UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 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): April 10, 2021

F-STAR THERAPEUTICS, INC.
(Exact Name of Registrant as Specified in Charter)

Delaware	**001-37718**	**52-2386345**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

Eddeva B920 Babraham Research Campus
Cambridge, United Kingdom CB22 3AT
(Address of Principal Executive Offices, and Zip Code)

+44-1223-497400
Registrant's Telephone Number, Including Area Code

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 (*see* General Instruction A.2. below):

☐ 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)**	**(Name of each exchange on which registered)**
Common stock, $0.0001 par value	**FSTX**	**The Nasdaq Stock Market (Nasdaq Capital Market)**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

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 8.01. Other Events.

On April 10, 2021, F-star Therapeutics, Inc. (the "Company") issued a press release announcing a poster presentation of preclinical data from FS222, a tetravalent bispecific antibody targeting both CD137 and PD-L1 at the 2021 American Academy of Cancer Research ("AACR") Annual Meeting, taking place virtually from April 10-15, 2021 and May 17-22, 2021. At the AACR 2021 Annual Meeting, the Company will be presenting a poster titled "FS222, a Tetravalent Bispecific Antibody Targeting CD137 and PD-L1, is Designed for Optimal CD137 Interactions Resulting in Potent T cell Activation Without Toxicity," which became available via on-demand viewing on April 10, 2021. A copy of each of the press release and the poster are attached hereto as Exhibits 99.1 and 99.2, respectively and each is incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits

Exhibit Number	Description
99.1	Press Release issued April 10, 2021.
99.2	Poster #1864, titled "FS222, a Tetravalent Bispecific Antibody Targeting CD137 and PD-L1, is Designed for Optimal CD137 Interactions Resulting in Potent T cell Activation Without Toxicity".
104	Cover Page Interactive File (the cover page tags are embedded within the Inline XBRL document).

SIGNATURES

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.

F-STAR THERAPEUTICS, INC.

Date: April 13, 2021

/s/ Darlene Deptula-Hicks
Darlene Deptula-Hicks
Chief Financial Officer

F-star Therapeutics Shows Differentiation of FS222 in 2021 AACR Poster

Study Confirms F-star's Bispecific Antibody Tetravalency is the Most Efficient Way to Induce Receptor Clustering and Activation

CAMBRIDGE, United Kingdom and CAMBRIDGE, Mass., April 10, 2021 (GLOBE NEWSWIRE) — F-star Therapeutics, Inc. (NASDAQ: FSTX), a clinical-stage biopharmaceutical company dedicated to developing next generation bispecific immunotherapies to transform the lives of patients with cancer, today announces that preclinical data from FS222, a potentially best-in-class tetravalent bispecific antibody targeting both CD137 and PD-L1 will be presented in a poster at the 2021 American Academy of Cancer Research (AACR) Annual Meeting, taking place virtually from April 10-15 and May 17-21. Poster #1864, entitled 'FS222, a Tetravalent Bispecific Antibody Targeting CD137 and PD-L1, is Designed for Optimal CD137 Interactions Resulting in Potent T cell Activation Without Toxicity' will be available via on-demand viewing starting today, April 10, at 8:30 a.m. ET.

FS222 targets PD-L1, the immune checkpoint protein that regulates the balance of activated T cells in the immune system and is overexpressed on many solid tumors and CD137, a co-stimulatory molecule from the tumor necrosis factor receptor superfamily (TNFRSF), which is widely known to be upregulated on tumor-reactive $CD8^+$ T cells or "killer T cells". Currently, only a minority of patients have a long-lasting response to monotherapies that block the PD-(L)1 pathway.

Neil Brewis, Chief Scientific Officer at F-star Therapeutics, said: "We are encouraged by the results of these latest preclinical studies of FS222, our tetravalent bispecific antibody targeting PD-L1 and CD137. This work further demonstrates that FS222's tetravalent binding mechanism is the most efficient and effective format for bispecific antibodies. The early onset of activity and T cell proliferation gives us confidence that FS222 will allow for a wide range of treatment options."

FS222 was designed to be a potent human CD137/PD-L1 tetravalent conditional agonist with a unique combination of high affinity PD-L1 binding, and moderate affinity, but with high avidity, binding to CD137 on activated T cells to result in optimal receptor clustering. Previously, FS222 has been shown to exhibit a favorable safety profile in preclinical safety studies.

