

**Strictly embargoed for publication until 7.30 a.m. on 22 September 2003**

## **INTERNATIONAL BIOTECHNOLOGY TRUST plc**

The Board of International Biotechnology Trust Plc today announces its unaudited Preliminary Results for the year ended 31 August 2003.

### **Summary**

- Strong recovery in the biotech market since the lows of July 2002
- Three unquoted IBT portfolio companies, together representing 16% of net assets (at 31 August 2003), have filed to go public on the NASDAQ, market conditions permitting
- Net asset value per share rose by 14.5% to 112.8p
- NASDAQ Biotech Index rose 48.1% (sterling adjusted), Merrill Lynch Small Cap Biotech Index rose by 26.5% (sterling adjusted) and the Bloomberg UK Biotech Index fell by 5.0%
- The return on IBT's quoted portfolio was 46.4% calculated on a monthly time-weighted return basis assuming mid-month cash flows, and 29.9% on an unweighted basis (ignoring the timing of transactions)
- Write-downs of two unquoted companies resulted in a fall in net assets for the year of £1.4 million or 2.9% of net assets at 31 August 2002
- New investments in seven quoted companies; sales of five quoted companies
- No new unquoted investments; follow-on investments in CancerVax and Affibody
- Total net assets at 31 August 2003: £53.9million (31 August 2002: £47.9 million)

Andrew Barker, Chairman, commented:

“After three years of falling stock markets I am pleased to be able to report better results following the recovery in markets generally and specifically the biotech sector. The valuations of the unquoted companies are based on tangible third party priced events, which include trade sales, initial public offerings (IPOs) and third party financings. We are encouraged that three of our unquoted companies, Aderis Pharmaceuticals, CancerVax and Eyetech Pharmaceuticals, (together representing 16% of net assets at 31 August 2003) have recently filed to go public on NASDAQ, market conditions permitting.

Investor sentiment towards the biotech sector is currently very positive. At the time of writing, although the biotech IPO window has yet to open in the US, twelve biotech companies have filed to go public, and IBT has investments in three of these. We believe that most of our portfolio companies, both quoted and unquoted, continue to make good progress and are generally well financed.

The fundamentals for the biotech industry remain intact with favourable demographics and high barriers to entry once products are approved. More and more biotech companies are turning profitable, product pipelines continue to widen and mature and there are more late stage compounds in development than ever before. The biggest issue facing the drug industry is a lack of new product opportunities and biotech companies are well placed to take advantage of this, as pharmaceutical companies are willing to enter rich strategic partnerships even at early development stages. The prospects for smaller biotech companies are consequently stronger than for some time.

The volatility of the biotech market does mean that IBT remains better suited to the longer-term investor as the short to medium term direction of the market remains difficult to predict. IBT offers investors exposure to an exciting industry with strong prospects through a portfolio of companies with strong upside potential, diversified across the private and public markets and by clinical area and geography.”

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## **CHAIRMAN'S STATEMENT**

### PERFORMANCE AND REVIEW

After three years of falling stock markets I am pleased to be able to report better results following the recovery in the markets generally and specifically the biotech sector. During the year to 31 August 2003, the net asset value (NAV) per share of International Biotechnology Trust (IBT) rose by 14.5% from 98.5p to 112.8p with the share price rising by 11.1% from 76.5p to 85.0p. During the period under review the NASDAQ Biotechnology Index (NBI) rebounded strongly and rose 48.1%, the Merrill Lynch Small Cap Biotech Index (MLSCI) rose by 26.5% and the Bloomberg UK Biotechnology Index fell by 5.0%, all in sterling terms.

We measure the performance of the Company in a number of different ways. The portfolio is predominantly composed of smaller biotech companies, which makes it difficult to compare the performance of IBT directly with the NBI, which is heavily weighted towards larger companies. We believe that an index which is more small cap focused is more useful, especially when looking at the performance of the quoted portfolio. The Merrill Lynch Small Cap Biotech Index currently consists of 117 biotech companies with market caps of less than US\$1bn. As mentioned previously, this index rose by 26.5% in sterling terms during the period under review.

IBT's smaller quoted holdings were hit badly during the correction in the market following the boom of 1999 and 2000, as investor focus moved towards the larger, profitable companies or those with projected near term earnings. The recent rally is the first post-bubble rally in which all the tiers of the market have benefited, although smaller biotech companies have still lagged their larger peers during the year under review. The performance of IBT's quoted portfolio has been calculated on a monthly time-weighted return basis (assuming mid-month cash flows) and showed a rise of 46.4%. The return on an unweighted basis (ignoring the timing of transactions) was 29.9%.

So far 2003 has been a much better year for the biotech market than 2002. The recovery in the value of biotech stocks has been driven by better general stock market conditions and an improvement in newsflow from the sector. There have been a run of regulatory approvals, strong clinical data (especially in the area of cancer) and better than anticipated earnings from a number of large, profitable companies.

