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## **INTERNATIONAL BIOTECHNOLOGY TRUST Plc**

The Board of International Biotechnology Trust Plc today announces its unaudited Preliminary Results for the year ended 31 August 2002.

### **SUMMARY**

- Net asset value per share fell by 51.5% to 98.5p
- NASDAQ Biotech Index fell 47.7% (in sterling terms) and the Bloomberg UK Biotech Index fell by 46.4%
- As announced at the half year, write-downs in unquoted companies resulted in a fall in net assets for the year of £6.1 million or 6.2% of net assets at 31 August 2001
- Total net assets at 31 August 2002: £47.9 million (31 August 2001: £98.7m)
- New investments in 6 quoted companies and 4 unquoted companies
- Sales of 7 quoted holdings and 2 unquoted companies

Andrew Barker, Chairman, commented:

“It was another year of significant stock market falls, particularly in the biotech sector, and our results reflect these difficult times. Continuing market declines have resulted in attractive valuations for many good quality biotech companies and IBT has taken advantage of this value and made a number of new investments. This has further strengthened the portfolio, which provides investors with an exposure to a dynamic industry through an exciting set of companies with strong upside potential, spread across the private and public markets, different clinical areas and varying stages of clinical development. However, both biotech and IBT remain more suited to the longer-term investor who is willing to weather the volatility, which looks set to continue, at least in the short-term.”

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## **CHAIRMAN'S STATEMENT**

### **Performance**

It was another year of significant stock market falls, particularly in the biotech sector, and our results reflect these difficult times. During the year to 31 August 2002, the net asset value ("NAV") per share of International Biotechnology Trust plc ("IBT") fell by 51.5% from 203.1p to 98.5p alongside a fall in the share price of 56.7% from 176.5p to 76.5p. This is in comparison to a fall in the NASDAQ Biotechnology Index ("NBI") of 47.7% in sterling terms and a fall in the Bloomberg UK Biotechnology Index of 46.4% during the same period.

Whilst the fall in NAV was predominantly due to the fall in the biotech market, an element was due to write-downs in the values of some of the inherited unquoted companies in the portfolio, as announced at the half year. Changes in the valuations of unquoted companies have resulted in a net fall in net assets for the year of £6.1 million or 6.2% of net assets at 31 August 2001. The fall in NAV during the year under review was 45.3% excluding these write-downs.

### **Review**

The year under review has been disappointing in performance terms for IBT. However, this should be viewed in the context of the weak overall market conditions, which have reduced investor tolerance for the type of risk found in the biotech sector. The biotech market typically goes through extreme cycles and the fall in the NBI during the last year follows the boom years of 1999 and 2000 when the index (in US dollar terms) rose from 437 and peaked at around 1600. At the end of the period under review the NBI had fallen back down to 489, close to the levels of early 1999.

Sentiment towards the sector seems worse than at any time in recent history with investors focusing on a number of high profile disappointments, and largely ignoring recent successes. The widening of the discounts for the biotech-focused investment trusts reflects this poor sentiment. At the time of writing, shares in IBT are trading on a discount of 31% to NAV, after widening from 13% to 22% during the reporting period.

IBT has a number of holdings in smaller quoted companies with very early stage pipelines, and these companies have been hit particularly hard as investor focus has moved towards the larger, profitable companies or those with projected near term earnings.

At 31 August 2002 the percentage of NAV in unquoted companies was 43%. Whilst new investments during the reporting period account for some of this increase, a large part is due to the falls in share prices of the quoted companies in the portfolio. Given that the guideline for unquoted investments was originally set at approximately 25% NAV, further unquoted investments are not planned in the near term. The Board keeps this matter under regular review, which includes monitoring the progress of the unquoted investments. If concerns arise regarding the valuation of these investments, appropriate action is taken immediately.

### **Valuation**

As is practice in the venture capital industry, the IBT portfolio is valued in accordance with the British Venture Capital Association (BVCA) guidelines. In certain circumstances quoted holdings are valued at discounts to their mid market prices. 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.

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, currently have board seats on ten of the portfolio companies. 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.

