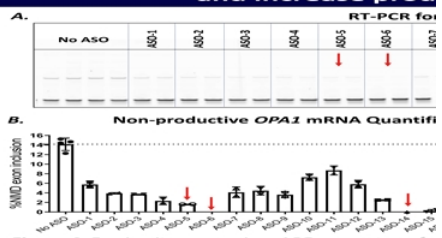



**Figure 4.** For *in vitro* screening, ASOs were transfe
a transfection agent. For effect on NMD exon, cell
RNA was isolated and used for RT-PCR (Panel A wi
cycloheximide treated cells were used for Taqman
**arrows highlight ASOs that reduce non-productiv
Among these, ASO-14 produces the most increas**

## ASO-14 decreases non-prod
## expression in a do

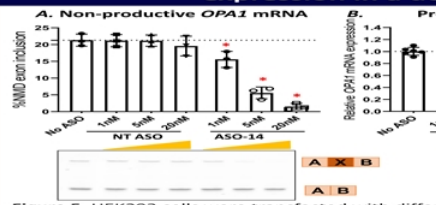
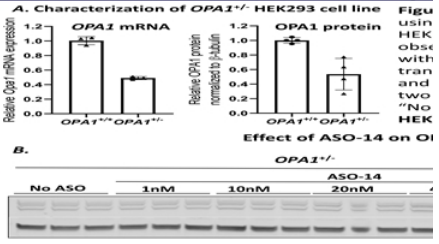



**Figure 5.** HEK293 cells were transfected with differ
hours after transfection and analyzed for impact o
(Panel B) similar to Figure 4. For protein analysis
western blots were probed with antibodies tar
different isoforms of OPA1. Data represent avera
compared to "No ASO" group). NT ASO targets un

## ASO-14 increases OPA1 e
## (O

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