At 31 August 2003, IBT's unquoted portfolio represented 42% of net assets (value £22.7m) against 43% (value £20.8m) at the previous financial year end. The valuations of the unquoted companies are based on tangible third party priced events, which include trade sales, initial public offerings (IPOs) and third party financings. We are encouraged that three of our unquoted companies, Aderis Pharmaceuticals, CancerVax and Eyetech Pharmaceuticals, (together representing 16% of net assets at 31 August 2003) have recently filed to go public on NASDAQ, market conditions permitting.

### BASIS OF VALUATION

As is practice in the venture capital industry, the IBT portfolio is valued in accordance with the British Venture Capital Association guidelines. The carrying valuations of unquoted companies are reviewed weekly and incorporate consideration of the progress of the underlying company against milestones made at the time of investment and any upcoming need to raise capital. In certain circumstances quoted holdings are valued at discounts to their mid market prices.

Ahead of each investment considerable due diligence is undertaken, making use of a comprehensive network of scientific and clinical advisers, with particular focus on management, science and valuation. Members of Schroder Ventures Life Sciences (SVLS), the investment adviser to IBT, have board seats on eight of the portfolio companies, at the

time of writing. This allows the performance of these companies to be closely monitored and the input of strategic and financial advice drawing on the experience of the SVLS team and their network of advisers, which include the IBT Scientific Advisory Board.

### CONTINUATION VOTE

The Articles of Association of the Company contain provisions requiring the Directors to put a proposal for the continuation of the Company to shareholders at the Annual General Meeting in 2003 and thereafter at two yearly intervals.

In considering whether to recommend to Shareholders that the Company continue in business as an investment trust, the Board of Directors has reviewed four particular aspects of its business:

- The prospects for the biotech sector
- The prospects for the portfolio
- The strength and depth of our management
- The appropriateness of the investment trust structure

We consider the fundamentals of the biotech sector to be compelling and these are outlined below and in the 'Investment Advisers' Review'. Our adviser, SVLS, has assembled a portfolio of quoted and unquoted, generally smaller, emerging biotech companies, which we believe to be well positioned to benefit from the increase in interest in the sector, especially the three unquoted companies that are potential IPO candidates. As I have said in previous statements, I believe that we have a leading team of advisers in SVLS, with considerable depth of skill, experience and resources. Finally, investment trusts, with their closed-end structures and boards of independent directors, have proved to be an effective vehicle for making long-term investments and we believe that this will continue to be the case.

For these reasons the Board of Directors is particularly excited about the prospects for your Company. Recent soundings with major shareholders indicate strong support for the Company to continue and the Directors intend to vote their 146,183 shares in favour of the ordinary resolution to continue in business as an investment trust.

### SHARE BUY-BACKS

At the Annual General Meeting held on 19 December 2002, the Directors were authorised to purchase for cancellation up to 14.99% of the shares in issue. Since that time, the Directors have utilised this authority to purchase a total of 800,000 shares for cancellation. We intend to continue to consider opportunities to purchase shares for cancellation in appropriate market conditions, at prices that would usefully enhance the net asset value for remaining shareholders and with the intention of reducing discount volatility. A resolution to renew the share buy-back authority is included in the notice of the Annual General Meeting.

### ANNUAL GENERAL MEETING

The Annual General Meeting will be held at 31 Gresham Street, London EC2V 7QA on 14 November 2003 at 3.00 p.m. A presentation will be made by Kate Bingham and other members of the SVLS team.

### OUTLOOK

Investor sentiment towards the biotech sector is currently very positive. At the time of writing, although the biotech IPO window has yet to open, twelve biotech companies have filed to go public in the US, and IBT has investments in three of these. We believe that our portfolio companies, both quoted and unquoted, continue to make good overall progress and are generally well financed.

The fundamentals of the biotech industry remain intact with favourable demographics and high barriers to entry once products are approved. More and more biotech companies are turning profitable, product pipelines continue to widen and mature and there are more late stage compounds in development than ever before. The biggest issue facing the drug industry is a lack of new product opportunities and biotech companies are well placed to take advantage of this, as pharmaceutical companies are willing to enter rich strategic partnerships even at early development stages. The prospects for smaller biotech companies are consequently stronger than for some time.

The volatility of the biotech market does mean that both IBT and the sector remain better suited to the longer-term investor, as the short to medium term direction of the market remains difficult to predict. IBT offers investors exposure to an exciting industry with strong prospects through a portfolio of companies with strong upside potential, diversified across the private and public markets and by clinical area and geography.

Andrew Barker  
Chairman

## **INVESTMENT ADVISERS REVIEW**

### SUMMARY

Investor sentiment regarding the biotech sector is much improved since the last Annual Report. The biotech market has rallied significantly and the recent approvals and strong clinical data underscore the progress that the industry is making in bringing new drugs to market. A reflection of this positive sentiment is the recent improvement in the share price and NAV of IBT and the filing of three unquoted portfolio companies to try and go public if the initial public offering (IPO) window opens.

### REVIEW

2002 was a difficult year for the biotech sector. Share prices were driven lower by the overall bear market, impending war in Iraq and a lack of appetite for risk. This led to a flight to quality and a lack of interest in the more volatile sectors including biotech. Newsflow from biotech companies was poor with corporate scandals and a number of drug candidate failures, which resulted in a heightened sensitivity of investors to the risks of clinical development.