### **Scientific Advisory Board ("SAB")**

The SAB has been expanded during the reporting period and now numbers four, providing IBT with a very valuable resource upon which to draw both scientific and clinical expertise. This advice is used to help identify new investment opportunities and in the management of portfolio companies. I would like to extend my congratulations to the Chairman of the SAB, Dr. Sydney Brenner, on sharing this year's Nobel Prize in Physiology and Medicine.

### **Share Buy-Back Facility**

To date, the Directors have not utilised the authority given to them at the 2001 Annual General Meeting to purchase shares for cancellation. Your Board will, however, 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. A resolution to renew the share buyback 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 Thursday 19<sup>th</sup> December 2002 at 12 noon. A presentation will be made by SVLS.

### **Outlook**

Continuing market declines have resulted in attractive valuations for many good quality biotech companies. IBT has taken advantage of this value and made a number of new investments. This has further strengthened the portfolio, which provides investors with an exposure to a dynamic industry through an exciting set of companies with strong upside potential, spread across the private and public markets, different clinical areas and varying stages of clinical development.

The fundamentals of the biotech sector remain compelling and while other sectors suffer declining earnings, more and more biotech companies are turning profitable and product pipelines continue to both widen and mature. Biotech companies have generated nearly a quarter of the drug candidates currently in development and are set to become the research and development engine of the drug industry.

We have experienced an extreme downturn in the biotech market and the timing of an upturn is difficult to predict. Investment in the both the biotech sector and IBT remain more suited to the longer-term investor who is willing to weather the volatility, which looks set to continue, at least in the short-term. That said, I continue to believe that we have a leading team of advisers in SVLS, with considerable depth of skill, experience and resources, which should be reflected in our results in due course.

**Andrew Barker**

**Chairman**

## **INVESTMENT ADVISERS REVIEW**

### **Schroder Ventures Life Sciences**

Schroder Ventures advised funds have invested in the life sciences industry since the early 1980's and to date have backed over 100 life science companies internationally. Schroder Ventures Life Sciences ("SVLS") was established in 1993 and currently has offices in Boston, London and San Francisco, in order to take advantage of the global nature of life sciences opportunities. The SVLS team is comprised of 24 professionals with a deep base of scientific, clinical, operational and life sciences investment experience.

In addition to IBT, SVLS advises three private equity funds with total commitments of approximately \$680m, focused on providing seed, start-up, early stage and expansion capital to life sciences companies primarily in the US and Europe.

### **Market Review**

The year under review has seen a severe correction in the biotech market with the NASDAQ biotech index falling by 47.7% in sterling terms. The backdrop to this poor performance has been a slump in the general markets and the growing intolerance of risk by investors. Technology stocks have generally held up better than biotech with the NASDAQ composite index falling by 31.7% in sterling terms during the reporting period.

The fall in the sector follows a frenzy of initial public offerings ("IPO's") and high valuations in 2000, which were driven by strong global market conditions and by the sequencing of the human genome and the perception that this would result in the rapid development of new therapeutics, driving earnings and profitability at a fast pace. The reality of the genomics revolution is that it is transformational but the fruits of this knowledge will not be commercialised for some years to come.

There have only been three biotech IPOs this year and the IPO window looks firmly closed for the coming months. A portfolio company, Aderis Pharmaceuticals, completed a series of investor roadshows in preparation for an IPO earlier this year, but the listing did not go ahead. Investor confidence in the IPO market was soured by the poor performance of the listing of DOV Pharmaceuticals, immediately before the Aderis listing was to become effective. This was disappointing but Aderis continues to make progress with its product pipeline and is well financed.

The biotech sell-off has contracted earnings multiples for profitable companies and lowered technology values for development stage companies. For loss-making companies, attention is focused on current cash positions and burn rates, with little value being accorded to future products. Many companies (including a number of portfolio companies) are trading at a discount to cash asset values and a number of companies have restructured to focus on their lead programs in order to conserve cash in the face of difficult market conditions. Overall, companies within the IBT portfolio remain generally well financed with twenty-two companies having two or more years of cash, seven with one or more and five with less than a year of cash. The remaining two companies have been written off. Of the five with less than a year of cash, one is expecting to start commercialisation of a product within the next year and to sign a marketing agreement, two are currently raising money, one is looking to partner out early stage programs and another has been sold since the end of the reporting period.

