

SCHEDULE 13G

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

Under the Securities Exchange Act of 1934
(Amendment No.)*

Opthea Limited

(Name of Issuer)

Ordinary Shares, no par value

(Title of Class of Securities)

68386J208**

(CUSIP Number)

December 31, 2020

(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 disclosures provided in a prior cover page.

The information required on 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 (the "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).

**This CUSIP applies to the American Depositary Shares, each representing eight Ordinary Shares

1	NAMES OF REPORTING PERSONS Baker Bros. Advisors LP		
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)		(a) <input type="checkbox"/> (b) <input type="checkbox"/>
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 33,963,240 (1)	
	6	SHARED VOTING POWER -0-	
	7	SOLE DISPOSITIVE POWER 33,963,240 (1)	
	8	SHARED DISPOSITIVE POWER -0-	
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 33,963,240 (1)		
10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)		<input type="checkbox"/>
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 9.8% (1)(2)		
12	TYPE OF REPORTING PERSON (See Instructions) IA, PN		

- (1) Includes 26,469,640 Ordinary Shares ("Ordinary Shares") of Opthea Limited (the "Issuer") that are represented by 3,308,705 American Depositary Shares ("ADS") and 7,493,600 Ordinary Shares that are represented by 936,700 ADS issuable upon the exercise of Pre-Funded Warrants (as defined in Item 4 and subject to the limitations as described therein) directly held by funds managed by the reporter (the "Funds"). Each ADS represents 8 Ordinary Shares of the Issuer.
- (2) Based on 337,664,169 Ordinary Shares of the Issuer outstanding as of October 20, 2020, as reported in the Issuer's Prospectus filed with the Securities and Exchange Commission ("SEC") on October 19, 2020, plus 7,493,600 Ordinary Shares that are represented by 936,700 ADS issuable upon the exercise of the Pre-Funded Warrants (as defined in Item 4 and subject to the limitations as described therein).

1	NAMES OF REPORTING PERSONS Baker Bros. Advisors (GP) LLC	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
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 33,963,240 (1)
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10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 9.8% (1)(2)	
12	TYPE OF REPORTING PERSON (See Instructions) HC, OO	

- (1) Includes 26,469,640 Ordinary Shares of the Issuer that are represented by 3,308,705 ADS and 7,493,600 Ordinary Shares that are represented by 936,700 ADS issuable upon the exercise of Pre-Funded Warrants (as defined in Item 4 and subject to the limitations as described therein) directly held by the Funds. Each ADS represents 8 Ordinary Shares of the Issuer.
- (2) Based on 337,664,169 Ordinary Shares of the Issuer outstanding as of October 20, 2020, as reported in the Issuer's Prospectus filed with the SEC on October 19, 2020, plus 7,493,600 Ordinary Shares that are represented by 936,700 ADS issuable upon the exercise of the Pre-Funded Warrants (as defined in Item 4 and subject to the limitations as described therein).

1	NAMES OF REPORTING PERSONS Felix J. Baker		
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) (a) <input type="checkbox"/> (b) <input type="checkbox"/>		
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 33,963,240 (1)	
	6	SHARED VOTING POWER -0-	
	7	SOLE DISPOSITIVE POWER 33,963,240 (1)	
	8	SHARED DISPOSITIVE POWER -0-	
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 33,963,240 (1)		
10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>		
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 9.8% (1)(2)		
12	TYPE OF REPORTING PERSON (See Instructions) IN, HC		

- (1) Includes 26,469,640 Ordinary Shares of the Issuer that are represented by 3,308,705 ADS and 7,493,600 Ordinary Shares that are represented by 936,700 ADS issuable upon the exercise of Pre-Funded Warrants (as defined in Item 4 and subject to the limitations as described therein) directly held by the Funds. Each ADS represents 8 Ordinary Shares of the Issuer.
- (2) Based on 337,664,169 Ordinary Shares of the Issuer outstanding as of October 20, 2020, as reported in the Issuer's Prospectus filed with the SEC on October 19, 2020, plus 7,493,600 Ordinary Shares that are represented by 936,700 ADS issuable upon the exercise of the Pre-Funded Warrants (as defined in Item 4 and subject to the limitations as described therein).