Smaller companies were hit the hardest in the sell off, which impacted the performance of IBT given its investment focus in this area. Many smaller companies were left trading below cash and some were delisted from the NASDAQ market, including one of IBT's portfolio investments, Essential Therapeutics.

The NASDAQ Biotech Index (NBI) bottomed at just over 400 in July 2002. At the time of writing the index had reached 798, a near doubling in dollar terms since the lows of 2002. This compares with the peak in the market in March 2000 when the index reached over 1600.

There have been a number of drivers of the recovery in the sector. Removal of the uncertainty around the conflict in Iraq, an increased appetite for risk and a broad bullish market direction have rewarded higher beta groups such as biotech and technology. However, the rally has not only been driven by improving general sentiment, but also by strengthening industry fundamentals. The NBI has significantly outperformed both the general market, rising by 48.1% in sterling terms, in comparison with rises of 8.1% in the S&P500 Index and 35.2% in NASDAQ Composite Index (which gives a reflection of the performance of technology stocks) during the year under review.

The initial rebound in biotech share prices was led by the large cap, profitable companies. However investor interest has extended beyond these limited names and into the smaller and earlier stage companies, which had suffered the most in the flight to liquidity of the previous years. The breadth of the recent rally has been notable as previous post-bubble rallies have been limited to the top tier of stocks. This has benefited the performance of IBT with some of the smaller cap holdings rising sharply in the year under review, for example Targeted Genetics which almost tripled in price. However, as noted in the Chairman's statement, the small caps still underperformed their larger peers in the year under review with the Merrill Lynch Small Cap Biotech Index (MLSCI) rising 26.5% in sterling terms in comparison with a 48.1% rise in the NBI.

The rally has been underpinned by the release of better than anticipated earnings by a number of large, profitable biotech companies, with sales of approved products going strongly. While earnings growth may be an issue in the pharmaceutical sector, biotech companies continue to post strong results with a number of companies recently moving into profitability.

Positive sentiment around the regulatory environment has also drawn interest to the sector. In contrast to the relatively low expectations following the disappointments of 2002, there

have been a string of timely drug approvals this year. New leadership at the Food and Drug Administration (FDA) already seems to be having an impact with eleven new biotech drug approvals in 2003, at the time of writing. The FDA appears to be committed to shortening the time it takes to review new drug applications and improving the predictability of the review process.

Recent approvals include two exciting first-in-class drugs in the cancer field. AstraZeneca's Iressa was approved for the treatment of advanced non-small cell lung cancer and Millennium Pharmaceutical's Velcade was approved for the treatment of relapsed and refractory multiple myeloma less than four months after the application was made. Both drugs were approved on the basis of Phase II trials rather than more typical larger controlled Phase III trials. First-in-class drugs typically attract additional scrutiny from the regulatory authority and these approvals illustrate the efforts of the FDA to be flexible about its approach to the evaluation of drug candidates that address life threatening diseases where little or no therapy is currently available.

A spate of positive recent clinical trial data has helped spur share prices. In May 2003, Genentech presented results from a Phase III trial of Avastin, which showed an improvement in the overall survival of colorectal cancer patients. Many investors were not expecting a positive outcome following poor data in breast cancer in 2002 and the results played a major role in rekindling interest in the sector. Avastin could be the first to market of a new class of drugs called angiogenesis inhibitors, which choke off the supply of blood to tumours.

Further encouraging clinical data was released by one of IBT's investments, Esperion Therapeutics. Esperion has a promising pipeline for the treatment of cardiovascular disease. These drug candidates are designed to increase levels of HDL (the so-called good cholesterol), and to reduce the build up of cholesterol-laden plaques in the arteries of patients. In June 2003, initial Phase II results were released showing a reduction in plaque volume in the arteries of patients with acute coronary syndromes. This is an exciting finding and we await the full details of the trial, which will be reported in the coming months.

Company pipelines continue to broaden and mature and many of the announcements made by later-stage portfolio companies are described later in the report. The pipelines of IBT's earlier stage investments have also made progress. KuDOS Pharmaceuticals started Phase II trials of its drug candidate, PaTrin, in metastatic melanoma and colorectal cancer patients. AnorMED started Phase II trials with AMD 3100 for stem cell transplant in cancer patients. Inflazyme's lead compound started a Phase IIa asthma study with partner Aventis, and Targeted Genetics and the Cystic Fibrosis Foundation initiated a Phase IIb trial in cystic fibrosis. Finally, Epimmune's HIV vaccine candidate entered Phase I/II trials and a second vaccine entered Phase I/II trials in lung cancer and colorectal cancer patients.

