# BlueBox Funds - BlueBox Precision Medicine Fund

## Investing in tomorrow's medicine, today

***This is a marketing communication**. Please refer to the Prospectus and KID of the Fund for more information on general terms, risks, and fees. Investors should only invest in the Fund once they have reviewed the Prospectus and KID before making any final investment decisions.*

Precision Medicine Fund

bluebox

### Annual Investor Report 2025—BlueBox Precision Medicine

2025 can be divided into two very different periods that closely mirror 2024. The first half saw significant headwinds for healthcare including the life sciences and biotechnology sub-sectors that the fund is focused on. With the subsequent half being much more positive.

The headwinds were the result of President Trump's liberation day in early April coinciding with Robert F. Kennedy Jr's job cuts at the Food and Drug Administration (FDA) and changes to grant awards at the National Institutes of Health (NIH). FDA staff cuts drove concerns about the ability of the industry to get drugs approved. While the NIH grant changes, driven in part by a political battle between leading universities and President Trump, affected researchers spending on new equipment and consumables in life sciences.

By the low point in mid-April the fund was down 22% for the year to date (the same as the S&P Select Biotechnology Index and 17% behind the S&P BMI Healthcare Index) as this was a perfect storm for our positioning.

In mid-April many companies were trading close to, or below, cash value. We reassessed the risk-reward of our pipeline stocks and found the downside be limited at a portfolio level, with significant upside, so increased our holdings in post-proof of concept pipeline companies that we knew well, adding around 5% of the AUM to this group, through stocks like Revolution Medicines, Nuvalent, Denali and Dyne therapeutics. A steady recovery followed and by mid-year the fund had closed half the deficit to the S&P BMI Healthcare Index and was down only 10% for the year to date.

As time passed it became clear that FDA was approving new drugs and that eventually the NIH grant money would begin to flow. The summer started with a steady stream of positive clinical data and increasing M&A in the sector, against the backdrop of a potentially slowing economy. By September there was more positive clinical trial data from several of the larger mid-cap biotechnology companies. Pfizer signed a drug pricing agreement with President Trump, which provided a blueprint for further deals by other companies, removing the worst-case scenario. Meanwhile M&A news continued coming through to year-end.

The fund did not own many of the companies that had positive data in September, in part because of our benchmark agnostic construction and specific focus on precision medicine but also some specific investment decisions we made. As a result, it lagged the initial rally but caught up in October and November. **For the full year the fund's S-class returned 31.3% net of fees vs 15.7% for the S&P BMI Healthcare Index and 35.6% for the S&P Select Biotechnology Index.**

2025 was characterized by significant volatility in both directions. Price appreciation post the April lows was multi-fold in some SMID cap biotech stocks so one different decision could have easily made a difference of 10% to total portfolio return.

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The fund returns for the year were driven by strong performance across all types of companies. More details on these are below.

**Since inception in February 2023 the fund's S-class was up 60% which is approximately 12% ahead of the S&P Select Biotechnology Index and 34% ahead of the S&P BMI Healthcare index, annualized returns have exceeded 18%, comparing well to our mid-teens goal.**

*Figure 1 – The BlueBox Precision Medicine Fund - S Class; S&P BMI Healthcare Index; S&P Select Biotechnology Index and MSCI ACWI World Index 31/12/2024-31/12/2025 (rebased to 100).*


Source: Bloomberg

**During the year the fund's top five positive contributors were:**

**Revolution Medicines** (+82%) contributed c.4.5% to return. Our decision to make it a top position in the April sell-off proved to be very helpful during the fourth quarter as the company provided additional data about its RAS targeting drugs in earlier stages of pancreatic cancer, while also completing recruitment in its first phase 3 in 2nd line metastatic pancreatic cancer, setting up results for 1H26. It also received an FDA Commissioners National Priority Voucher, a new scheme aiming to approve a drug within 1-2 months instead of the usual 8-12 months, setting up a potential launch in late 2026/early 2027.

## Annual Investor Report 2025—BlueBox Precision Medicine

**Guardant Health** (+160%) contributed c.3%. The company has executed well as it rolled out its new colorectal cancer screening test, Shield. It has also added lung cancer screening to the same test. Its larger existing oncology testing offering that selects precision medicines for diagnosed patients accelerated in the third quarter. All three led to higher long-term guidance and earnings estimates.