1	NAMES OF REPORTING PERSONS Julian C. Baker	
2	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions) (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
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 33,963,240 (1)
	6	SHARED VOTING POWER -0-
	7	SOLE DISPOSITIVE POWER 33,963,240 (1)
	8	SHARED DISPOSITIVE POWER -0-
9	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 33,963,240 (1)	
10	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>	
11	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 9.8% (1)(2)	
12	TYPE OF REPORTING PERSON (See Instructions) IN, HC	

- (1) Includes 26,469,640 Ordinary Shares of the Issuer that are represented by 3,308,705 ADS and 7,493,600 Ordinary Shares that are represented by 936,700 ADS issuable upon the exercise of Pre-Funded Warrants (as defined in Item 4 and subject to the limitations as described therein) directly held by the Funds. Each ADS represents 8 Ordinary Shares of the Issuer.
- (2) Based on 337,664,169 Ordinary Shares of the Issuer outstanding as of October 20, 2020, as reported in the Issuer's Prospectus filed with the SEC on October 19, 2020, plus 7,493,600 Ordinary Shares that are represented by 936,700 ADS issuable upon the exercise of the Pre-Funded Warrants (as defined in Item 4 and subject to the limitations as described therein).

Schedule 13G

Item 1(a) Name of Issuer:

Opthea Limited (the "Issuer")

Item 1(b) Address of Issuer's Principal Executive Offices:

650 Chapel Street, Level 4

South Yarra, Victoria, Australia 3141

Item 2(a) Name of Person Filing:

This Schedule 13G is being filed jointly by Baker Bros. Advisors LP (the "Adviser"), Baker Bros. Advisors (GP) LLC (the "Adviser GP"), Felix J. Baker and Julian C. Baker (collectively, the "Reporting Persons").

Item 2(b) Address of Principal Business Office or, if None, Residence:

The business address of each of the Reporting Persons is:

c/o Baker Bros. Advisors LP

860 Washington Street, 3rd Floor

New York, NY 10014

(212) 339-5690

Item 2(c) Citizenship:

The Adviser is a limited partnership organized under the laws of the State of Delaware. The Adviser GP is a limited liability company organized under the laws of the State of Delaware. The citizenship of each of Julian C. Baker and Felix J. Baker is the United States of America.

Item 2(d) Title of Class of Securities

Ordinary Shares, no par value per share ("Ordinary Shares").

Item 2(e) CUSIP Number

68386J208

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

- (a) Broker or dealer registered under Section 15 of the Exchange Act.
- (b) Bank as defined in section 3(a)(6) of the Exchange Act.
- (c) Insurance company as defined in section 3(a)(19) of the Exchange Act.
- (d) Investment company registered under section 8 of the Investment Company Act of 1940.
- (e) An investment adviser in accordance with Rule 13d-1(b)(1)(ii)(E).
- (f) An employee benefit plan or endowment fund in accordance with Rule 13d-1(b)(1)(ii)(F).
- (g) A parent holding company or control person in accordance with Rule 13d-1(b)(1)(ii)(G).
- (h) A savings association as defined in Section 3(b) of the Federal Deposit Insurance Act.
- (i) A church plan that is excluded from the definition of an investment company under section 3(c)(14) of the Investment Company Act of 1940.
- (j) Group, in accordance with Rule 13d-1(b)(1)(ii)(J).

Item 4. Ownership.

Items 5 through 9 and 11 of each of the cover pages to this Schedule 13G are incorporated herein by reference. Set forth below is the aggregate number of Ordinary Shares represented by American Depositary Shares (“ADS”) directly held by each of Baker Brothers Life Sciences, L.P. (“Life Sciences”) and 667, L.P. (“667”, and together with Life Sciences, the “Funds”) which may be deemed to be indirectly beneficially owned by the Reporting Persons, as well as Ordinary Shares represented by ADS that may be acquired upon exercise of pre-funded warrants with no expiration date with an exercise price of \$0.00001 per ADS (“Pre-Funded Warrants”), subject to the limitations on exercise described below. Each ADS represents 8 Ordinary Shares of the Issuer.