The biotech sector has benefited from corporate activity as product acquisitions are used to diversify pipelines and revenue streams. There were a number of mergers and acquisitions (M&A) announcements from within IBT's investment portfolio. Novuspharma agreed to merge with Cell Therapeutics (CTIC) adding a late stage drug candidate, pixantrone, to CTIC's pipeline. OSI Pharmaceuticals acquired Cell Pathways, adding a marketed oncology product and expanding its pipeline through an earlier stage therapeutic platform. Inflazyme bought GlycoDesign to expand further in the area of inflammation and to boost cash reserves. CancerVax brought in an early stage pipeline of angiogenesis inhibitors through the acquisition of Cell-Matrix, and Corvas merged with Dendreon Corporation. Finally, Galen announced in July 2003 that it was in preliminary discussions with a potential acquirer, although these talks were terminated without the emergence of a bid for the company.

There have been some acquisitions of biotech companies by pharmaceutical companies, for example Johnson & Johnson's acquisition of one of IBT's investments, 3-Dimensional Pharmaceuticals. However, these acquisitions have been limited in number as

pharmaceutical companies have tended to avoid depressing earnings by buying unprofitable biotech companies.

As patent expiries loom, the reliance of pharmaceutical companies on biotech to replenish dwindling pipelines has increased the price that these companies are willing to pay for synergistic assets. This has continued to be demonstrated through a variety of deals, although the number of collaborations has not increased noticeably. Within the portfolio, in December 2002, EyeTech announced a major deal with Pfizer for Macugen, which is in Phase II/III trials for age-related macular degeneration (AMD), and Phase II trials for diabetic macular edema. EyeTech received a \$100m upfront payment and could receive a further \$645m in milestones, contingent on regulatory approvals and successful commercialisation.

An unquoted IBT portfolio company, Sunesis, announced deals with both Merck & Co. and Biogen during the year under review. With Merck, Sunesis entered a research collaboration to discover oral therapeutics for Alzheimer's disease and with Biogen, a collaboration was initiated to discover therapeutics for inflammatory and auto-immune diseases.

Another example of a licensing deal by an IBT portfolio company, although with a larger biotech rather than a pharmaceutical company, was the co-development agreement between Micromet and Medimmune for the Phase I stage anti-cancer agent MT103. MT103 is the most advanced of Micromet's novel class of antibody derivatives, Bi-Specific T Cell Engagers (BiTEs). Micromet will receive milestone payments based on successful development and commercialisation, as well as royalties on North American sales. In addition, the parties will collaborate to develop up to six new BiTE drug candidates.

The combination of solid earnings, product approvals, strong clinical data and partnering has meant that momentum has continued to build in the biotech market. This has allowed issuers to aggressively tap both the secondary and convertible markets in order to bolster cash reserves. Many of the convertible debt financings have incorporated attractive terms for issuers due to the low interest rate environment and volatility of the sector.

The surge in financing activity has allowed many of IBT's portfolio companies to extend their cash runways including Alexion Pharmaceuticals, Aradigm, Esperion Therapeutics, Indevus Pharmaceuticals, Inspire Pharmaceuticals, Nektar Therapeutics, OSI Pharmaceuticals, Sirna Therapeutics (formerly Ribozyme Therapeutics) and Targeted Genetics.

Despite the flurry of secondary financings there have not been any biotech IPOs since April 2002. Only one healthcare company has gone public this year, a profitable managed care company called Molina Healthcare. It is possible that an IPO window for biotech companies may open in the USA later this year, market conditions permitting. The later stage, higher quality private companies with nearer term revenue/profit opportunities are best positioned to be able to take advantage of any such opening. At the time of writing a number of biotech companies have filed to try and go public on the NASDAQ market. Examples from IBT's portfolio include Aderis Pharmaceuticals, CancerVax and EyeTech Pharmaceuticals.

Aderis has four product candidates in development for six indications. The most advanced of these is a transdermal patch partnered with Schwarz Pharma, in Phase III trials for Parkinson's disease and in Phase IIb for the treatment of Restless Legs syndrome. CancerVax has a therapeutic cancer vaccine, in Phase III trials for the treatment of advanced stage melanoma and EyeTech has been described previously.

Financing of unquoted biotech companies has held up relatively well, despite the correction in the market since 2000. With the biotech IPO window being closed for the last year, private equity funds have had to fund existing portfolio companies for longer and new investments have tended to be made in later stage companies closer to a potential revenue stream. Financing rounds have generally been larger in size in order to fund companies for longer and deals are taking longer to complete as investors have become more valuation sensitive.

2003 has been characterised by a much better mix of news from the sector. However, as should be expected, given the risks of drug development, there have been some disappointments and setbacks. Examples from within the portfolio include Essential Therapeutics. Essential failed to achieve common shareholder consent to the conversion of \$60m convertible preferred stock into common and the company was delisted from NASDAQ in May 2003. The company filed for Chapter 11 and the final initial hearing on its plan of reorganisation is planned for October 2003. If this plan is approved, it is likely that the company will be relaunched as a private company using the remaining cash left from the \$60m preferred investment. If the plan is not approved, then it is likely that the company will be wound up with cash distributed back to its preferred shareholders, which include IBT.

