

Fund Objective

The main objective of the Fund is to seek long-term capital growth by investing mainly in shares of companies that have their principle business in the pharmaceuticals, biotechnology and life science sectors, or profiting from them. The Fund invests globally, is actively managed and is not benchmark constrained.

Investment Theme — Precision Medicine

Precision Medicine is the fundamental revolution in drug discovery and patient treatment of the 21st century. Traditional medicine is being transformed into patient specific solutions that treat disease at its underlying cause. This intersection of a genomic and biotechnology revolution is changing lives, now.

Investment Manager

Lead Portfolio Manager

Mark Dainty

MPharm, FCA



BlueBox Precision Medicine Fund Performance

Performance to 31.08.2023	1 month	YTD
BlueBox Precision Medicine Fund	- 1.4 %	4.8 %
S&P BMI Healthcare Index ¹	- 1.5 %	5.2 %

¹ S&P Global BMI Healthcare INDEX is Net Total Return, calculated since launch of BBPM on 28 February 2023.

Investment Manager Biography

Mark joined BlueBox in 2022 to launch the BlueBox Precision Medicine Fund. He has been researching and investing in the Healthcare sector since 2006. Prior to BlueBox he was the Lead Portfolio Manager of a pharmaceuticals and biotechnology fund at Norges Bank Investment Management for 6 years. He also spent 3 years at Blackrock as a global healthcare analyst and 6 years at Citi in a leading equity research team covering European pharmaceuticals. He holds a Masters in Pharmacy and became a Chartered Accountant (FCA) with KPMG. This combination is critical for evaluating businesses that create lasting value through innovation in the biopharmaceutical sector.

What is Precision Medicine?

Precision Medicine is a transformational change in what humanity can do to improve people's lives. It is a more targeted approach to medicine than the one-size-fits-all methods of the last 100+ years. It exists at the intersection of major advances in genomics, biotechnology, chemistry, molecular biology and computing power. It enables scientists to understand the underlying biological drivers of an increasing number of diseases. Once the underlying cause of a disease is elucidated through molecular biology and genomics, much more effective medicines can be developed using the latest technology in biotechnology and chemistry. All of this is supported by ever increasing computing power.

Precision Medicines address the underlying driver of a disease and eligible patients may be selected using a diagnostic test. By targeting the specific driver, the benefit of precision medicine is much greater than traditional medicine. Furthermore, patients without the relevant driver are unlikely to benefit and can be treated with an alternative, avoiding unnecessary side effects and saving money.

Approvals of precision medicines started accelerating in 2010 and have continued to do so. Originally these started in rare genetic diseases and certain subsets of oncology. There is plenty of growth in these areas but it is also expanding into new, more common diseases. This underpins our belief that there are decades of growth ahead for the field.

Top 10 Holdings

Argenx	6.1 %
Vertex Pharmaceuticals	5.9 %
BioMarin Pharmaceutical	5.2 %
Sartorius Stedim	4.8 %
Natera Inc	4.5 %
Regeneron Pharmaceuticals	4.4 %
Danaher	4.1 %
Blueprint Medicines	4.1 %
Alnylam Pharmaceuticals	4.0 %
Thermo Fisher Scientific	3.9 %
Total	47.0 %

Top Countries

United States	72.7 %
Belgium	6.1 %
France	4.8 %
United Kingdom	4.3 %
Denmark	3.4 %
Switzerland	3.4 %
Italy	3.1 %
Cash & equivalents	2.2 %

Market Capitalisation

Mega cap (>\$100bn)	11.4 %
Large cap – upper (\$50bn - \$100bn)	10.4 %
Large cap – lower (\$10bn - \$50bn)	35.7 %
Mid cap (\$1bn - \$10bn)	31.5 %
Small cap (<\$1bn)	8.8 %
Cash & equivalents	2.2 %

Sector Allocation

Biotechnology	62.3 %
Life Sciences	31.4 %
Pharmaceuticals	4.1 %
Cash & equivalents	2.2 %

Top 10 Holdings, Top Countries, Market Capitalisation & Sector Allocation as of 31.08.2023

Mark Dainty's Monthly Comment

The fund was down 1.4% in August, well ahead of the S&P Select Biotechnology Index (-5.8%) and just ahead of the S&P BMI Healthcare Index (-1.5%). Healthcare outperformed broader global equity markets by c.1.5% in August.

In the first six months of its life the fund has returned 4.8%, which is 8.8% ahead of the S&P Select Biotechnology Index and broadly in line with the S&P BMI Healthcare Index.