The information set forth below is based on 337,664,169 Ordinary Shares outstanding as of October 20, 2020 as reported in the Issuer’s Prospectus filed with the Securities and Exchange Commission (“SEC”) on October 19, 2020, plus 7,493,600 Ordinary Shares represented by 936,700 ADS issuable upon the exercise of the Pre-Funded Warrants, subject to the limitations on exercise described below. Such percentage figures are calculated in accordance with Rule 13d-3 under the Securities Exchange Act of 1934, as amended.

Name	Number of Ordinary Shares we own or have the right to acquire within 60 days	Percent of Class Outstanding
667, L.P.	2,713,816	0.8%
Baker Brothers Life Sciences, L.P.	31,249,424	9.0%
Total	33,963,240	9.8%

The Pre-Funded Warrants are only exercisable to the extent that after giving effect to such exercise the holders thereof, their affiliates and any persons who are members of a Section 13(d) group with the holders or its affiliates would beneficially own in the aggregate, for purposes of Rule 13d-3 under the Exchange Act, no more than 9.99% of the outstanding ADS (“Maximum Percentage”). By written notice to the Issuer, the Funds may from time to time increase or decrease the Maximum Percentage applicable to that Fund to any other percentage not in excess of 19.99%. Any such increase will not be effective until the 61st day after such notice is delivered to the Issuer. As a result of this restriction, the number of ADS that may be issued upon exercise of the Pre-Funded Warrants by the above holders may change depending upon changes in the outstanding ADS.

Pursuant to the management agreements, as amended, among the Adviser, the Funds and their respective general partners, the Funds’ respective general partners relinquished to the Adviser all discretion and authority with respect to the investment and voting power of the securities held by the Funds and thus the Adviser has complete and unlimited discretion and authority with respect to the Funds’ investments and voting power over investments.

The Adviser GP, Felix J. Baker and Julian C. Baker as managing members of the Adviser GP, and the Adviser may be deemed to be beneficial owners of securities of the Issuer directly held by the Funds.

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

If this statement is being filed to report the fact that as of the date hereof the reporting person has ceased to be the beneficial owner of more than five percent of the class of securities, check the following []. N/A

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

N/A

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

The information in Item 4 is incorporated herein by reference.

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

N/A

Item 9. Notice of Dissolution of Group.

N/A

Item 10. Certification.

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were acquired and are held in the ordinary course of business and 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.

February 16, 2021

BAKER BROS. ADVISORS LP

By: Baker Bros. Advisors (GP) LLC, its general partner

By: /s/ Scott L. Lessing

Name: Scott L. Lessing

Title: President

BAKER BROS. ADVISORS (GP) LLC

By: /s/ Scott L. Lessing

Name: Scott L. Lessing

Title: President

/s/ Julian C. Baker

Julian C. Baker

/s/ Felix J. Baker

Felix J. Baker

AGREEMENT

In accordance with Rule 13d-1(k)(1) under the Securities Exchange Act of 1934, as amended, the undersigned hereby agree that this Statement on Schedule 13G relating to the Ordinary Shares of Opthea Limited is being filed with the Securities and Exchange Commission on behalf of each of them.

February 16, 2021

BAKER BROS. ADVISORS LP

By: Baker Bros. Advisors (GP) LLC, its general partner

By: /s/ Scott L. Lessing

Name: Scott L. Lessing

Title: President

BAKER BROS. ADVISORS (GP) LLC

By: /s/ Scott L. Lessing

Name: Scott L. Lessing

Title: President

/s/ Julian C. Baker

Julian C. Baker

/s/ Felix J. Baker

Felix J. Baker