The most extreme falls in share prices have been seen in companies with very small market capitalisations (microcaps) and early stage pipelines, despite good operational progress in many cases. In times of uncertainty investor interest concentrates on the larger, profitable companies or those with very late stage product pipelines and a near term chance of earnings.

This has severely impacted the performance of IBT. An example of this is Essential Therapeutics, which is trading at a dollar a share, down from just under four dollars at the start of the period under review. This is despite a planned restructuring to focus on clinical development rather than earlier stage research, and an acquisition that brought in an interesting compound that is already in the clinic.

Positive news has tended to be overlooked by investors and there has been a spate of bad news from the sector, which has depressed sentiment. This included the ImClone scandal and concerns over Elan's accounting practices. In addition there have been a number of late stage product failures including Cubist's injectable antibiotic for pneumonia and Emisphere's oral heparin formulation. These failures have reminded investors of the risks of drug development although, given that there are more late-stage drugs in the pipeline than ever before, more late-stage failures should be expected.

The FDA appears to be taking a more cautious approach to the approval of drugs following a series of product withdrawals. The perceived increase in regulatory risk has increased the discount rate that investors use to value biotech stocks, however, history has shown that many of the drug candidates initially held up by the FDA, are ultimately approved. Recent drug approvals have largely been ignored by investors, for example Gilead's HIV drug Viread, IDEC's Zevalin for Non-Hodgkins Lymphoma and portfolio company, Atrix Labs' two formulations of Eligard for the treatment of advanced prostate cancer.

However, more recently newsflow from the sector has begun to improve with good earnings numbers from the larger biotech companies and two well-subscribed follow-ons for Telik and Trimeris. In addition Biogen's Amevive for psoriasis and AstraZeneca's oral cancer drug Iressa both received positive reviews from FDA advisory panels. Most importantly for sentiment, a new Commissioner for the FDA was nominated in September. The Agency has been without a Head since President Bush came to office and this new leadership may help reduce some of the delays in decision-making. In addition the third Prescription Drug User Fee Act was passed in June, which should improve funding for the agency and increase the number of reviewers and external advisers.

## **Fundamentals**

The correction in the biotech market overshadows strong fundamentals for the sector; an increasing supply of new potential drugs driven by scientific innovation, high barriers to entry for competition and the demand dynamics of an ageing population coupled with increased drug usage. Biotechnology drugs generally treat serious, life-threatening, and unmet medical needs, so revenues and earnings are generally insensitive to changes in the macroeconomic environment. The industry comprises an unprecedented and growing number of profitable companies, a plethora of products on the market and more than 350 products in late-stage clinical trials (Phase II or beyond) and while many of these products will not succeed, many of them will.

Pharmaceutical companies are relying more and more on biotech companies to supply them with in-licensing opportunities in order to meet double-digit earnings growth expectations. Their own pipelines are generally lacklustre and they face looming key patent expiries and declining R&D productivity. There is typically strong competition to in-license late stage products and the balance of power in negotiating these deals has swung firmly in favour of biotech companies. An example of a significant late stage transaction is GlaxoSmithKline's \$270m licensing of portfolio company Adolor's Phase III compound Alvimopan. Given the nature of this competition, pharma companies may start in-licensing some of the more plentiful earlier stage compounds, which should translate into richer incentives for biotech to partner out these programs. This could allow biotech companies to bolster their increasingly precious cash piles and to reduce

risk by diversifying pipelines whilst retaining more of the rewards of a successful product candidate.

## **Mergers and Acquisitions**

Following the consolidation seen in the sector last year, which saw major acquisitions by Amgen, Medimmune, and Millennium, merger and acquisitions (“M&A”) activity has been slow in 2002 and the few deals that have been announced have not materially helped the performance of the biotech market.

