

Form 604Corporations Act 2001
Section 671B**Notice of change of interests of substantial holder**To Company Name/Scheme Opthea LimitedACN/ARSN ACN 006 340 567**1. Details of substantial holder (1)**Name Baker Bros. Advisors LP and each of the persons and entities set out in Annexure AACN N/AThere was a change in the interests of the
substantial holder on 23 August 2022The previous notice was given to the company on 21 June 2021
The previous notice was dated 21 June 2021**2. Previous and present voting power**

The total number of votes attached to all the voting shares in the company or voting interests in the scheme that the substantial holder or an associate (2) had a relevant interest (3) in when last required, and when now required, to give a substantial holding notice to the company or scheme, are as follows:

Class of securities (4)	Previous notice		Present notice	
	Person's votes	Voting power (5)	Person's votes	Voting power (5)
Ordinary units	29,696,496	8.46%	28,763,289	7.1%

3. Changes in relevant interests

Particulars of each change in, or change in the nature of, a relevant interest of the substantial holder or an associate in voting securities of the company or scheme, since the substantial holder was last required to give a substantial holding notice to the company or scheme are as follows:

Date of change	Person whose relevant interest changed	Nature of change (6)	Consideration given in relation to change (7)	Class and number of securities affected	Person's votes affected
See Annexure C	667, L.P. Baker Brothers Life Sciences, L.P.	As set forth in Annexure C	As set forth in Annexure C	As set forth in Annexure C	As set forth in Annexure C

4. Present relevant interests

Particulars of each relevant interest of the substantial holder in voting securities after the change are as follows:

Holder of relevant interest	Registered holder of securities	Person entitled to be registered as holder (8)	Nature of relevant interest (6)	Class and number of securities	Person's votes
667, L.P.	667, L.P.	667, L.P.	Registered holder with power to vote or dispose of the shares	584,793 ordinary shares	584,793
667, L.P.	667, L.P.	667, L.P.	Relevant interest under Corporations Act s608(8) by way of American Depositary Shares	1,715,192 ordinary shares subject to 214,399 American Depositary Shares	1,715,192
Baker Brothers Life Sciences, L.P.	Baker Brothers Life Sciences, L.P.	Baker Brothers Life Sciences, L.P.	Registered holder with power to vote or dispose of the shares	6,647,368 ordinary shares	6,647,368
Baker Brothers Life Sciences, L.P.	Baker Brothers Life Sciences, L.P.	Baker Brothers Life Sciences, L.P.	Relevant interest under Corporations Act s608(8) by way of American Depositary Shares	19,815,936 ordinary shares subject to 2,476,992 American Depositary Shares	19,815,936
Each of the substantial shareholders	Each entity listed above in relation to the shares specified in respect of that entity	Each entity listed above in relation to the shares specified in respect of that entity	Deemed relevant interest by virtue of control by each of Julian Baker and Felix Baker of each of the other substantial holders	7,232,161 ordinary shares	7,232,161
Each of the substantial shareholders	Each entity listed above in relation to the shares specified in respect of that entity	Each entity listed above in relation to the shares specified in respect of that entity	Deemed relevant interest by virtue of control by each of Julian Baker and Felix Baker of each of the other substantial holders	21,531,128 ordinary shares subject to 2,691,391 American Depositary Shares	21,531,128

5. Changes in association

The persons who have become associates (2) of, ceased to be associates of, or have changed the nature of their association (9) with, the substantial holder in relation to voting interests in the company or scheme are as follows:

Name and ACN/ARSN (if applicable)	Nature of association
N/A	

6. Addresses

The addresses of persons named in this form are as follows:

Name	Address
Each of the substantial holders	860 Washington Street, 3 rd Floor New York New York 10014

Signature

print name Alexandra A. Toohey

capacity Chief Financial Officer

sign here

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Alexandra Tooley date 24 August 2022
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DIRECTIONS