Weston Medical announced manufacturing problems with its needle-free drug delivery device and the assets of the company were sold to Aradigm for approximately \$2m. Crucell had a difficult year and refocused on vaccine development and although Aradigm announced the start of its first inhaled insulin Phase III trial with Novo Nordisk, it subsequently announced a one-year delay to the program due to manufacturing issues. Epimmune cancelled a merger agreement with Anosys and announced cost cutting measures and is considering alternative strategies going forward.

It is difficult to predict the direction the market will take from here, in the short term at least. There remain a number of potential FDA approvals on the horizon, including compounds from three of IBT's portfolio companies - Inspire's diquafasol for dry eye; XOMA's Raptiva for psoriasis; and Indevus' Trosipium for overactive bladder.

More late-stage clinical trial data is expected to be released over the next year. Examples from the IBT portfolio include data from OSI Pharmaceuticals, which has an EGFR inhibitor in Phase III trials for lung cancer and Adolor which will report the results of two further Phase III trials of its potential treatment for post-surgical constipation resulting from the use of opioids for pain relief.

The fundamentals of the industry remain strong and IBT's portfolio companies continue to make good overall progress and are generally well funded. The broad rally across all tiers means that stock picking will be key and deep due diligence will continue to be fundamental in the selection of new investments.

The next year will be an exciting time for IBT, although there are likely to be some delays and surprises at portfolio companies, as should be expected from the nature of the industry. An opening of the IPO window could allow some of the unquoted portfolio companies to gain a listing and Aderis, CancerVax and EyeTech are well positioned to try and take advantage of such an opportunity. However an IPO window requires the backdrop of a good overall market environment, which in turn relies on positive economic and political conditions.

### **PORTFOLIO SUMMARY AT 31 AUGUST 2003**

IBT has investments in 36 companies - 25 quoted companies (representing 51% of NAV) and 11 unquoted companies (comprising 42% of NAV). The remaining 7% is made up of cash, money market instruments and other net current assets. Given the level of unquoted investments, no new unquoted investments are planned in the short term.

Members of SVLS sat on the Board of 9 of the 36 portfolio companies at the end of the year under review – Aderis Pharmaceuticals, Affibody, CancerVax, Epimmune, Eyetech Pharmaceuticals, Galen Group, Genosis, KuDOS Pharmaceuticals and Micromet. Since 31 August 2003, the SVLS representative on the board of Epimmune has resigned.

In terms of the geographical split of the portfolio, 63% of NAV is invested in the US, 4% in Canada, 8% in the UK/Ireland and 18% in Continental Europe. By sub-sector, 80% of NAV is

invested in biopharmaceuticals, 5% in drug delivery, 1% in medical devices and 7% in other areas. The remaining 7% is made up of cash, money market instruments and other net current assets.

Analysing the investments by the stage of their most advanced product in drug development; eight companies have products on the market, three have filed for approval, ten are in Phase III trials, eight are in Phase II or Phase I/II, and three are in preclinical development. Of the remaining four, one is in late stage testing for a diagnostic device and the other three are platform technology companies.

In terms of the cash positions of the portfolio companies, it is estimated that at 31 August 2003, seventeen have two or more years of cash (41% of NAV), fifteen have between one and two years of cash (47% of NAV) and four have less than a year of cash (5% of NAV). The companies with less than a year of cash are Auxilium, Axxima, Genosis and publicly quoted Epimmune. Genosis has raised money since 31 August 2003, Auxilium has fundraising plans, Axxima is exploring M&A opportunities and Epimmune is considering alternative strategies.

The portfolio gives investors a broad spread of exposure to different stages of clinical development across a variety of different clinical areas – cancer, infectious disease, diabetes, central nervous system disorders, women’s health, urology, cardiovascular complications, rheumatoid arthritis, asthma, psoriasis, ophthalmology and management of the side effects of opioids for pain relief.

#### Ten largest quoted investments

Investment	Value £'000	% of NAV	Country
OSI Pharmaceuticals	2,703	5.01	USA
Atrix Laboratories	2,273	4.22	USA
XOMA	2,073	3.84	USA
Encysive Pharmaceuticals	1,803	3.34	USA
Esperion Therapeutics	1,750	3.24	USA
Novuspharma	1,734	3.22	Italy
Nektar Therapeutics	1,450	2.69	USA
Inflazyme	1,232	2.28	Canada
Aradigm	1,099	2.04	USA
AnorMED	1,040	1.93	Canada
<b>Total</b>	<b>17,157</b>	<b>31.81</b>	

#### Unquoted investments

Investment	Value £'000	% of NAV	Country
Micromet	3,658	6.78	Germany
Aderis Pharmaceuticals	3,161	5.86	USA
EyeTech Pharmaceuticals	3,161	5.86	USA
Sunesis Pharmaceuticals	3,161	5.86	USA
Affibody	3,025	5.61	Sweden
CancerVax	2,161	4.01	USA
KuDOS Pharmaceuticals	1,400	2.60	UK
Essential Therapeutics	948	1.76	USA
Axxima Pharmaceuticals	864	1.60	Germany
Auxilium Pharmaceuticals	632	1.17	USA
Genosis	518	0.96	USA
<b>Total</b>	<b>22,689</b>	<b>42.07</b>	

## VALUATION

During the year under review the net effect of the change in the Directors valuations of unquoted companies was a net reduction in NAV for the year of £1.4m. This represents a decrease of 6.7% on the valuation of the unquoted portfolio at 31 August 2002. The value of unquoted investments at 31 August 2003 was £22.7m (£20.8m at 31 August 2002). The holdings in CancerVax and Axxima were written down by £0.2m (total cost £2.5m) and £1.2m (cost £1.4m) respectively during the period under review. CancerVax was written down to the price of the August 2003 financing round in which IBT invested £0.4m. The valuation of Axxima was written down to a best estimate of a fair market value. Currency gains increased the valuation of the unquoted portfolio by £0.6m during the period under review.