However, there are reasons why M&A may start to pick up. The weak equity market conditions make it difficult for companies to raise cash, which should increase the pressure for consolidation. This is most likely to occur between cash rich companies seeking to expand their pipelines and those companies with interesting products but limited financing. Well-funded private companies wanting to gain a listing but restrained by the lack of an IPO window could also benefit from the acquisition of a cash-strapped public company. In addition the need to bolster product pipelines, bring in new capabilities and to increase liquidity and critical mass to attract large investors continue to be compelling reasons for M&A. Examples from the portfolio include Essential’s purchase of Maret Pharmaceuticals to bring in a clinical stage compound, the acquisition of ChemOvation by KuDOS to bring chemistry capabilities in-house and the purchase of Cell-Matrix by CancerVax to broaden its oncology pipeline.

## **INVESTMENT ACTIVITY**

### **Summary**

During the reporting period investments were made in six new quoted companies – Adolor, Esperion Therapeutics, Essential Therapeutics, Crucell, Alexion Pharmaceuticals and 3-Dimensional Pharmaceuticals. Following the end of the reporting period an investment was made in the quoted company, XOMA. Further investments were made in five existing quoted holdings – Epimmune, Aspect Medical, AnorMED, Novuspharma and Atrix Labs. Seven quoted holdings were sold and four quoted holdings were reduced in size.

In the unquoted portfolio four new investments were made - KuDOS Pharmaceuticals, Genosis, Auxilium Pharmaceuticals and CancerVax, and there were two follow-on investments in Axxima Pharmaceuticals and Eyetech Pharmaceuticals. Subsequent to the reporting period a follow-on investment was made in Affibody. Two unquoted companies were sold.

### **Quoted Companies**

#### **New Investments**

**Adolor** (£0.4m investment) is a US-based company focused on the reduction of side effects of currently marketed opioids used for pain relief. The lead compound is called Alvimopan and is in Phase III clinical trials for two indications: post-operative ileus (loss of bowel function following surgery) and opioid bowel dysfunction (severe constipation in chronic opioid users), both of which represent large unmet medical needs. Data from these trials is expected in the first half of 2003 and Adolor hope to file a New Drug Application (NDA) with the FDA by the end of 2003 for the surgical indication.

Alvimopan is partnered with GlaxoSmithKline (“GSK”), which provides a strong endorsement of the compound and will allow Adolor to tap into GSK’s extensive marketing infrastructure. Since 31 August 2002, a further £0.1m has been invested in the company, increasing the total invested to £0.5m.

**Esperion Therapeutics** (£0.1m investment) is a US-based company with a broad pipeline of clinical and preclinical drug candidates for the treatment of cardiovascular and metabolic diseases. The focus of the company is to enhance the effects of HDL (high density lipoproteins, the so-called good cholesterol) and several different drug candidates have been developed to mimic and enhance naturally occurring biological processes that remove excess cholesterol from the walls of arteries and transport it to the liver where it is eliminated from the body.

Traditional management of elevated cholesterol focuses on reducing levels of LDL (low density lipoproteins) and uses statins in an outpatient setting, which are good at reducing LDL but may increase HDL in some cases. There are few drugs on the market for the treatment of low HDL and the drug candidates in development at Esperion have been designed to act as complementary therapy with the current agents for cholesterol therapy. Specifically, two products are in Phase II trials, one is entering Phase II and an IND is expected to be filed for another by the end of the year.

Esperion has a seasoned management team with impressive depth. The management team includes several members from major pharma companies, such as Parke Davis, Pfizer and Bristol-Myers Squibb, who have had prior success with development and launch of several cholesterol management medications in use today. The CEO Roger Newton was the co-discoverer of Lipitor, a statin with sales of \$6 billion in 2001.

Since 31 August 2002, a further £0.7m has been invested in the company, increasing the total invested to £0.8m.

As detailed in the previous Annual Report a commitment was made in August 2001 to invest £5.3m in **Essential Therapeutics** and this was completed in October 2001. Essential now has an emerging pipeline of product candidates in the anti-infective and haematology/oncology areas. Since the investment, there has been a broadening of the management team and the pure research capability has been significantly cut back in order to focus resources on preclinical and clinical development. In March 2002, Essential announced the acquisition of Maret Pharmaceuticals bringing in a Phase I stage compound. This may have uses in the prevention of thrombocytopenia, anaemia and infection in patients following chemotherapy or bone marrow transplantation and three Phase II trials are planned. The company has also entered into a new collaborative agreement with Fujisawa Pharmaceutical in the area of novel antibiotics, and J&J has initiated Phase I clinical trials with Essential's cephalosporin candidate.