Tetravalent binding by FS222 demonstrated optimal activity in multiple preclinical pharmacology studies, outperforming classic heterodimeric bispecific antibodies. These data showed that there was no evidence of a hook effect, or bell-shaped dose response curve, *in vitro*, and coupled with FS222's favorable safety profile, presents a potentially broad and differentiated therapeutic window. A murine surrogate mAb^2 for FS222 had peripheral immunopharmacology, as shown by $CD8^+$ T cell proliferation, at high dose levels, mirroring the *in vitro* data, whereby the tetravalent FS222 surrogate mAb^2 outperforms other lower valency formats.

In January 2021, F-star announced that the first patient had been dosed in a Phase 1 clinical trial of FS222, a multicenter, open-label, first-in-human trial to evaluate the safety, tolerability, and early signs of efficacy of FS222 in adult patients diagnosed with advanced malignancies. The adaptive study design will allow for the early exploration of clinical activity of FS222 in a range of selected solid tumors that will guide future targeted clinical development.

About F-star Therapeutics, Inc.

F-star is a clinical-stage biopharmaceutical company developing tetravalent bispecific antibodies for a paradigm shift in cancer therapy. By developing medicines that seek to block tumor immune evasion, the Company's goal is to offer patients greater and more durable benefits than current immuno-oncology treatments. Through its proprietary tetravalent, bispecific natural antibody (mAb^{2}™) format, F-star's mission is to generate highly differentiated best-in-class drug candidates with monoclonal antibody-like manufacturability. For more information visit www.f-star.com and follow us on LinkedIn and Twitter.

Forward Looking Statements

Certain statements contained in this press release regarding matters that are not historical facts, are forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995, known as the PSLRA. These include statements regarding management's intentions, plans, beliefs, expectations or forecasts for the future and, therefore, you are cautioned not to place undue reliance on them. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. F-star undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise, except to the extent required by law. Such forward-looking statements are based on our expectations and involve risks and uncertainties; consequently, actual results may differ materially from those expressed or implied in the statements due to a number of factors, including those discussed in F-star's Annual Report on Form 10-K, as well as subsequent Quarterly Reports on Form 10-Q and other documents to be filed from time to time with the SEC. New factors emerge from time to time and it is not possible for us to predict all such factors, nor can we assess the impact of each such factor on the business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. Forward-looking statements included in this communication are based on information available to F-star as of the date of this communication. F-star does not assume any obligation to update such forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

For further information, please contact:

For investor inquiries
Lindsey Trickett
VP Investor Relations & Communications
+1 240-543-7970
lindsey.trickett@f-star.com

For media inquiries
Helen Shik
Shik Communications LLC
+1 617-510-4373
Shik.Helen10@gmail.com

FS222, a Tetravalent Bispecific Antibody Targeting CD137 and PD-L1, is Designed for Optimal CD137 Interactions Resulting in Potent T cell Activation Without Toxicity

Matthew A Lakins, Jose Munoz-Olaya, Christel Veyssier, Daniel Jones, Emma Goodman, Quincy Kaka, Jennifer Ofoedu, Ryan Fiehler, Robert Hughes, Cristian Gradinaru, Daniel Gliddon, Michelle Morrow, Neil Brewis

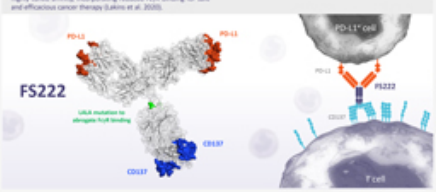
F-star Therapeutics Inc., Babraham Research Campus, Cambridge, UK

Background

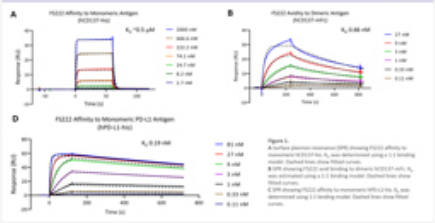
CD137 (4-1BB, TNFRSF9) is expressed on activated lymphocytes, and its clustering leads to receptor agonism resulting in lymphocyte proliferation and pro-inflammatory cytokine release. First-generation CD137 antibodies for cancer therapy were high affinity and enabled for FcγR engagement with either severe toxicity or weak activity limiting their therapeutic benefit (Qi, X et al. 2019). Next generation CD137 approaches remain a promising area for bispecific antibodies designed to redirect T cell activity to the tumor whilst limiting unwanted toxicities. We have rationally designed and developed a unique tetravalent bispecific antibody with natural architecture, targeting CD137 and PD-L1 through highly tuned affinity, incorporating reduced FcγR binding for safe and efficacious cancer therapy (Lakins et al. 2020).