The valuation of Essential Therapeutics was changed during the year under review to an unquoted basis and is included as an unquoted holding. This change in valuation basis was because the company was delisted from NASDAQ. While the common shares of Essential are still thinly traded, IBT holds a preferred redeemable instrument that is not quoted. The preferred shareholders have issued redemption notices and the SVLS representative on the board of the company has resigned. Since Essential could not repay the \$60m originally invested by the preferred shareholders, the Chapter 11 process was initiated to enable the company to reorganise. The holding is valued at £0.9m (cost £5.3m) taking into account the stage the company has reached in Chapter 11 proceedings. The valuation is believed to be a conservative estimate of IBT's interest in Essential following the resolution of the court process after which it is expected that the preferred shareholders will own 100% of the company. The company reported \$16m of cash and marketable securities at end June 2003.

At 31 August 2003 the holdings in Aderis, Affibody, Auxilium, EyeTech, Genosis, KuDOS and Sunesis are held at cost (total value £15.0m), Axxima, CancerVax and Essential Therapeutics have been written down from their original cost (total value £4.0m), and Micromet has been written up (value £3.7m). This equates to 66% of the unquoted portfolio held at cost, 18% written down and 16% written up by value. The unquoted portfolio, excluding ValiGen and Entigen, is now valued at 81% of original cost (including the initial cost of Essential).

To recap, the carrying valuations of each of the unquoted companies are reviewed weekly and incorporate consideration of the progress of the underlying company against milestones made at the time of investment and any upcoming need to raise capital. Strategic equity investments, such as Pfizer's equity investment in EyeTech are not used as a basis for valuing unquoted companies.

Of the 25 quoted investments, five are held at a discount to their mid market prices at 31 August 2003, due to disposal restrictions, including limited liquidity – AnorMED, Epimmune, Galen, Inflazyme, and LION. The effect of these discounts was to reduce the NAV by £0.9m at 31 August 2003.

## INVESTMENT ACTIVITY

### UNQUOTED COMPANIES

As the percentage of NAV invested in unquoted investments remains high, no new investments have been made in the unquoted portfolio during the year under review. An investment of £0.4m was made in August 2003 in existing portfolio company, **CancerVax** (total investment £2.1m). CancerVax raised \$41m in the financing and has subsequently filed to go public on NASDAQ, market conditions permitting.

Following a commitment made in August 2001, the second tranche of an investment (£1.4m) was made in **Affibody** (total investment £2.7m). Affibody continues to make good progress

developing antibodies (small peptide binders similar to antibodies) in the areas of protein separation, affinity ligands for drug discovery, diagnostics and biotherapeutics. The company's collaboration with Amersham in the area of bioseparations is progressing well and the company has met its milestones. Affibody is well financed with cash estimated to last until the end of 2005.

In May 2003, **Auxilium's** investors agreed to guarantee a revolving line of credit of \$10m to the company in proportion to their investments and in return for warrants. IBT's share of the guarantee is £0.1m and is shown as a contingent liability in the accounts. Auxilium's testosterone gel, Testim has been approved for sale in the US and the UK for use in treating men with low testosterone levels, and was launched in the USA in February 2003. The sales ramp has been disappointing due to difficulties with pre-marketing and a stronger than expected competitor response. However, it appears that Testim is now making up an increasing share of new testosterone prescriptions as physicians recognise the benefit of the product over alternative gels. Auxilium is likely to need to raise another round of private finance in which IBT is likely to participate (up to £0.5m).

**Genosis**, the infertility diagnostics company, has completed its clinical trials for the female fertility test and has filed for regulatory approval for the female test. The final tooling and manufacturing of the male fertility test has been somewhat delayed, although the male device appears to have the necessary accuracy and sensitivity. This has delayed clinical testing. Since 31 August 2003 an investment of £0.2m has been made in Genosis in order to fund the completion of the trials for the male test (total investment £0.7m).

There were no exits from unquoted investments during the period under review.

#### QUOTED COMPANIES

New investments were made in seven quoted companies – Cambridge Antibody Technology Group (CAT), Encysive Pharmaceuticals, Galen Holdings, Indevus Pharmaceuticals, Inspire Therapeutics, Progenics Pharmaceuticals and XOMA.