- (1) If there are a number of substantial holders with similar or related relevant interests (eg. a corporation and its related corporations, or the manager and trustee of an equity trust), the names could be included in an annexure to the form. If the relevant interests of a group of persons are essentially similar, they may be referred to throughout the form as a specifically named group if the membership of each group, with the names and addresses of members is clearly set out in paragraph 6 of the form.
 - (2) See the definition of 'associate' in section 9 of the Corporations Act 2001.
 - (3) See the definition of 'relevant interest' in sections 608 and 671B(7) of the Corporations Act 2001.
 - (4) The voting shares of a company constitute one class unless divided into separate classes.
 - (5) The person's votes divided by the total votes in the body corporate or scheme multiplied by 100.
 - (6) Include details of:
 - (a) any relevant agreement or other circumstances because of which the change in relevant interest occurred. If subsection 671B(4) applies, a copy of any document setting out the terms of any relevant agreement, and a statement by the person giving full and accurate details of any contract, scheme or arrangement, must accompany this form, together with a written statement certifying this contract, scheme or arrangement; and
 - (b) any qualification of the power of a person to exercise, control the exercise of, or influence the exercise of, the voting powers or disposal of the securities to which the relevant interest relates (indicating clearly the particular securities to which the qualification applies).See the definition of 'relevant agreement' in section 9 of the Corporations Act 2001.
 - (7) Details of the consideration must include any and all benefits, money and other, that any person from whom a relevant interest was acquired has, or may, become entitled to receive in relation to that acquisition. Details must be included even if the benefit is conditional on the happening or not of a contingency. Details must be included of any benefit paid on behalf of the substantial holder or its associate in relation to the acquisitions, even if they are not paid directly to the person from whom the relevant interest was acquired.
 - (8) If the substantial holder is unable to determine the identity of the person (eg. if the relevant interest arises because of an option) write 'unknown'.
 - (9) Give details, if appropriate, of the present association and any change in that association since the last substantial holding notice.
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Annexure A

Page 1 of 1 of Annexure "A" referred to in ASIC Form 604 – Notice of change of interests of substantial holder, signed by me and dated 24 August 2022.

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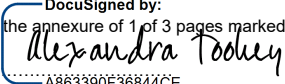
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Alexandra A. Toohy, Chief Financial Officer

Baker Bros. Advisors LP
Felix Baker
Julian Baker
Baker Bros. Advisors (GP) LLC
Baker Biotech, Capital (GP), LLC
Baker Biotech Capital, L.P.
Bakers Life Sciences, Capital (GP), LLC
Baker Brothers Life Sciences Capital, L.P.
Baker Brothers Life Sciences, L.P.
667, L.P.

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This is the annexure of 1 of 3 pages marked C mentioned in the Form 604 signed by me and dated 24 August 2022

