4D pharma plc

Transforming how diseases are treated

4D pharma plc
Interim Report 2019

We are pioneers in harnessing bacteria as a novel and revolutionary class of medicines:

Live Biotherapeutics

What we do

We understand that bacteria in the human intestine – known as the gut microbiome – have an important function in many diseases.

Importantly, we understand *how* they function and how they could be used as a revolutionary new class of medicines known as Live Biotherapeutics.

Our deep understanding of bacterial functionality enables us to develop Live Biotherapeutics for a large number of diseases including cancer, gastrointestinal disease, respiratory disease and central nervous system ("CNS") disease.

What sets us apart

- We are targeting a new, safer approach to drug development
- We are a fully integrated microbiome company with the capability to progress from research to production to clinic
- We have a well established manufacturing facility capable of producing products for clinical trial supply and beyond
- We understand mechanism: how our products exert their therapeutic effects and act as a drug
- We have developed and wholly own the largest intellectual property estate in the field

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Highlights

Financial highlights

- Net assets as at 30 June 2019 of £35.0 million (30 June 2018: £58.7 million and 31 December 2018: £45.8 million).
- Cash and cash equivalents and short-term deposits at 30 June 2019 of £12.9 million (30 June 2018: £36.6 million and 31 December 2018: £26.2 million).
- Loss and comprehensive income for the six months ended 30 June 2019 of £11.3 million (30 June 2018: £11.3 million; 12 months ended 31 December 2018: £24.3 million).
- Research and development expenditure for the six months ended 30 June 2019 of £10.8 million (30 June 2018: £11.8 million; 12 months ended 31 December 2018: £24.9 million).

Operational and clinical highlights

- Commencement of a Phase I/II study of MRx0518 in combination with Keytruda in collaboration with MSD (tradename of Merck & Co., Inc., Kenilworth, N.J., USA). The two-part study is evaluating the safety, tolerability and preliminary clinical benefit of the combination in patients with melanoma, non-small-cell lung carcinoma ("NSCLC"), renal and bladder cancers who have relapsed on prior anti-PD-1 therapy.
- Commencement of a Phase Ib study of MRx0518 as a monotherapy in the neoadjuvant setting. The two-part study will evaluate the safety, tolerability and anti-tumour immunological effects of MRx0518 in patients with multiple solid tumour types.
- Presentation of first data of 4D's second-generation immuno-oncology candidate, MRx1299, outlining the mechanism of action and preliminary efficacy in preclinical models. Publication of the mechanism of action of MRx0518, outlining the bacterial effector molecule and host receptor which mediate its therapeutic effect.
- Appointment of two new Non-Executive Directors. The Company has welcomed Ed Baracchini, PhD, and Professor Axel Glasmacher, who bring significant biopharma industry experience to the Board of Directors.

Since the period end

- Appointment of Sandy Macrae, currently CEO of US-based Sangamo Therapeutics, as a Non-Executive Director.
- Commencement of a Phase I/II study of MRx-4DP0004 in patients with poorly controlled asthma. The study will enrol 90 asthma patients not adequately controlled on their current inhaler maintenance therapy. This is the world's first clinical study of a Live Biotherapeutic in patients with poorly controlled asthma.

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Chairman and Chief Executive Officer's Joint Review

David Norwood, Non-Executive Chairman, and Duncan Peyton, Chief Executive Officer

Live Biotherapeutics: transforming the way we treat disease

Proof-of-concept data on the horizon

The microbiome space, with 4D at the forefront, has continued to deliver a large body of data supporting the role of the microbiome in a variety of diseases. Given the nascent stage of the field, what has been lacking thus far is robust clinical proof-of-concept data to validate the overwhelming body of preclinical evidence.

We want 4D to be the first to deliver this data and have continued to invest in our clinical operations. So far in 2019, we have commenced three key studies in cancer and asthma and continue to make progress with our Phase II study in IBS. Before the end of the year, we expect to see the first readouts from these studies, with more to follow in 2020.

Differentiation: beyond the gut

The influence of the gut microbiome in organs which are anatomically distant from the gut is now widely accepted. The academic community, as well as microbiome industry leaders such as 4D, have continued to present work that demonstrates the impact that Live Biotherapeutics can have in diseases such as cancer, Alzheimer's disease and Parkinson's disease.

