

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

**FORM S-8  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933**

**Zynerba Pharmaceuticals, Inc.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or Other Jurisdiction of  
Incorporation or Organization)

**26-0389433**  
(I.R.S. Employer  
Identification Number)

**80 W. Lancaster Avenue, Suite 300**  
(Address of Principal Executive Offices)

**19333**  
(Zip Code)

**ZYNERBA PHARMACEUTICALS, INC.  
AMENDED AND RESTATED 2014 OMNIBUS INCENTIVE COMPENSATION PLAN**  
(Full Title of the Plan)

**Armando Anido**  
**Chairman and Chief Executive Officer**  
**Zynerba Pharmaceuticals, Inc.**  
**80 W. Lancaster Avenue, Suite 300**  
**Devon, PA 19333**  
(Name and address of agent for service)

**(484) 581-7505**  
(Telephone number, including area code, of agent for service)

**with a copy to:**

**Rachael M. Bushey, Esq.**  
**Jennifer L. Porter, Esq.**  
Pepper Hamilton LLP  
3000 Two Logan Square  
18<sup>th</sup> and Arch Streets  
Philadelphia, PA 10193  
(215) 981-4331

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

|                         |                          |  |                           |                                     |
|-------------------------|--------------------------|--|---------------------------|-------------------------------------|
| Large accelerated filer | <input type="checkbox"/> |  | Accelerated filer         | <input checked="" type="checkbox"/> |
| Non-accelerated filer   | <input type="checkbox"/> |  | Smaller reporting company | <input type="checkbox"/>            |
|                         |                          |  | Emerging growth company   | <input checked="" type="checkbox"/> |

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 7(a)(2)(B) of the Securities Act.

**CALCULATION OF REGISTRATION FEE**

| Title of Securities<br>to be Registered   | Amount<br>to be<br>Registered (1) | Proposed<br>Maximum<br>Offering Price<br>Per Share (2) | Proposed<br>Maximum<br>Aggregate<br>Offering Price (2) | Amount of<br>Registration Fee |
|-------------------------------------------|-----------------------------------|--------------------------------------------------------|--------------------------------------------------------|-------------------------------|
| Common Stock, par value \$0.001 per share | 1,500,000 shares                  | \$ 4.66                                                | \$ 6,990,000.00                                        | \$ 847.19                     |

(1) Represents shares of common stock, \$0.001 par value per share, of the Registrant (the "Common Stock") that were added to the shares authorized for

issuance under the Zynerba Pharmaceuticals, Inc. Amended and Restated 2014 Omnibus Incentive Compensation Plan, as amended (the "Plan"), on January 2, 2019 pursuant to an "evergreen" provision contained in the Plan. Pursuant to such provision, as of the first trading day of January of each year, the number of shares authorized for issuance under the Plan is increased to the lesser of (i) ten percent (10%) of the issued and outstanding shares of Common Stock as of the last trading day in December of the immediately preceding calendar year, or (ii) 1,500,000 shares of Common Stock. Pursuant to Rule 416 of the Securities Act of 1933, as amended (the "Securities Act"), this registration statement shall also cover any additional shares of Common Stock which become issuable under the Plan by reason of any stock dividend, stock split, recapitalization or other similar transaction effected without the receipt of consideration which results in an increase in the number of the outstanding shares of the Registrant.

(2) This estimate is made pursuant to Rule 457(h) of the Securities Act. The price shown is based upon the average of the high and low prices reported for the Common Stock on the NASDAQ Global Market on March 7, 2019.

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#### EXPLANATORY NOTE

This Registration Statement is being filed for the purpose of registering an additional 1,500,000 shares of common stock, \$0.001 par value per share (the “Common Stock”), of Zynerba Pharmaceuticals, Inc. (the “Registrant”) that were added to the shares authorized for issuance under the Zynerba Pharmaceuticals, Inc. Amended and Restated 2014 Omnibus Incentive Compensation Plan, as amended (the “Plan”) for which a Registration Statement on Form S-8 relating to the same employee benefit plan is effective.

The Registrant previously filed the Registration Statements on Form S-8 (File Nos. 333-207973, 333-216968 and 333-223597) with the Securities and Exchange Commission (the “Commission”) to register 4,209,030 shares of Common Stock that were authorized for issuance under the Plan. Upon the effectiveness of this Registration Statement, an aggregate of 5,709,030 shares of Common Stock will be registered for issuance from time to time under the Plan. Pursuant to General Instruction E to Form S-8, the contents of the Registration Statements on Form S-8 (File Nos. 333-207973, 333-216968 and 333-223597) filed with the Commission on November 13, 2015, March 27, 2017 and March 12, 2018, are incorporated herein by reference except to the extent supplemented, amended or superseded by the information set forth herein. Only those items of Form S-8 containing new information not contained in the earlier registration statements are presented herein.