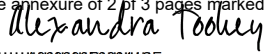

 Alexandra A. Tooney, Chief Financial Officer

Annexure C

Date of Change*	Person whose relevant interest change	Nature of Change (4)	Consideration given in relation to change (5)	Class of securities affected (6)	Number of Securities affected	Person's votes affected
8-Jul-2021	667, L.P.	4,880 Ordinary Shares borrowed under securities lending arrangement	N/A	Ordinary Shares	4,880	4,880
8-Jul-2021	Baker Brothers Life Sciences, L.P.	56,420 Ordinary Shares borrowed under securities lending arrangement	N/A	Ordinary Shares	56,420	56,420
8-Jul-2021	667, L.P.	Open market sales of 4,880 Ordinary Shares	AUD 6,832	Ordinary Shares	4,880	4,880
8-Jul-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 56,420 Ordinary Shares	AUD 78,988	Ordinary Shares	56,420	56,420
30-Aug-2021	667, L.P.	Open market sales of 17,872 Ordinary Shares in the form of 2,234 ADS	\$ 18,435.10	ADS	2,234	17,872
30-Aug-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 206,648 Ordinary Shares in the form of 25,831 ADS	\$ 213,158.91	ADS	25,831	206,648
31-Aug-2021	667, L.P.	1,144 Ordinary Shares in the form of 143 ADS borrowed under securities lending arrangement	N/A	ADS	143	1,144
31-Aug-2021	Baker Brothers Life Sciences, L.P.	13,256 Ordinary Shares in the form of 1,657 ADS borrowed under securities lending arrangement	N/A	ADS	1,657	13,256
31-Aug-2021	667, L.P.	Open market sales of 1,144 Ordinary Shares in the form of 143 ADS	\$ 1,183	ADS	143	1,144
31-Aug-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 13,256 Ordinary Shares in the form of 1,657 ADS	\$ 13,711	ADS	1,657	13,256
10-Sep-2021	667, L.P.	1,912 Ordinary Shares in the form of 239 ADS borrowed under securities lending arrangement	N/A	ADS	239	1,912
10-Sep-2021	Baker Brothers Life Sciences, L.P.	22,088 Ordinary Shares in the form of 2,761 ADS borrowed under securities lending arrangement	N/A	ADS	2,761	22,088
10-Sep-2021	667, L.P.	Open market sales of 1,912 Ordinary Shares in the form of 239 ADS	\$ 1,962	ADS	239	1,912
10-Sep-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 22,088 Ordinary Shares in the form of 2,761 ADS	\$ 22,669	ADS	2,761	22,088
10-Sep-2021	667, L.P.	13,164 Ordinary Shares borrowed under securities lending arrangement	N/A	Ordinary Shares	13,164	13,164
10-Sep-2021	Baker Brothers Life Sciences, L.P.	152,195 Ordinary Shares borrowed under securities lending arrangement	N/A	Ordinary Shares	152,195	152,195
10-Sep-2021	667, L.P.	Open market sales of 13,164 Ordinary Shares	AUD 19,052	Ordinary Shares	13,164	13,164
10-Sep-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 152,195 Ordinary Shares	AUD 220,272	Ordinary Shares	152,195	152,195
27-Sep-2021	667, L.P.	Open market sales of 768 Ordinary Shares in the form of 96 ADS	\$ 768	ADS	96	768
27-Sep-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 8,832 Ordinary Shares in the form of 1,104 ADS	\$ 8,832	ADS	1,104	8,832
14-Oct-2021	667, L.P.	Open market sales of 60,568 Ordinary Shares in the form of 7,571 ADS	\$ 57,738	ADS	7,571	60,568
14-Oct-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 700,232 Ordinary Shares in the form of 87,529 ADS	\$ 667,519	ADS	87,529	700,232
18-Oct-2021	667, L.P.	Open market sales of 11,941 Ordinary Shares	AUD 15,357	Ordinary Shares	11,941	11,941
18-Oct-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 138,059 Ordinary Shares	AUD 177,558	Ordinary Shares	138,059	138,059
19-Oct-2021	667, L.P.	Open market sales of 4,935 Ordinary Shares	AUD 6,360	Ordinary Shares	4,935	4,935
19-Oct-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 57,063 Ordinary Shares	AUD 73,537	Ordinary Shares	57,063	57,063
20-Oct-2021	667, L.P.	Open market sales of 2,216 Ordinary Shares	AUD 2,829	Ordinary Shares	2,216	2,216
20-Oct-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 25,622 Ordinary Shares	AUD 32,706	Ordinary Shares	25,622	25,622
21-Oct-2021	667, L.P.	Open market sales of 448 Ordinary Shares in the form of 56 ADS	\$ 427	ADS	56	448
21-Oct-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 5,152 Ordinary Shares in the form of 644 ADS	\$ 4,914	ADS	644	5,152
21-Oct-2021	667, L.P.	Open market sales of 502 Ordinary Shares	AUD 643	Ordinary Shares	502	502
21-Oct-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 5,808 Ordinary Shares	AUD 7,442	Ordinary Shares	5,808	5,808
22-Oct-2021	667, L.P.	Open market sales of 4,384 Ordinary Shares	AUD 5,619	Ordinary Shares	4,384	4,384
22-Oct-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 50,687 Ordinary Shares	AUD 64,960	Ordinary Shares	50,687	50,687
25-Oct-2021	667, L.P.	Open market sales of 2,143 Ordinary Shares	AUD 2,750	Ordinary Shares	2,143	2,143
25-Oct-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 24,782 Ordinary Shares	AUD 31,798	Ordinary Shares	24,782	24,782
26-Oct-2021	667, L.P.	Open market sales of 6,838 Ordinary Shares	AUD 8,709	Ordinary Shares	6,838	6,838
26-Oct-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 79,055 Ordinary Shares	AUD 100,684	Ordinary Shares	79,055	79,055
27-Oct-2021	667, L.P.	Open market sales of 1,774 Ordinary Shares	AUD 2,257	Ordinary Shares	1,774	1,774
27-Oct-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 20,515 Ordinary Shares	AUD 26,105	Ordinary Shares	20,515	20,515
28-Oct-2021	667, L.P.	Open market sales of 1,524 Ordinary Shares	AUD 1,939	Ordinary Shares	1,524	1,524
28-Oct-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 17,614 Ordinary Shares	AUD 22,414	Ordinary Shares	17,614	17,614
29-Oct-2021	667, L.P.	Open market sales of 5,922 Ordinary Shares	AUD 7,617	Ordinary Shares	5,922	5,922
29-Oct-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 68,464 Ordinary Shares	AUD 88,065	Ordinary Shares	68,464	68,464