4D is now leading the development of Live Biotherapeutics that target diseases which manifest at sites away from the gut. As well as launching numerous clinical studies, we have continued to publish our research in the fields of cancer and asthma in leading scientific journals and at international conferences throughout 2019. More recently, our research team have utilised the MicroRx® platform to target the gut–brain axis, identifying new candidates for neurodegenerative conditions such as Parkinson's disease. These indications have been historically challenging for the pharmaceutical industry and Live Biotherapeutics represent a novel therapeutic approach that could fundamentally change the way these diseases are treated. This year, we have presented our work in this space for the first time; identifying single-strain Live Biotherapeutic candidates with striking effects on neurodegeneration and neuroinflammation that could represent a new paradigm in the treatment of neurodegenerative disease.

Delivering clinical progress

Oncology

So far in 2019, 4D has initiated two parallel studies to evaluate MRx0518 in different clinical settings, capturing the full spectrum of cancer disease stages.

The first of these two studies, being conducted in collaboration with MSD, is evaluating the combination of MRx0518 and MSD's Keytruda® in patients with advanced malignancies. The gut microbiome is known to influence patient response to checkpoint inhibitors, such as Keytruda®, which have transformed treatment for patients with late-stage disease. Although these therapies can be highly efficacious, only a minority of patients respond and there is a significant unmet need to find novel combinations which can boost response rates.

The patients enrolled in this study will have already received multiple previous lines of therapy and represent a population with very high unmet need and limited treatment options. The trial is assessing the potential for MRx0518 to re-engage the immune system in patients with melanoma, non-small-cell lung cancer, renal and bladder cancers who have lost response to prior checkpoint inhibitor therapy. Recruitment for the study is progressing well and we anticipate completion of Part A of the study, which will assess the safety and tolerability of MRx0518 in 12 patients, by the end of 2019, with preliminary efficacy data from this cohort to follow shortly after in 2020.

The second study, in collaboration with Imperial College London, is evaluating MRx0518 as a neoadjuvant monotherapy in newly diagnosed patients who have not previously received treatment for their cancer. The study employs a novel design, whereby patients are dosed with MRx0518 in the 2–4 week period following diagnosis and prior to surgery. In addition to being treatment naïve, study participants will not be administered concurrent therapies during the MRx0518 dosing period. This allows for a 'clean' evaluation of the anti-tumour immunological effects of MRx0518 in patients for the first time. We expect to see the first readouts from this study in 2020.

Asthma

Continuing our push towards diseases beyond the GI tract, we have initiated a Phase I/II study of MRx-4DP0004, in patients with poorly controlled asthma. Despite the availability of inhaler treatments, many asthma patients still struggle to achieve adequate control of their disease. MRx-4DP0004 has a unique mechanism of action, targeting both neutrophilic and eosinophilic airway inflammation, which may mean that it is able to treat patients in a way not currently possible with existing therapies.

The clinical study, which is led by Professor Chris Brightling, will enrol up to 90 patients who are not adequately controlled on their current inhaler maintenance therapy and will be offered MRx-4DP0004 as an add-on. As a first-in-man study, the primary endpoint will be safety and tolerability; however, the study will also assess a suite of secondary endpoints to assess the effects of MRx-4DP0004 on a range of efficacy metrics. Recruitment for this study is progressing well and we anticipate a readout before the end of 2020.

Chairman and Chief Executive Officer's Joint Review continued

David Norwood, Non-Executive Chairman, and Duncan Peyton, Chief Executive Officer

Delivering clinical progress continued

Irritable Bowel Syndrome

We continue to make progress with our Phase II study of Blautix in patients with IBS-C and IBS-D. This study, which is one of the largest Live Biotherapeutic trials ever conducted, is illustrative of our commitment to generating robust clinical data sets to demonstrate the efficacy of our products. In 2019, we significantly expanded the number of clinical study sites across the US and Europe and are pleased with the impact that has had on patient recruitment. We anticipate that the first readout from this study, an interim analysis of the microbiome data from a subset of patients, will be available early in Q4 this year.

Additions to the Board of Directors

Over the coming months and through 2020, we expect key data readouts from ongoing clinical studies in oncology, IBS and asthma, the results of which will have significant impact on the Company's development strategy and long-term value. We have brought in additional leadership and experience to our Board of Directors to help guide the Company through this critical period of our development and beyond.