**PART II**

**INFORMATION REQUIRED IN THE REGISTRATION STATEMENT**

**Item 3. Incorporation of Documents by Reference.**

The following documents of the Registrant filed with the Commission are incorporated by reference in this Registration Statement as of their respective dates:

- (a) The Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2018, filed with the Commission on March 11, 2019;
- (b) The Registrant's Current Reports on Form 8-K (other than portions thereof furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits accompanying such reports that are related to such items) filed on January 4, 2019, February 20, 2019, February 26, 2019 and March 7, 2019; and
- (c) The description of the Registrant's Common Stock contained in the Form 8-A filed with the Commission on July 30, 2015 pursuant to the Securities Exchange Act of 1934, as amended (the "Exchange Act"), including any amendment or report filed for the purpose of further updating such description.

All documents subsequently filed by the Registrant pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act prior to the filing of a post-effective amendment which indicates that all securities offered hereby have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference into this Registration Statement and to be a part hereof from the date of filing of such documents; provided, however, that documents or information deemed to have been furnished and not filed in accordance with Commission rules shall not be deemed incorporated by reference into this Registration Statement. Any statement contained herein or in a document, all or a portion of which is incorporated or deemed to be incorporated by reference herein, shall be deemed to be modified or superseded for purposes of this Registration Statement to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or amended, to constitute a part of this Registration Statement.

**Item 8 Exhibits.**

| Exhibit No. | Description                                                                                                                                                                                                                                                                                |
|-------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 4.1         | <a href="#"><u>Sixth Amended and Restated Certificate of Incorporation of Zynerba Pharmaceuticals, Inc., effective August 10, 2015 (incorporated herein by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-37526) filed on August 10, 2015).</u></a> |
| 4.2         | <a href="#"><u>Amended and Restated By-laws of Zynerba Pharmaceuticals, Inc., effective August 10, 2015 (incorporated herein by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-37526) filed on August 10, 2015).</u></a>                            |
| 5.1         | <a href="#"><u>Opinion of Pepper Hamilton LLP (filed herewith).</u></a>                                                                                                                                                                                                                    |
| 10.1        | <a href="#"><u>Zynerba Pharmaceuticals, Inc. Amended and Restated 2014 Omnibus Incentive Compensation Plan (incorporated herein by reference to Exhibit 10.19(A) to the Registrant's Registration Statement on Form S-1 (File No. 333-205355) filed on June 30, 2015).</u></a>             |
| 10.2        | <a href="#"><u>Amendment to Amended and Restated 2014 Omnibus Incentive Compensation Plan (incorporated herein by reference to Exhibit 10.19(B) to the Registrant's Amendment No. 1 to Registration Statement on Form S-1 (File No. 333-205355) filed on July 23, 2015).</u></a>           |
| 23.1        | <a href="#"><u>Consent of KPMG LLP (filed herewith).</u></a>                                                                                                                                                                                                                               |
| 23.2        | <a href="#"><u>Consent of Pepper Hamilton LLP (included in Exhibit 5.1).</u></a>                                                                                                                                                                                                           |
| 24.1        | <a href="#"><u>Power of Attorney (included in signature page to this Registration Statement).</u></a>                                                                                                                                                                                      |

## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Devon, Commonwealth of Pennsylvania, on this 11th day of March, 2019.

### ZYNERBA PHARMACEUTICALS, INC.

By: /s/ Armando Anido  
Name: Armando Anido  
Title: Chief Executive Officer and Chairman of the Board of Directors