This return has been achieved even though most of the precision medicine enablers in the portfolio have been detractors. Despite the mixed performance from this group it remains an important part of the portfolio. The headwinds are a mixture of industry wide and company specific, and 2Q23 earnings showed divergent trends. Natera (+30% in Aug.) performed well with the roll out of its blood based circulating DNA (ctDNA) tests for cancer exceeding estimates, supported by operational progress also improving margins. On the other hand, there was poorer performance at Illumina (-14%) which is contending with a range of issues that we believe can be overcome with time. Interestingly the bioprocessing companies (manufacturing tech/services for biologic drugs) have posted positive returns since the end of June, despite guidance downgrades/2Q misses. The reaction to 2Q commentary on customer de-stocking bottoming has been positive. We have probably passed the worst in share price terms as the market starts to discount a return to growth.

Other stock specific news of note in the month was as follows:

Novo Nordisk is our only mega-cap pharmaceutical holding due to its fast growth, R&D culture and a growing commitment to precision medicine via its acquisition of an RNA company and various cell therapy programs. The Precision Medicine efforts have been overshadowed by the value created from the rapid uptake of the diabetes and obesity drugs, Ozempic and Wegovy. Novo and Lilly, the two main players in this market, are now the largest pharmaceutical companies in the world at c.\$422bn and \$526bn respectively. Good news in obesity continued with a large trial showing that Wegovy reduces the risk of heart attack, stroke and cardiovascular death in obese, non-diabetic, patients with a history of cardiovascular disease. This supports the class and increases the potential for wider reimbursement, especially in the US Government Medicare program for over 65's. The data pushed the shares up 17% in August. There is no doubt the opportunity is very large and Novo is an excellent company in many aspects. However, we are limiting its size in the fund and its place is under consideration for various reasons.

Rhythm Pharmaceuticals is an obesity company that is completely precision medicine focused as its drug, Imcivree, treats specific forms of obesity at the causal genetic pathway (melanocortin). In August it rose 46% due to good 2Q sales and reports that France has started to reimburse use of its drug for hypothalamic obesity (HO), where surgery disrupts melanocortin signalling and causes obesity. HO can increase the drug's addressable population by 2-3x. The early reimbursement is notable because there is only phase 2 data so far and it is not approved by regulators. This is a rare outcome that is a major validation of the phase 2 data and the unmet need. It clearly bodes well for the future. Phase 3 data in this indication is due in 4Q24 but sales from France should appear soon.

Blueprint Medicines was down 25% in the month but is flat since the end of April. Expectations had risen into 2Q results and while the company beat consensus it was clearly not enough. We had trimmed a little prior to results and have recently added back to target weight.

Design Therapeutics - The company reported disappointing phase 1 data for its lead product in a rare disease called Friedrich's ataxia. The company aims to treat genetic diseases caused by specific types of repeating DNA sequences. The mechanism appeared to be active to some degree, but a safety issue due to formulation prevented further investigation of higher doses. The data has raised our concern about the other programs enough that we decided to exit. The stock was down c.66% in August at our exit price, thankfully it was only a 50bp position, further highlighting our risk management strategy in the earliest stage companies. As always we reserve the right to change our mind pending further data.

There is plenty of news flow ahead for our portfolio companies, which supports our conviction that we are at the beginning of a multi-decade growth trend of more targeted Precision Medicines. The BlueBox Precision Medicine Fund aims to capture this growth through both drug developers and enablers of Precision Medicine.

Portfolio Construction

Asset Class	Equity
Number of Securities	25 - 45
Weight	10% maximum
Turnover	Low (typically 30 - 40%)
Market Cap	Mainly Targeting \$1 bn - \$80 bn
Geographic Allocation	Global
Cash	Minimal cash, always below 10%
Benchmark	Flexible, not benchmark oriented

Key Facts

Fund Base Currency	USD
Liquidity	Daily
Fund Type	UCITS
Legal Status	SICAV
Domicile	Luxembourg
Auditor	PwC
Custodian	Northern Trust Global Services SE
Launch Date	28 February 2023

Share Classes

	S Acc. Retail	A Acc. Retail	I Acc. Institutional
Min. Initial Investment:	\$ 10,000.-	\$ 10,000.-	\$ 150,000.-
Annual Management Fee:	1.0% AUM \$100m - \$150m: 0.5% AUM >\$150m: 0%	1.5 %	1.0%
Launch Date:	28 Feb 2023	14 Jun 2023	
USD			
ISIN:	LU2519375591	LU2519372499	LU2519373547
Bloomberg Ticker:	BLUBSUA LX	BLUBAUA LX	BLURUA LX
EUR			
ISIN:		LU2519375161	LU2519373380
Bloomberg Ticker:		BLUBFAE LX	BLUBIEA LX
GBP			
ISIN:		LU2519375245	LU2519373463
Bloomberg Ticker:		BLURAGA LX	BLURBIA LX

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