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This is the annexure of 2 of 3 pages marked C mentioned in the Form 604 signed by me and dated 24 August 2022



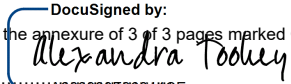
Alexandra A. Tooley, Chief Financial Officer

Annexure C

1-Nov-2021	667, L.P.	Open market sales of 2,869 Ordinary Shares	AUD 3,653	Ordinary Shares	2,869	2,869
1-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 33,175 Ordinary Shares	AUD 42,245	Ordinary Shares	33,175	33,175
2-Nov-2021	667, L.P.	Open market sales of 466 Ordinary Shares	AUD 593	Ordinary Shares	466	466
2-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 5,392 Ordinary Shares	AUD 6,861	Ordinary Shares	5,392	5,392
3-Nov-2021	667, L.P.	Open market sales of 1,121 Ordinary Shares	AUD 1,442	Ordinary Shares	1,121	1,121
3-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 12,966 Ordinary Shares	AUD 16,683	Ordinary Shares	12,966	12,966
5-Nov-2021	667, L.P.	Open market sales of 4,460 Ordinary Shares	AUD 5,597	Ordinary Shares	4,460	4,460
5-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 51,562 Ordinary Shares	AUD 64,705	Ordinary Shares	51,562	51,562
8-Nov-2021	667, L.P.	Open market sales of 1,144 Ordinary Shares in the form of 143 ADS	\$ 1,072.50	ADS	143	1,144
8-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 13,256 Ordinary Shares in the form of 1,657 ADS	\$ 12,427.44	ADS	1,657	13,256
8-Nov-2021	667, L.P.	Open market sales of 11,941 Ordinary Shares	AUD 15,288	Ordinary Shares	11,941	11,941
8-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 138,059 Ordinary Shares	AUD 176,757	Ordinary Shares	138,059	138,059
9-Nov-2021	667, L.P.	Open market sales of 768 Ordinary Shares in the form of 96 ADS	\$ 726.72	ADS	96	768
9-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 8,832 Ordinary Shares in the form of 1,104 ADS	\$ 8,357.24	ADS	1,104	8,832
10-Nov-2021	667, L.P.	Open market sales of 192 Ordinary Shares in the form of 24 ADS	\$ 180.00	ADS	24	192
10-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 2,208 Ordinary Shares in the form of 276 ADS	\$ 2,069.99	ADS	276	2,208
10-Nov-2021	667, L.P.	Open market sales of 2,549 Ordinary Shares	AUD 3,199	Ordinary Shares	2,549	2,549
10-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 29,474 Ordinary Shares	AUD 36,993	Ordinary Shares	29,474	29,474
12-Nov-2021	667, L.P.	Open market sales of 768 Ordinary Shares in the form of 96 ADS	\$ 720.24	ADS	96	768
12-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 8,832 Ordinary Shares in the form of 1,104 ADS	\$ 8,282.72	ADS	1,104	8,832
11-Nov-2021	667, L.P.	Open market sales of 11,941 Ordinary Shares	AUD 15,059	Ordinary Shares	11,941	11,941
11-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 138,059 Ordinary Shares	AUD 174,106	Ordinary Shares	138,059	138,059
15-Nov-2021	667, L.P.	Open market sales of 7,120 Ordinary Shares in the form of 890 ADS	\$ 6,741.09	ADS	890	7,120
15-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 82,280 Ordinary Shares in the form of 10,285 ADS	\$ 77,901.28	ADS	10,285	82,280
17-Nov-2021	667, L.P.	Open market sales of 47,848 Ordinary Shares in the form of 5,981 ADS	\$ 43,063.58	ADS	5,981	47,848
17-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 553,200 Ordinary Shares in the form of 69,150 ADS	\$ 497,884.38	ADS	69,150	553,200
17-Nov-2021	667, L.P.	Open market sales of 408 Ordinary Shares	AUD 511.02	Ordinary Shares	408	408
17-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 4,715 Ordinary Shares	AUD 5,905.54	Ordinary Shares	4,715	4,715
19-Nov-2021	667, L.P.	Open market sales of 356 Ordinary Shares	AUD 441.44	Ordinary Shares	356	356
19-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 4,120 Ordinary Shares	AUD 5,108.80	Ordinary Shares	4,120	4,120
22-Nov-2021	667, L.P.	Open market sales of 453 Ordinary Shares	AUD 562.58	Ordinary Shares	453	453
22-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 5,236 Ordinary Shares	AUD 6,502.59	Ordinary Shares	5,236	5,236
24-Nov-2021	667, L.P.	Open market sales of 1,311 Ordinary Shares	AUD 1,589.09	Ordinary Shares	1,311	1,311
24-Nov-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 15,158 Ordinary Shares	AUD 18,373.31	Ordinary Shares	15,158	15,158
13-Dec-2021	667, L.P.	Open market sales of 7,961 Ordinary Shares	AUD 9,570.71	Ordinary Shares	7,961	7,961
13-Dec-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 92,039 Ordinary Shares	AUD 110,649.29	Ordinary Shares	92,039	92,039
14-Dec-2021	667, L.P.	Open market sales of 23,882 Ordinary Shares	AUD 29,690.10	Ordinary Shares	23,882	23,882
14-Dec-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 276,118 Ordinary Shares	AUD 343,269.90	Ordinary Shares	276,118	276,118
15-Dec-2021	667, L.P.	Open market sales of 2,240 Ordinary Shares	AUD 2,816.80	Ordinary Shares	2,240	2,240