### POWER OF ATTORNEY

KNOW ALL BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Armando Anido and James Fickenschler, as his or her true and lawful attorney-in-fact and agent, with the full power of substitution, for him or her and in his or her name, place or stead, in any and all capacities, to sign any and all amendments to this registration statement (including post-effective amendments), and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

| <u>Signature</u>                                      | <u>Title</u>                                                                                    | <u>Date</u>    |
|-------------------------------------------------------|-------------------------------------------------------------------------------------------------|----------------|
| <u>/s/ Armando Anido</u><br>Armando Anido             | Chief Executive Officer and Chairman of the Board of Directors<br>(Principal Executive Officer) | March 11, 2019 |
| <u>/s/ James Fickenschler</u><br>James Fickenschler   | Chief Financial Officer<br>(Principal Financial and Accounting Officer)                         | March 11, 2019 |
| <u>/s/ John Butler</u><br>John Butler                 | Director                                                                                        | March 11, 2019 |
| <u>/s/ Warren D. Cooper</u><br>Warren D. Cooper       | Director                                                                                        | March 11, 2019 |
| <u>/s/ William J. Federici</u><br>William J. Federici | Director                                                                                        | March 11, 2019 |
| <u>/s/ Thomas L. Harrison</u><br>Thomas L. Harrison   | Director                                                                                        | March 11, 2019 |
| <u>/s/ Daniel L. Kisner</u><br>Daniel L. Kisner       | Director                                                                                        | March 11, 2019 |
| <u>/s/ Kenneth I. Moch</u><br>Kenneth I. Moch         | Director                                                                                        | March 11, 2019 |
| <u>/s/ Pamela Stephenson</u><br>Pamela Stephenson     | Director                                                                                        | March 11, 2019 |



3000 Two Logan Square  
Eighteenth and Arch Streets  
Philadelphia, PA 19103-2799  
215.981.4000  
Fax 215.981.4750

March 11, 2019

Board of Directors  
Zynerba Pharmaceuticals, Inc.  
80 W. Lancaster Avenue, Suite 300  
Devon, PA 19333

Ladies and Gentlemen:

We are acting as counsel to Zynerba Pharmaceuticals, Inc., a Delaware corporation (the “**Company**”), in connection with its registration statement on Form S-8, as amended (the “**Registration Statement**”), filed with the Securities and Exchange Commission under the Securities Act of 1933, as amended (the “**Act**”), relating to the proposed offering of up to 1,500,000 shares of common stock, par value \$0.001 per share, of the Company (the “**Shares**”), all of which Shares are issuable pursuant to the Zynerba Pharmaceuticals, Inc. Amended and Restated 2014 Omnibus Incentive Compensation Plan, as amended (the “**Plan**”). This opinion letter is furnished to you at your request to enable you to fulfill the requirements of Item 601(b)(5) of Regulation S-K, 17 C.F.R. § 229.601(b)(5), in connection with the Registration Statement.

For purposes of this opinion letter, we have examined copies of such agreements, instruments and documents as we have deemed an appropriate basis on which to render the opinions hereinafter expressed. In our examination of the aforesaid documents, we have assumed the genuineness of all signatures, the legal capacity of all natural persons, the accuracy and completeness of all documents submitted to us, the authenticity of all original documents, and the conformity to authentic original documents of all documents submitted to us as copies (including telecopies). As to all matters of fact, we have relied on the representations and statements of fact made in the documents so reviewed, and we have not independently established the facts so relied on. This opinion letter is given, and all statements herein are made, in the context of the foregoing.

This opinion letter is based as to matters of law solely on the Delaware General Corporation Law, as amended. We express no opinion herein as to any other statutes, rules or regulations.

Based upon, subject to and limited by the foregoing, we are of the opinion that following (i) effectiveness of the Registration Statement, (ii) issuance of the Shares pursuant to the terms of the Plan, and (iii) receipt by the Company of the consideration for the Shares specified in the resolutions of the Board of Directors or a duly authorized committee thereof, the Plan and any underlying award agreements or letters, the Shares will be validly issued, fully paid, and nonassessable.

This opinion letter has been prepared for use in connection with the Registration Statement. We assume no obligation to advise you of any changes in the foregoing subsequent to the effective date of the Registration Statement.

We hereby consent to the filing of this opinion letter as Exhibit 5.1 to the Registration Statement. In giving this consent, we do not thereby admit that we are an “expert” within the meaning of the Act.

Very truly yours,

/s/ PEPPER HAMILTON LLP

PEPPER HAMILTON LLP

**Consent of Independent Registered Public Accounting Firm**

The Board of Directors  
Zynerba Pharmaceuticals, Inc.:

We consent to the use of our report dated March 11, 2019, with respect to the consolidated balance sheets of Zynerba Pharmaceuticals, Inc. and subsidiary as of December 31, 2018 and 2017, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2018, and the related notes (collectively, the consolidated financial statements), incorporated herein by reference.

/s/ KPMG LLP

Philadelphia, Pennsylvania  
March 11, 2019

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