

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

SCHEDULE 13G
Under the Securities Exchange Act of 1934

(Amendment No. __)*

ZYNERBA PHARMACEUTICALS, INC.

(Name of Issuer)

Common Stock, par value \$0.001 per share

(Title of Class of Securities)

98986X109

(CUSIP Number)

October 5, 2015

(Date of Event Which Requires Filing of this Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

- Rule 13d-1(b)
- Rule 13d-1(c)
- Rule 13d-1(d)

*The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter the disclosures provided in a prior cover page.

The information required in the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

-
1. Names of Reporting Persons.
I.R.S. Identification Nos. of above persons (entities only).

RA Capital Management, LLC

2. Check the Appropriate Box if a Member of a Group (See Instructions)
(a)
(b)
-

3. SEC Use Only
-

4. Citizenship or Place of Organization **Massachusetts**
-

Number of Shares Beneficially Owned by Each Reporting Person With	5. Sole Voting Power	0 shares
	6. Shared Voting Power	578,575 shares
	7. Sole Dispositive Power	0 shares
	8. Shared Dispositive Power	578,575 shares

9. Aggregate Amount Beneficially Owned by Each Reporting Person
578,575 shares
-

10. Check if the Aggregate Amount in Row (9) Excludes
Certain Shares (See Instructions)
-

11. Percent of Class Represented by Amount in Row (9)
6.6%
-

12. Type of Reporting Person (See Instructions)
IA
-
-
-

-
1. Names of Reporting Persons.
I.R.S. Identification Nos. of above persons (entities only).

Peter Kolchinsky

-
2. Check the Appropriate Box if a Member of a Group (See Instructions)
(a)
(b)

-
3. SEC Use Only

-
4. Citizenship or Place of Organization **United States**

Number of Shares Beneficially Owned by Each Reporting Person With	5. Sole Voting Power	0 shares
	6. Shared Voting Power	578,575 shares
	7. Sole Dispositive Power	0 shares
	8. Shared Dispositive Power	578,575 shares

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9. Aggregate Amount Beneficially Owned by Each Reporting Person
578,575 shares

-
10. Check if the Aggregate Amount in Row (9) Excludes
Certain Shares (See Instructions)

-
11. Percent of Class Represented by Amount in Row (9)
6.6%

-
12. Type of Reporting Person (See Instructions)
IN
-
-

1. Names of Reporting Persons.
I.R.S. Identification Nos. of above persons (entities only).

RA Capital Healthcare Fund, L.P.

2. Check the Appropriate Box if a Member of a Group (See Instructions)
(a)
(b)

3. SEC Use Only

4. Citizenship or Place of Organization **Delaware**

Number of Shares Beneficially Owned by Each Reporting Person With	5. Sole Voting Power	0 shares
	6. Shared Voting Power	476,932 shares
	7. Sole Dispositive Power	0 shares
	8. Shared Dispositive Power	476,932 shares

9. Aggregate Amount Beneficially Owned by Each Reporting Person
476,932 shares

10. Check if the Aggregate Amount in Row (9) Excludes
Certain Shares (See Instructions)

11. Percent of Class Represented by Amount in Row (9)
5.5%

12. Type of Reporting Person (See Instructions)
PN (Limited Partnership)

CUSIP No. 98986X109

Item 1.

(a) **Name of Issuer:** Zynerba Pharmaceuticals, Inc. (the "Issuer").

(b) **Address of the Issuer's Principal Executive Offices:** 80 W. Lancaster Avenue, Suite 300, Devon, PA 19333.

Item 2.

(a) **Name of Person Filing:** This joint statement on Schedule 13G is being filed by Peter Kolchinsky, RA Capital Management, LLC ("Capital"), and RA Capital Healthcare Fund, L.P. (the "Fund"). Mr. Kolchinsky, Capital and the Fund are collectively referred to herein as the "Reporting Persons."

(b) **Address of Principal Business Office:** The principal business office of the Reporting Persons is c/o RA Capital Management, LLC, 20 Park Plaza, Suite 1200, Boston, MA 02116.

(c) **Citizenship:** Capital is a Massachusetts limited liability company. The Fund is a Delaware limited partnership. Mr. Kolchinsky is a United States citizen.

(d) **Title and Class of Securities:** Common stock ("Common Stock")

(e) **CUSIP Number:** 98986X109

Item 3. If this statement is filed pursuant to §§240.13d-1(b) or 240.13d-2(b) or (c), check whether the person filing is a:

Not applicable.

Item 4. Ownership:

Provide the following information regarding the aggregate number and percentage of the class of securities of the issuer identified in Item 1.