Early in 2019, we welcomed Ed Baracchini, PhD, and Professor Axel Glasmacher as Non-Executive Directors, both of whom bring a wealth of experience in the biopharmaceutical industry. Having previously held roles as Chief Business Officer at Xencor and SVP Business Development at Metabasis Therapeutics, among others, Ed Baracchini has brought valuable biotech commercial expertise to the board. Professor Axel Glasmacher most recently held the role of SVP and Head of Oncology Global Clinical R&D at Celgene. His work led to the approvals of Revlimid®, Idhifa®, and Vidaza® and his track record of developing novel therapeutics through to approval will be of great value to the Company.

More recently, we welcomed Dr. Sandy Macrae as Non-Executive Director, bringing over 20 years of pharmaceutical industry experience to our board. Dr. Macrae currently serves as President and CEO of Sangamo Therapeutics, Inc, a role he has held since 2016. During this time the company has seen its market capitalisation increase from around $350 million to approximately $1.35 billion at the time of his appointment. We look forward to working with him at this exciting time in the Company's development.

Conclusion

In the first half of this year, we have laid the foundations for clinical success through the initiation of key studies in oncology and asthma, as well as continuing to make good progress in our Phase II trial in IBS. The second half of 2019 will see the first readouts from these studies, with further data expected throughout 2020. The next 6–12 months promise to be an exciting time for 4D pharma.

David Norwood
Non-Executive Chairman

Duncan Peyton
Chief Executive Officer
27 September 2019

Group Statement of Total Comprehensive Income

For the six months to 30 June 2019

	Notes	**Unaudited six months ended 30 June 2019 £000**	Unaudited six months ended 30 June 2018 £000	Audited year to 31 December 2018 £000
Research and development costs		**(10,796)**	(11,829)	(24,908)
Administrative expenses		**(2,337)**	(1,969)	(4,212)
Foreign currency (losses)/gains		**(739)**	605	749
Other operating income		**16**	—	—
Operating loss		**(13,856)**	(13,193)	(28,371)
Finance income		**65**	190	282
Finance expense		**(286)**	(167)	(348)
Loss before taxation		**(14,077)**	(13,170)	(28,437)
Taxation	4	**2,086**	2,520	4,747
Loss for the period		**(11,991)**	(10,650)	(23,690)
Other comprehensive income				
Exchange differences on translating foreign operations		**658**	(652)	(601)
Loss for the period and total comprehensive income for the period		**(11,333)**	(11,302)	(24,291)
Loss per share				
Basic and diluted for the period	5	**(18.31)p**	(16.26)p	(36.17)p

Group Statement of Financial Position

At 30 June 2019

	Notes	**At 30 June 2019 £000**	At 30 June 2018 £000	At 31 December 2018 £000
Assets				
Non-current assets				
Property, plant and equipment		**5,686**	5,001	4,865
Intangible assets		**14,258**	14,515	14,445
Taxation receivables		**247**	84	137
		20,191	19,600	19,447
Current assets				
Inventories		**288**	262	290
Trade and other receivables		**1,713**	2,193	1,248
Taxation receivables		**7,470**	6,442	5,393
Short-term investments and cash on deposit		**—**	15,151	10,174
Cash and cash equivalents		**12,895**	21,405	16,053
		22,366	45,453	33,158
Total assets		**42,557**	65,053	52,605
Liabilities				
Current liabilities				
Trade and other payables	6	**3,380**	3,251	5,177
		3,380	3,251	5,177
Non-current liabilities				
Deferred tax		**965**	965	966
Other payables	6	**3,244**	2,165	699
		4,209	3,130	1,665
Total liabilities		**7,589**	6,381	6,842
Net assets		**34,968**	58,672	45,763
Capital and reserves				
Share capital		**164**	164	164
Share premium		**108,296**	108,296	108,296
Merger reserve		**958**	958	958
Translation reserve		**725**	16	67
Other reserve		**(864)**	(864)	(864)
Share-based payments reserve		**699**	628	708
Retained earnings		**(75,010)**	(50,526)	(63,566)
Total equity		**34,968**	58,672	45,763

Approved by the Board and authorised for issue on 27 September 2019.