Methods

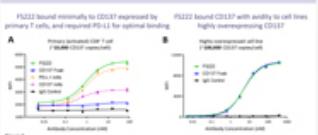
A CD137/PD-L1 bispecific mAb² antibody (FS222) was generated by introducing a bivalent affinity-optimised CD137 binding Frab into a human IgG1 bivalent PD-L1 mAb. LALA mutations were introduced to abrogate FcγR activity. To elucidate its mechanism of action, FS222's binding valency was assessed by chemically-crosslinked mass spectrometry mapping (XL/MS). Immune pharmacology models were also used to evaluate PD-L1 dependent FS222 agonism against variants with differing valency for each target.



1. By design, FS222 bound PD-L1 with high affinity and specifically interacted with CD137 through highly tuned affinity to result in optimal receptor clustering



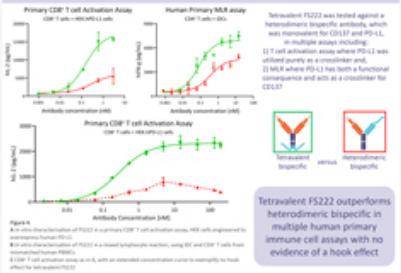
2. FS222's natural IgG1 architecture, tetravalency and highly tuned affinity resulted in ideal cell binding



3. FS222 tetravalency was demonstrated unequivocally using crosslinking mass spectrometry mapping (XL/MS)

FS222's natural structure presents an opportunity to bind each target bivalently and simultaneously. In a dynamic equilibrium system, FS222 bound CD137 and PD-L1 antigens tetravalently.

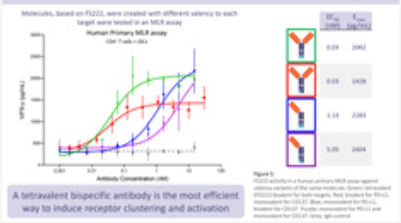
4. Tetravalent FS222 outperformed a heterodimeric bispecific antibody in multiple *in vitro* functional assays without hook effect



Tetravalent FS222 was tested against a heterodimeric bispecific antibody, which was monovalent for CD137 and PD-L1, in multiple assays including: 1) T cell activation assay where PD-L1 was utilized purely as a crosslinker and, 2) MLR where PD-L1 has both a functional consequence and acts as a crosslinker for CD137.

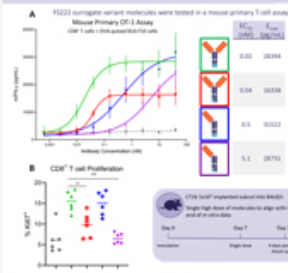
Tetravalent FS222 outperforms heterodimeric bispecific in multiple human primary immune cell assays with no evidence of a hook effect

5. Tetravalency resulted in full PDx blockade and optimal CD137 agonism in a human primary mixed lymphocyte reaction



A tetravalent bispecific antibody is the most efficient way to induce receptor clustering and activation

6. Tetravalent FS222 surrogate mAb² provided optimal *in vitro* activity and enhanced CD8⁺ T cell proliferation *in vivo*



Conclusion

FS222 was designed to be a potent human anti-CD137/PD-L1 tetravalent condition agonist with a unique combination of high affinity PD-L1 binding, and moderate af with high avidity binding to CD137 on activated T cells. Previously, FS222 has been to exhibit a favourable safety profile with immunopharmacology of non-human pr safety studies.

Tetravalent binding by FS222 was required for optimal activity in multiple preclinica pharmacology studies, outperforming classical heterodimeric bispecific antibodies was no evidence of a hook effect *in vitro*, and coupled with FS222's favourable safe profile, presents a potentially very broad therapeutic window. FS222 surrogate mA peripheral immunopharmacology, as shown by CD8⁺ T cell proliferation, at high do levels, mirroring the *in vitro* data whereby tetravalent FS222 surrogate outperform lower valency formats.

In many tumor settings, checkpoint inhibitors only provide moderate clinical benef for many of those patients there is a strong mechanistic rationale for clinical outco be improved with FS222 administration. We believe FS222 presents a unique oppo versus high affinity and/or low valency CD137 binding bispecific molecules, by ope a broad therapeutic window.

AACR Virtual Annual Meeting 2021 | 09 – 14 April | Poster Number: 2384

Qi, X., Li, F., Wu, Y. et al. (2019) *Nat Comm* 10, 2141 **DOI: 10.1038/s41467-019-10088-1**
Lakins et al. (2020). *Clin Cancer Res* April 28 2020 **DOI: 10.1158/1078-0432.CCR-19-2958**