(a) Amount Beneficially Owned:**

RA Capital Management, LLC – 578,575 shares
Peter Kolchinsky – 578,575 shares
RA Capital Healthcare Fund, L.P. – 476,932 shares

(b) Percent of Class:**

RA Capital Management, LLC – 6.6%
Peter Kolchinsky – 6.6%
RA Capital Healthcare Fund, L.P. – 5.5%

(c) Number of shares as to which such person has:

(i) sole power to vote or to direct the vote **

RA Capital Management, LLC - 0 shares
Peter Kolchinsky - 0 shares
RA Capital Healthcare Fund, L.P. - 0 shares

(ii) shared power to vote or to direct the vote**

RA Capital Management, LLC – 578,575 shares
Peter Kolchinsky – 578,575 shares
RA Capital Healthcare Fund, L.P. – 476,932 shares

(iii) sole power to dispose or to direct the disposition of**

RA Capital Management, LLC - 0 shares
Peter Kolchinsky - 0 shares
RA Capital Healthcare Fund, L.P. - 0 shares

(iv) shared power to dispose or to direct the disposition of**

RA Capital Management, LLC – 578,575 shares
Peter Kolchinsky – 578,575 shares
RA Capital Healthcare Fund, L.P. – 476,932 shares

** RA Capital Management, LLC (“Capital”) is the general partner of RA Capital Healthcare Fund, L.P. (the “Fund”) and serves as investment adviser for a separately managed account (the “Account”). Peter Kolchinsky is the manager of Capital. Mr. Kolchinsky, Capital and the Fund are referred to herein collectively as the “Reporting Persons.” As the investment adviser to the Fund and the Account, Capital may be deemed a beneficial owner, for purposes of Section 13(d) of the Securities Exchange Act of 1934 (the “Act”), of any securities of the Issuer owned by the Fund or the Account. As the manager of Capital, Mr. Kolchinsky may be deemed a beneficial owner, for purposes of Section 13(d) of the Act, of any securities of the Issuer beneficially owned by Capital. Capital is a registered investment adviser within the meaning of Rule 13d-1(b)(1)(ii)(E) and Rule 16a-1(a)(v), and Mr. Kolchinsky is a parent or control person of Capital within the meaning of Rule 13d-1(b)(1)(ii)(G) and Rule 16a-1(a)(1)(vii). Capital and Mr. Kolchinsky disclaim beneficial ownership of the securities reported in this Schedule 13G Statement (the “Statement”) other than for the purpose of determining their obligations under Section 13(d) of the Act, and neither the filing of the Statement nor the filing of this Amendment shall not be deemed an admission that either Capital or Mr. Kolchinsky is or was the beneficial owner of such securities for any other purpose.

Item 5. Ownership of Five Percent or Less of a Class:

Not applicable.

Item 6. Ownership of More than Five Percent on Behalf of Another Person:

Not applicable.

CUSIP No. 98986X109

Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent Holding Company or Control Person:

Not applicable.

Item 8. Identification and Classification of Members of the Group:

Not applicable.

Item 9. Notice of Dissolution of Group:

Not applicable.

Item 10. Certification:

By signing below I hereby certify that, to the best of my knowledge and belief, the securities referred to above were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect.

SIGNATURE

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

DATE: October 14, 2015

RA CAPITAL MANAGEMENT, LLC

By: /s/ Rajeev Shah

Rajeev Shah
Authorized Signatory

PETER KOLCHINSKY

/s/ Peter Kolchinsky

RA CAPITAL HEALTHCARE FUND, L.P.

By: RA Capital Management, LLC
Its: General Partner

By: /s/ Rajeev Shah

Rajeev Shah
Authorized Signatory

Exhibit 1

JOINT FILING AGREEMENT

This Joint Filing Agreement, dated as of October 14, 2015, is by and among RA Capital Management, LLC, Peter Kolchinsky, and RA Capital Healthcare Fund, L.P. (the foregoing are collectively referred to herein as the "Filers").

Each of the Filers may be required to file with the United States Securities and Exchange Commission a statement on Schedule 13G and/or 13D with respect to Common Shares, par value \$0.001 per share of Zynerba Pharmaceuticals, Inc. beneficially owned by them from time to time.

Pursuant to and in accordance with Rule 13(d)(1)(k) promulgated under the Securities Exchange Act of 1934, as amended, the Filers hereby agree to file a single statement on Schedule 13G and/or 13D (and any amendments thereto) on behalf of each of such parties, and hereby further agree to file this Joint Filing Agreement as an exhibit to such statement, as required by such rule.

This Joint Filing Agreement may be terminated by any of the Filers upon one week's prior written notice or such lesser period of notice as the Filers may mutually agree.

Executed and delivered as of the date first above written.

RA CAPITAL MANAGEMENT, LLC

By: /s/ Rajeev Shah

Rajeev Shah
Authorized Signatory

PETER KOLCHINSKY

/s/ Peter Kolchinsky

RA CAPITAL HEALTHCARE FUND, L.P.

By: RA Capital Management, LLC
Its: General Partner

By: /s/ Rajeev Shah

Rajeev Shah
Authorized Signatory