Duncan Peyton
Director
27 September 2019

Group Statement of Changes in Equity

For the six months to 30 June 2019

	Share capital £000	Share premium £000	Merger reserve £000	Translation reserve £000	Other reserve £000	Share-based payment reserve £000	Retained earnings £000	Total £000
At 1 January 2018	164	108,296	958	668	(864)	440	(39,876)	69,786
Loss and total comprehensive income for the period	—	—	—	—	—	—	(10,650)	(10,650)
Foreign currency gains/losses arising on consolidation of subsidiaries	—	—	—	(652)	—	—	—	(652)
Issue of share-based compensation	—	—	—	—	—	188	—	188
At 30 June 2018	164	108,296	958	16	(864)	628	(50,526)	58,672
Loss and total comprehensive income for the year	—	—	—	—	—	—	(13,040)	(13,040)
Foreign currency gains/losses arising on consolidation of subsidiaries	—	—	—	51	—	—	—	51
Issue of share-based compensation	—	—	—	—	—	80	—	80
At 31 December 2018	164	108,296	958	67	(864)	708	(63,566)	45,763
Loss and total comprehensive income for the year	—	—	—	—	—	—	(11,991)	(11,991)
Foreign currency gains/losses arising on consolidation of subsidiaries	—	—	—	658	—	—	—	658
Issue of share-based compensation	—	—	—	—	—	538	—	538
Non-vesting share-based compensation	—	—	—	—	—	(547)	547	—
At 30 June 2019	**164**	**108,296**	**958**	**725**	**(864)**	**699**	**(75,010)**	**34,968**

Group Cash Flow Statement

For the six months to 30 June 2019

	Unaudited six months ended 30 June 2019 £000	Unaudited six months ended 30 June 2018 £000	Audited year to 31 December 2018 £000
Loss after taxation	**(11,991)**	(10,650)	(23,690)
Adjustments for:			
Depreciation of property, plant and equipment	**531**	443	905
Amortisation of intangible assets	**144**	148	296
Loss on disposal of property, plant and equipment	**29**	—	1
Finance income	**(65)**	(190)	(282)
Finance expense	**286**	167	348
Share-based compensation	**538**	188	268
Cash flows from operations before movements in working capital	**(10,528)**	(9,894)	(22,154)
Changes in working capital:			
Decrease/(increase) in inventories	**2**	(9)	(37)
(Increase)/decrease in trade and other receivables	**(584)**	393	1,894
Increase in taxation receivables	**(2,190)**	(2,164)	(1,166)
Increase/(decrease) in trade and other payables	**187**	(1,614)	(1,474)
Cash outflow from operating activities	**(13,113)**	(13,288)	(22,937)
Cash flows from investing activities			
Purchases of property, plant and equipment	**(271)**	(259)	(537)
Purchase of software and other intangibles	**(18)**	(4)	(4)
Acquisition of subsidiaries net of cash acquired	**—**	—	(660)
Interest received	**76**	115	378
Monies drawn from deposit	**10,174**	22,982	27,959
Net cash inflow from investing activities	**9,961**	22,834	27,136
Cash flows from financing activities			
Hire purchase payments	**(6)**	(6)	(10)
Interest paid	**—**	—	(1)
Net cash outflow from financing activities	**(6)**	(6)	(11)
(Decrease)/increase in cash and cash equivalents	**(3,158)**	9,540	4,188
Cash and cash equivalents at the start of the year	**16,053**	11,865	11,865
Cash and cash equivalents at the end of the year	**12,895**	21,405	16,053

The cash outflow of £660,000 in respect of the acquisition of subsidiaries net of cash acquired relates to the investment by the Group in 4D Pharma León S.L.U. in 2016. The outflow in the financial year to 2018 represents the final instrument of deferred consideration concerning successful GMP certification attained during the previous reporting period.

Notes to the Interim Financial Report

For the six months ended 30 June 2019

1. Basis of preparation

The Group's half-yearly financial information, which is unaudited, consolidates the results of 4D pharma plc and its subsidiary undertakings up to 30 June 2019. The Group's accounting reference date is 31 December. 4D pharma plc's shares are quoted on the AIM Market of the London Stock Exchange ("AIM").

The Company is a public limited liability company incorporated, registered and domiciled in the UK. The consolidated financial information is presented in round thousands of Pounds Sterling (£000).

The financial information for the six months ended 30 June 2019 and 30 June 2018 are unaudited.

Full audited financial statements of the Group in respect of the period ended 31 December 2018, which received an unqualified audit opinion and did not contain a statement under section 498(2) or (3) of the Companies Act 2006, have been delivered to the Registrar of Companies.

The accounting policies used in the preparation of the financial information for the six months ended 30 June 2019 are in accordance with the recognition and measurement criteria of International Financial Reporting Standards as adopted by the European Union ("IFRS") and are consistent with those which will be adopted in the annual financial statements for the year ending 31 December 2019.