##### **CAT** (£0.5m investment)

CAT is a Cambridge, UK-based antibody platform and therapeutics company. The company's primary areas of therapeutic focus are auto-immune disorders and oncology. CAT's most advanced program is HUMIRA, an antibody which is partnered with Abbott and has been launched in the US for rheumatoid arthritis and been approved in Europe. CAT has seven other antibodies in clinical development, the most advanced of which is Trabio in Phase III trials for the prevention of post-operative scarring in patients with glaucoma.

##### **Encysive Therapeutics** (£1.1m investment)

Encysive is a US-based company developing therapeutics for cardiovascular and inflammatory diseases, the most advanced of which is Sitaxsentan, which is in a pivotal trial for Pulmonary Arterial Hypertension (PAH). The company expects to report data from the trial towards the end of 2004 and to announce a marketing partner thereafter. Sitaxsentan appears to offer a significant improvement in treatment over the traditional practice of care, a continuous infusion by implanted catheter. Currently there is only one oral drug available for PAH patients, and data to date suggest that the clinical profile of Sitaxsentan may be superior.

##### **Indevus Pharmaceuticals** (£0.4m investment)

Indevus is a US-based company with drug candidates in development for overactive bladder, anxiety, stroke, HIV, pain and inflammation and serious fungal infections. Indevus acquires the rights to developmental compounds and uses its team to advance the clinical program, either independently or with a partner. Indevus' lead compound, Trospium, is for the treatment of overactive bladder. Currently marketed products can cause side effects including dry mouth and data suggest that Trospium may have similar efficacy to marketed

products but with a more favourable side effect profile. Indevus licensed the US rights to Trospium from Madaus who market the product in Europe. Trospium was filed for approval in the US in April 2003 and the search for a marketing partner is underway.

**Progenics Pharmaceuticals** (£0.4m investment)

Progenics is a US-based company. Its most advanced product candidate is methylnaltrexone, a compound in Phase III trials designed to reduce the side effects of currently marketed opioids used for pain relief. Progenics is developing the compound in three parallel clinical programs. A Phase III trial is underway for opioid-induced bowel dysfunction in advanced medical illness, a Phase II trial has started in post-surgical constipation and finally a Phase I study in patients taking opioids chronically is planned for later this year. The compound is currently unpartnered.

The final three new investments were discussed in detail in the 2003 Interim Report.

**Galen Holdings** (£0.5m investment)

Galen is a speciality pharmaceutical company focused on women's health, dermatology and urology. During the year under review, the company significantly broadened its product portfolio. Galen strengthened its position in the dermatology market through a co-promotion agreement with Bristol-Myers Squibb and development agreement with Leo Pharma in the area of psoriasis. In June 2003, Galen's Femring was launched in the USA. Femring is the first vaginal estrogen product indicated to treat both the hot flushes and vaginal symptoms associated with menopause. Galen also bolstered its position in women's health through the acquisition of the rights to three marketed products from Pfizer.

**Inspire Therapeutics** (£0.3m investment)

Inspire's lead drug candidate, diquafasol, is for the treatment of dry eye, and was filed for approval in the USA in mid 2003. In May 2003, Inspire announced data from a PIII trial for allergic rhinitis, which did not meet its primary endpoint. Although this was a large potential market, the dry eye compound and potential size of the dry eye market mean that this remains an interesting investment.

**XOMA** (£1.0m investment)

XOMA's lead drug candidate is Raptiva, an antibody for moderate to severe psoriasis partnered with Genentech in the US, and Serono in Europe. Raptiva has been filed for approval in both areas and an FDA Advisory panel in September 2003 unanimously recommended its approval. Although the FDA is not bound by the recommendation of its advisory committees it generally follows their advice.

A further £0.4m was invested in **Adolor** (total investment £0.8m) and a net investment of £0.4m was made in **Esperion Therapeutics** (total investment £0.5m).

Adolor's lead compound, Alvimopan is in Phase III clinical trials for post-surgical constipation resulting from the use of opioids for pain relief. Data from the first of these three trials was reported in April 2003 and was mixed – the primary endpoint of recovery of gastrointestinal function was met in one of the dosage groups but the time to hospital discharge did not show as much of a reduction as anticipated. Data from the other two trials is expected later this year or early next and should allow a better evaluation of the clinical profile of the compound.

The positive initial Phase II data announced by Esperion has been described and more details are expected in the coming months. The company's pipeline continues to progress with two product candidates in Phase II, and another two in Phase I. However, the inadvertent acquisition by a shareholder of a third of the company has resulted in an overhang of stock in the market which will need to be carefully managed.

The holdings in **Arque**, **Aspect Medical**, **Corvas International**, **3 – Dimensional Pharmaceuticals** and **Weston Medical** were sold in their entirety.

The holdings in **Alexion Pharmaceuticals, AnorMED, Crucell, Forest Labs, OSI Pharmaceuticals, Sirna Therapeutics** and **Targeted Genetics** were reduced in size.

