

PROSPECTUS SUPPLEMENT  
(To Prospectus dated October 14, 2021)



**\$22,356,446**

## **Common Stock**

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This prospectus supplement (this "**Supplement**") amends and supplements the information in our prospectus, dated October 14, 2021 (the "**Base Prospectus**"), the shelf registration statement on Form S-3 of which the Prospectus (as defined below) is a part (the "**Registration Statement**"), and our prospectus supplement, dated October 14, 2021 (the "**Prospectus Supplement**" and together with the Base Prospectus, the "**Prospectus**"), relating to the offer and sale of shares of common stock, par value \$0.00001 per share ("**Common Stock**"), of Taysha Gene Therapies, Inc. (the "**Company**") having an aggregate offering price of up to \$150,000,000 from time to time through the Sales Agents (as defined below). This Supplement should be read in conjunction with the Prospectus, and is qualified by reference thereto, except to the extent that the information herein amends or supersedes the information contained in the Prospectus. This Supplement is not complete without, and may only be delivered or utilized in connection with, the Prospectus and any future amendments or supplements thereto.

In accordance with the terms of the sales agreement, dated August 10, 2021, as amended by that certain amendment No. 1, dated March 30, 2022 (the "**Sales Agreement**"), by and among the Company, Goldman Sachs & Co. LLC ("**Goldman**"), Wells Fargo Securities, LLC ("**Wells Fargo**") and SVB Securities LLC (f/k/a SVB Leerink LLC) ("**SVB Securities**"), we may offer and sell shares of our Common Stock from time to time through Goldman, Wells Fargo and SVB Securities, acting as sales agents (the "**Sales Agents**").

We are now subject to General Instruction I.B.6 of Form S-3, which limits the amounts that we may sell under the Registration Statement of which this Supplement and the Prospectus form a part. The aggregate market value of our Common Stock held by non-affiliates pursuant to General Instruction I.B.6 of Form S-3 is \$67,069,341, which was calculated based on 38,107,580 shares of our outstanding Common Stock held by non-affiliates on March 27, 2023, at a price of \$1.76 per share, the closing price of our Common Stock on January 27, 2023. We have not offered any securities pursuant to Instruction I.B.6 during the prior twelve calendar month period that ends on and includes the date of this prospectus supplement. As a result of the limitations of General Instruction I.B.6, and in accordance with the terms of the Sales Agreement, we are registering the offer and sale of shares of our Common Stock having an aggregate offering price of up to \$22,356,446 from time to time through the Sales Agents.

Our Common Stock is listed on the Nasdaq Global Market under the symbol "TSHA." On March 27, 2023, the last reported sales price of our Common Stock was \$0.695 per share.

**Investing in our Common Stock involves risks. Before buying any shares, you should read the discussion of material risks of investing in our Common Stock in "Risk Factors" beginning on page 7 of the Prospectus, and in the risks discussed under similar headings in the documents incorporated by reference in this prospectus supplement and the Prospectus, as they may be amended, updated or modified periodically in our reports filed with the Securities and Exchange Commission.**

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement and the Prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Goldman Sachs & Co. LLC

Wells Fargo Securities

SVB Securities

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The date of this prospectus supplement is March 29, 2023.