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Alexandra A. Tooley, Chief Financial Officer

Annexure C

15-Dec-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 25,903 Ordinary Shares	AUD 32,573.02	Ordinary Shares	25,903	25,903
16-Dec-2021	667, L.P.	Open market sales of 3,155 Ordinary Shares	AUD 4,004.33	Ordinary Shares	3,155	3,155
16-Dec-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 36,472 Ordinary Shares	AUD 46,290.26	Ordinary Shares	36,472	36,472
22-Dec-2021	667, L.P.	Open market sales of 665 Ordinary Shares	AUD 862.17	Ordinary Shares	665	665
22-Dec-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 7,694 Ordinary Shares	AUD 9,975.27	Ordinary Shares	7,694	7,694
29-Dec-2021	667, L.P.	Open market sales of 4,457 Ordinary Shares	AUD 5,734.38	Ordinary Shares	4,457	4,457
29-Dec-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 51,525 Ordinary Shares	AUD 66,292.07	Ordinary Shares	51,525	51,525
31-Dec-2021	667, L.P.	Open market sales of 339 Ordinary Shares	AUD 454.26	Ordinary Shares	339	339
31-Dec-2021	Baker Brothers Life Sciences, L.P.	Open market sales of 3,918 Ordinary Shares	AUD 5,250.12	Ordinary Shares	3,918	3,918
12-Jan-2022	667, L.P.	Open market sales of 733 Ordinary Shares	AUD 965.73	Ordinary Shares	733	733
12-Jan-2022	Baker Brothers Life Sciences, L.P.	Open market sales of 8,469 Ordinary Shares	AUD 11,157.91	Ordinary Shares	8,469	8,469
13-Jan-2022	667, L.P.	Open market sales of 800 Ordinary Shares	AUD 1,050.40	Ordinary Shares	800	800
13-Jan-2022	Baker Brothers Life Sciences, L.P.	Open market sales of 9,245 Ordinary Shares	AUD 12,138.69	Ordinary Shares	9,245	9,245
14-Jan-2022	667, L.P.	Conversion of 39,830 ADS to 318,640 Ordinary Shares	N/A	Ordinary Shares	318,640	318,640
14-Jan-2022	Baker Brothers Life Sciences, L.P.	Conversion of 460,170 ADS to 3,681,360 Ordinary Shares	N/A	Ordinary Shares	3,681,360	3,681,360
23-Aug-2022	667, L.P.	77,390 Ordinary Shares returned under securities lending arrangement	N/A	Ordinary Shares	77,390	77,390
23-Aug-2022	Baker Brothers Life Sciences, L.P.	875,820 Ordinary Shares returned under securities lending arrangement	N/A	Ordinary Shares	875,820	875,820
23-Aug-2022	667, L.P.	3,056 Ordinary Shares in the form of 382 ADS returned under securities lending arrangement	N/A	ADS	382	3,056
23-Aug-2022	Baker Brothers Life Sciences, L.P.	35,344 Ordinary Shares in the form of 4,418 ADS returned under securities lending arrangement	N/A	ADS	4,418	35,344
24-Aug-2022	667, L.P.	Purchase of 276,645 Ordinary Shares in a private placement	AUD 318,141.75	Ordinary Shares	276,645	276,645
24-Aug-2022	Baker Brothers Life Sciences, L.P.	Purchase of 3,069,980 Ordinary Shares in a private placement	AUD 3,530,477.00	Ordinary Shares	3,069,980	3,069,980

*New York time