**Rhythma Pharmaceuticals** (+91%) contributed c.3% after reporting phase 2 data for its in-licensed oral drug, targeting the same melanocortin pathway as its existing daily injectable, Imcivree. The oral drug can not only extend the IP lifecycle but has fewer side effects and may expand patient uptake. The company also reported positive phase 2 data in Prader-Willi syndrome for Imcivree, a new indication not in consensus estimates. Rhythm is set for a transformational 2026 as it rolls out Imcivree into hypothalamic obesity (approval expected in April) and new phase 3 data in genetic forms of obesity.

**Avidity Bioscience**s (+141%) added c.3% after it received an acquisition proposal from Novartis in October. We recycled the capital into other positions shortly after the news.

**Wave Life Sciences** (+37%) added c.2%. We added to our position ahead of critical phase 1 data for WVE-007 a silencing RNAi therapy for obesity that targets a genetically validated target, Activin E. This proved to be a good decision as the data showed the ability to reduce visceral and subcutaneous fat while sparing muscle, with a single injection. The stock was up nearly 3x in a week and subsequently settled to around twice the pre-release price. With more updates to come in 2026 on this and its other lead program we have maintained a mid-sized position.

**The five main detractors during the year were:**

**Rocket Pharmaceuticals** (-72%) detracted c.3%. In May a safety event occurred in its gene therapy trial for the severe cardiac condition, Danon disease. We felt the issue could be overcome so we decided to hold on to the position. Rocket quickly aligned with the FDA to resume the trial with different dosing. The rest of the cardiac gene therapy pipeline has continued to advance. We expect the company to recover through time as it proves its ability to execute.

**Replimune** (-77%) – detracted c.1.5% as the FDA declined to approve its oncolytic virus therapy for late-stage melanoma in July. We decided to exit the position at that time as it wasn't obvious that the concerns could be addressed easily with the available capital.

## Annual Investor Report 2025—BlueBox Precision Medicine

**Bicycle Therapeutics** (-49%) suffered from a lack of major news flow in 2026 to change investor perceptions about the viability of its programs. The company is one of the remaining ones to still trade at a low EV, despite plenty of capital on the balance sheet. Its lead program is an improved drug conjugate targeting chemotherapy to Nectin-4 expressing tumours, with the aim of providing similar activity to Pfizer's Padcev in bladder cancer, but with less toxicity. The market does not believe this will lead to value creation. At the same time, the company has steadily evolved its focus to more novel approaches such as a precision medicine approach targeting Nectin-4 amplification in lung and breast cancer and advancing an early-stage pipeline of radio-pharmaceuticals for cancer. 2026 should see data emerge starting to prove these programs.

**Maravai** (-52%) detracted c.1%. Poor execution had already taken the stock down significantly in 2024, and we should have exited then. In 2025 there was pressure evident in research budgets which put any recovery at risk and the new US administration had taken a negative view on mRNA vaccines and research further increasing the risks, so we decided to put the capital elsewhere.

**Immunovant** (-40%) detracted c.1%. The stock sold off during the period to mid-April. At that time, we sold the stock and put the capital into other positions that had fallen further and had news flow that was likely to drive returns sooner. This was purely a decision about optimising timing and risk-reward.

### Outlook

The fundamentals for the sector are good, innovation continues to be strong, and the regulatory environment is generally supportive albeit with some volatility in timelines and personnel at the FDA. The funding environment is also good as increased M&A activity has enabled capital to be recycled. While valuations are not at the distressed levels they were in April, they are by no means exuberant. Since the market is rewarding investors for taking risk it appears to be a good time to deploy capital.

Precision Medicine's reach continues to expand, as evidenced by the growth in genetic cancer testing and screening, as well as newly approved medicines or pipeline clinical data for everything from rare diseases to oncology, nephrology, neurology and metabolic diseases.

Precision Medicine is beneficial to all stakeholders – patients, society, payers, the industry and investors. All the pieces are in place for the fund to continue benefiting from the growth in precision medicine through both the companies developing, selling and enabling it.

### Mark Dainty, Lead Manager - BlueBox Precision Medicine