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UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, DC 20549

**SCHEDULE 13G**

Under the Securities Exchange Act of 1934

(Amendment No. 1)\*

**Opthea Limited**

(Name of Issuer)

**Ordinary Shares, no par value**

(Title of Class of Securities)

**68386J208\*\***

(CUSIP Number)

**December 31, 2021**

(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

<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> Baker Bros. Advisors LP
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>
<b>3</b>	<b>SEC USE ONLY</b>
<b>4</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> Delaware
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>5</b> <b>SOLE VOTING POWER</b> 26,427,521 (1)
	<b>6</b> <b>SHARED VOTING POWER</b> -0-
	<b>7</b> <b>SOLE DISPOSITIVE POWER</b> 26,427,521 (1)
	<b>8</b> <b>SHARED DISPOSITIVE POWER</b> -0-
<b>9</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 26,427,521 (1)
<b>10</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>
<b>11</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b> 7.5% (1)(2)
<b>12</b>	<b>TYPE OF REPORTING PERSON (See Instructions)</b> IA, PN

(1) Includes 25,569,528 Ordinary Shares (“Ordinary Shares”) of Opthea Limited (the “Issuer”) that are represented by 3,196,191 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”). Each ADS represents 8 Ordinary Shares of the Issuer.

(2) Based on 351,939,280 Ordinary Shares of the Issuer outstanding as of December 31, 2021, as reported in the Issuer’s Registration Statement on Form F-3 filed with the Securities and Exchange Commission (the “SEC”) on February 1, 2022.



<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> Baker Bros. Advisors (GP) LLC		
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>		
<b>3</b>	<b>SEC USE ONLY</b>		
<b>4</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> Delaware		
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>5</b>	<b>SOLE VOTING POWER</b> 26,427,521 (1)	
	<b>6</b>	<b>SHARED VOTING POWER</b> -0-	
	<b>7</b>	<b>SOLE DISPOSITIVE POWER</b> 26,427,521 (1)	
	<b>8</b>	<b>SHARED DISPOSITIVE POWER</b> -0-	
<b>9</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 26,427,521 (1)		
<b>10</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>		
<b>11</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b> 7.5% (1)(2)		
<b>12</b>	<b>TYPE OF REPORTING PERSON (See Instructions)</b> HC, OO		

(1) Includes 25,569,528 Ordinary Shares of the Issuer that are represented by 3,196,191 ADS directly held by the Funds. Each ADS represents 8 Ordinary Shares of the Issuer.

(2) Based on 351,939,280 Ordinary Shares of the Issuer outstanding as of December 31, 2021, as reported in the Issuer's Registration Statement on Form F-3 filed with the SEC on February 1, 2022.



<b>1</b>	<b>NAMES OF REPORTING PERSONS</b> Felix J. Baker		
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>		
<b>3</b>	<b>SEC USE ONLY</b>		
<b>4</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> United States		
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>5</b>	<b>SOLE VOTING POWER</b> 26,427,521 (1)	
	<b>6</b>	<b>SHARED VOTING POWER</b> -0-	
	<b>7</b>	<b>SOLE DISPOSITIVE POWER</b> 26,427,521 (1)	
	<b>8</b>	<b>SHARED DISPOSITIVE POWER</b> -0-	
<b>9</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 26,427,521 (1)		
<b>10</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>		
<b>11</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b> 7.5% (1)(2)		
<b>12</b>	<b>TYPE OF REPORTING PERSON (See Instructions)</b> IN, HC		

(1) Includes 25,569,528 Ordinary Shares of the Issuer that are represented by 3,196,191 ADS directly held by the Funds. Each ADS represents 8 Ordinary Shares of the Issuer.

(2) Based on 351,939,280 Ordinary Shares of the Issuer outstanding as of December 31, 2021, as reported in the Issuer's Registration Statement on Form F-3 filed with the SEC on February 1, 2022.



<b>1</b>	<b>NAMES OF REPORTING PERSONS</b>  Julian C. Baker		
<b>2</b>	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b>  (a) <input type="checkbox"/> (b) <input type="checkbox"/>		
<b>3</b>	<b>SEC USE ONLY</b>		
<b>4</b>	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b>  United States		
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	<b>5</b>	<b>SOLE VOTING POWER</b>  26,427,521 (1)	
	<b>6</b>	<b>SHARED VOTING POWER</b>  -0-	
	<b>7</b>	<b>SOLE DISPOSITIVE POWER</b>  26,427,521 (1)	
	<b>8</b>	<b>SHARED DISPOSITIVE POWER</b>  -0-	
<b>9</b>	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b>  26,427,521 (1)		
<b>10</b>	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b>  <input type="checkbox"/>		
<b>11</b>	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b>  7.5% (1)(2)		
<b>12</b>	<b>TYPE OF REPORTING PERSON (See Instructions)</b> IN, HC		

(1) Includes 25,569,528 Ordinary Shares of the Issuer that are represented by 3,196,191 ADS directly held by the Funds. Each ADS represents 8

Ordinary Shares of the Issuer.

- (2) Based on 351,939,280 Ordinary Shares of the Issuer outstanding as of December 31, 2021, as reported in the Issuer's Registration Statement on Form F-3 filed with the SEC on February 1, 2022.
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### Amendment No. 1 to Schedule 13G

This Amendment No. 1 to Schedule 13G amends and restates the previously filed Schedule 13G filed by Baker Bros. Advisors LP (the “Adviser”), Baker Bros. Advisors (GP) LLC (the “Adviser GP”), Julian C. Baker and Felix J. Baker (collectively, the “Reporting Persons”). Except as supplemented herein, such statements, as heretofore amended and supplemented, remain in full force and effect.

**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 Amendment No. 1 is being filed jointly by 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, 3<sup>rd</sup> 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

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**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 Amendment No. 1 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. Each ADS represents 8 Ordinary Shares of the Issuer.

The information set forth below is based on 351,939,280 Ordinary Shares outstanding as of December 31, 2021 as reported in the Issuer’s Registration Statement on Form F-3 filed with the Securities and Exchange Commission (“SEC”) on February 2, 2022. Such percentage figures are calculated in accordance with Rule 13d-3 under the Securities Exchange Act of 1934, as amended.

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Name	Number of Ordinary Shares we own or have the right to acquire within 60 days	Percent of Class Outstanding
667, L.P.	2,105,319	0.6%
Baker Brothers Life Sciences, L.P.	24,322,202	6.9%
<b>Total</b>	<b>26,427,521</b>	<b>7.5%</b>

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.

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**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 14, 2022

**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

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