## International Biotechnology Trust plc

### Unaudited Preliminary Results

#### Unaudited Statement of Total Return (incorporating the Revenue Account)

	For the year end 31 August 2003			For the year end 31 August 2002		
	Revenue £'000	Capital £'000	Total £'000	Revenue £'000	Capital £'000	Total £'000
Gains/(losses) on investments	–	7,613	7,613	–	(49,532)	(49,532)
Exchange gains/(losses) on currency balances	–	53	53	–	(28)	(28)
Income	112	–	112	278	–	278
Management fees	(638)	–	(638)	(804)	–	(804)
Administrative expenses	(488)	–	(488)	(758)	–	(758)
<b>Net (deficit)/return on ordinary activities before taxation</b>	<b>(1,014)</b>	<b>7,666</b>	<b>6,652</b>	<b>(1,284)</b>	<b>(49,560)</b>	<b>(50,844)</b>
Tax on ordinary activities	–	–	–	–	–	–
<b>Net (deficit)/return on ordinary activities after taxation</b>	<b>(1,014)</b>	<b>7,666</b>	<b>6,652</b>	<b>(1,284)</b>	<b>(49,560)</b>	<b>(50,844)</b>
<b>Transfer (from)/to reserves</b>	<b>(1,014)</b>	<b>7,666</b>	<b>6,652</b>	<b>(1,284)</b>	<b>(49,560)</b>	<b>(50,844)</b>
<b>(Deficit)/surplus per share</b>	<b>(2.09)p</b>	<b>15.82p</b>	<b>13.73p</b>	<b>(2.64)p</b>	<b>(101.94)p</b>	<b>(104.58)p</b>

The revenue column of this statement is the profit and loss account of the Company.  
All revenue and capital items in the above statement derive from continuing operations.

## International Biotechnology Trust plc

### Unaudited Balance Sheet as at 31 August

	2003 £'000	2003 £'000	2002 £'000	2002 £'000
<b>Fixed assets</b>				
Investments		49,911		43,584
<b>Current assets</b>				
Debtors	73		153	
Investments	2,742		1,889	
Cash at bank	1,615		2,912	
	4,430		4,954	
<b>Creditors: amounts falling due within one year</b>	410		643	
<b>Net current assets</b>		4,020		4,311
<b>Net assets</b>		53,931		47,895
<b>Capital and reserves</b>				
Called up share capital		11,954		12,154
Capital redemption reserve		11,043		10,843
Share purchase reserve		66,467		67,083
Capital reserve		(26,512)		(34,178)
Revenue reserve		(9,021)		(8,007)
<b>Equity shareholders' funds</b>		53,931		47,895
<b>Net asset value per share</b>		112.79p		98.52p

# International Biotechnology Trust plc

## Unaudited Cash Flow Statement

	For the year ended 31 August 2003 £'000	For the year ended 31 August 2002 £'000
<b>Operating activities</b>		
Income	56	283
Management fees paid	(617)	(852)
Other cash payments	(537)	(729)
<b>Net cash outflow from operating activities</b>	<b>(1,098)</b>	<b>(1,298)</b>
<b>Servicing of finance</b>		
Interest paid	–	–
<b>Cash outflow from servicing of finance</b>	<b>–</b>	<b>–</b>
<b>Taxation</b>		
UK income tax recovered	–	67
<b>Tax recovered</b>	<b>–</b>	<b>67</b>
<b>Capital expenditure and financial investment</b>		
Purchase of investments	(7,838)	(25,579)
Disposal of investments	8,994	19,816
<b>Net cash inflow/(outflow) from capital expenditure and financial investment</b>	<b>1,156</b>	<b>(5,763)</b>
<b>Net cash inflow/(outflow) before management of liquid resources and financing</b>	<b>58</b>	<b>(6,994)</b>
<b>Management of liquid resources</b>	<b>(793)</b>	<b>2,777</b>
<b>Financing</b>		
Repurchase of shares for cancellation	(615)	–
<b>Net cash outflow from financing</b>	<b>(615)</b>	<b>–</b>
<b>Net cash outflow</b>	<b>(1,350)</b>	<b>(4,217)</b>

### Notes:

#### 1. Audit status

The financial information set out in the announcement does not constitute the Company's statutory accounts for the year ended 31 August 2003 or 31 August 2002. The financial information for the year ended 31 August 2002 is derived from the statutory accounts for that year which have been delivered to the Registrar of Companies. The auditors reported on

those accounts; their report was unqualified and did not contain a statement under section 237(2) or (3) of the Companies Act 1985. The statutory accounts for the year ended 31 August 2003 will be finalised on the basis of the financial information presented by the Directors in this preliminary announcement and will be delivered to the Registrar of Companies following the Company's Annual General Meeting.

This announcement is prepared on the basis of the accounting policies as set out in the most recently published set of annual financial statements.

## **2. Annual General Meeting**

The Annual General Meeting of International Biotechnology Trust plc will be held at 3pm on 14 November 2003 at 31 Gresham Street, London, EC2V 7QA.

## **3. Annual Report and Accounts**

The Annual Report and Accounts will be mailed to registered shareholders at their registered addresses in October 2003 and from the date of release copies of the Annual Report will be made available to the public at the Company's registered office, 31 Gresham Street, London EC2V 7QA.