Whilst the financial information included has been prepared in accordance with the recognition and measurement criteria of IFRS, the financial information does not contain sufficient information to comply with IFRS.

4D pharma plc has not applied IAS 34 Interim Financial Reporting, which is not mandatory for UK AIM listed groups, in the preparation of this interim financial report.

2. Going concern

The Group and parent company are subject to a number of risks similar to those of other development stage pharmaceutical companies. These risks include, amongst others, generation of revenues in due course from the development portfolio and risks associated with research, development and obtaining regulatory approval of its products. Ultimately, the attainment of profitable operations is dependent on future uncertain events which include obtaining adequate financing to fulfil the Group's commercial and development activities and generating a level of revenue to support the Group's cost structure.

The Directors have prepared detailed financial forecasts and cash flows looking beyond twelve months from the date of the approval of these financial statements. In developing these forecasts, the Directors have made assumptions based upon their view of the current and future economic conditions that are expected to prevail over the forecast period. The Directors estimate that the cash held by the Group together with known receivables will be sufficient to support the current level of activities into the fourth quarter of 2019. The Directors are continuing to explore sources of finance available to the Group and have a reasonable expectation that they will be able to secure sufficient cash inflows into the Group to continue its activities for not less than twelve months from the date of approval of these accounts. They have therefore prepared the financial statements on a going concern basis.

Because the additional finance is not committed at the date of approval of these financial statements, these circumstances represent an uncertainty as to the Group's ability to continue as a going concern. Should the Group be unable to obtain further finance such that the going concern basis of preparation were no longer appropriate, adjustments would be required including provisions to reduce the balance sheet values of assets to their recoverable amounts, and to provide for future liabilities that may arise.

3. Significant accounting policies

For periods commencing 1 January 2019 and onwards "IFRS 16 Leases" came into effect. IFRS 16 distinguishes leases and service contracts on the basis of whether an identifiable asset is controlled by a customer. Distinctions of operating leases (off Statement of Financial Position) and finance leases (on Statement of Financial Position) are removed for lessee accounting and are replaced by a model where a right-of-use and corresponding liability have to be recognised for all leases (i.e. all on Statement of Financial Position) except for short-term leases and low value assets.

Having undertaken a review of outstanding leases the Group have adopted the modified retrospective approach with no reserves adjustment after due consideration of the impact on the overall financial results. The adoption of this approach resulted in the Group recognising additional right-of-use property lease assets and lease liabilities of £1,186,274. In addition, the overall effect of the changes arising through the recognition of interest and depreciation, whilst removing items formerly recognised as operating leases, is an increase in loss for the period to 30 June 2019 of £52,330.

Notes to the Interim Financial Report continued

For the six months ended 30 June 2019

4. Taxation

The tax credit is made up as follows:

	Unaudited six months ended 30 June 2019 £000	Unaudited six months ended 30 June 2018 £000	Audited year to 31 December 2018 £000
Current income tax			
Total current income tax	**2,086**	2,520	4,760
Adjustment in respect of prior years	**—**	—	(13)
Total income tax credit recognised in the year	**2,086**	2,520	4,747

5. Loss per share

Basic and diluted

	Unaudited six months ended 30 June 2019 £000	Unaudited six months ended 30 June 2018 £000	Audited year to 31 December 2018 £000
Loss for the year attributable to equity shareholders	**(11,991)**	(10,650)	(23,690)
Weighted average number of shares			
Ordinary shares in issue	**65,493,842**	65,493,842	65,493,842
Basic loss per share (pence)	**(18.31)p**	(16.26)p	(36.17)p

The basic and diluted loss per share are the same as the effect of share options is anti-dilutive.

6. Other payables

	Unaudited six months ended 30 June 2019 £000	Unaudited six months ended 30 June 2018 £000	Audited year to 31 December 2018 £000
Non-current payables			
Contingent consideration	**2,145**	2,144	684
Hire purchase and finance leases	**1,099**	21	15
	3,244	2,165	699

Contingent consideration

The non-current contingent consideration is made up as follows:

	Unaudited six months ended 30 June 2019 £000	Unaudited six months ended 30 June 2018 £000	Audited year to 31 December 2018 £000
Brought forward	**2,325**	1,979	1,979
Unwinding of discount	**195**	165	346
	2,520	2,144	2,325
Analysed as follows:			
Within one year	**375**	—	1,641
More than one year	**2,145**	2,144	684
	2,520	2,144	2,325

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