The final three new investments were described in the interim report - Crucell, Alexion Pharmaceuticals and 3-Dimensional Pharmaceuticals ("3DP").

**Crucell** (£1.9m investment) is a Dutch biotechnology company focused on the discovery and development of novel antibodies and vaccines. It has announced a number of smaller partnerships and licences since the investment was made but a partner for its flu vaccine program or another interesting antibody deal is required to drive the share price higher.

**Alexion Pharmaceuticals** (£1.8m investment) is a US-based company focused on the development of a novel class of anti-inflammatory compounds known as complement inhibitors. The lead compound is in Phase III trials for the reduction of complications during coronary artery bypass graft surgery with cardiopulmonary bypass, and Phase II myocardial infarction trials. Data in the latter indication is expected later this year.

**3DP** (£1.9m investment) is a chemistry-focused drug discovery company based in the USA. 3DP uses its drug discovery platform to find orally available small molecule drug candidates. The interesting product pipeline is at very early stage and the share price should be driven higher as the pipeline broadens and matures.

Subsequent to the end of the reporting period £0.4m was invested in the US-based company, **XOMA**. XOMA has expertise and capabilities in the development and manufacture of antibody therapeutics and has a healthy pipeline of biologics. Risk is diversified by partial ownership of a number of different compounds and deals are in place with Genentech, Onyx and Millennium. The company's lead candidate is Raptiva, which was originated by Genentech. Raptiva is a humanized monoclonal antibody in Phase III for moderate to severe psoriasis and Phase II for rheumatoid arthritis. Favorable Phase III trial results in psoriasis were reported in 2001, however, in April of this year Genentech announced that the filing for regulatory approval of Raptiva would be delayed due to discrepancies in pharmacokinetic properties between material produced at small and commercial scales. In September 2002, the companies announced that a Phase III trial using solely commercial material achieved its primary endpoint and that they plan to file for approval by the end of 2002.

### **Follow-on Investments**

In December 2001, IBT participated in a PIPE (public investment in private equity) in **Epimmune**, increasing its investment by £1.4m to £6.2m. Epimmune has designed therapeutic drug candidates to treat disease by stimulating the body's immune system to respond aggressively to infections and certain types of tumour. The company has also designed preventative drug candidates to protect against disease by teaching the immune system to react quickly when exposed to infectious agents. Epimmune has started a Phase I/II HIV vaccine trial and expects to file an IND for a lung and colorectal cancer vaccine early in 2003.

A further £2.7m was invested in **Aspect Medical** (total investment £3.4m), £1.1m in **AnorMED** (total investment £5.8m but subsequent sales reduced this to £5.0m), £0.7m in **Novuspharma** (total investment £2.6m), and £0.6m in **Atrix Laboratories** (total investment £2.0m).

### **Sales**

The holdings in **Biocompatibles**, **Biogen** and **Elan** were sold in their entirety during the period, along with the remaining holdings in **CeNeS Pharmaceuticals**, **Onyx Pharmaceuticals** and **Vernalis Group**. In December 2001, Medimmune acquired **Aviron**, which resulted in a net gain of £1.1m for IBT.

The holdings in **OSI Pharmaceuticals**, **Corvas**, **Ribozyme Pharmaceuticals**, and **Forest Labs** were reduced in size during the period under review.

### **Unquoted Companies**

#### **New investments**

In March 2002, as reported in the interim report, IBT invested £2.1m in **CancerVax**, an unquoted US-based company. CancerVax's CANVAXIN is a therapeutic cancer vaccine containing at least 30 known tumour and melanoma-associated antigens which are believed to enhance the overall immune response to cancer. CANVAXIN has been administered to over 2,000 patients and is currently in Phase III clinical trials for the treatment of advanced stage melanoma, a disease with few effective or well-tolerated treatments. In May of this year the FDA put a hold on enrollment in the PIII trial and asked for certain information related to the production, characterisation and testing of the vaccine. We do not believe that the hold on new patient enrollment is the result of clinical practice or safety concerns related to the vaccine as patients already receiving CANVAXIN were permitted to continue to do so and patients already deemed to have met the eligibility criteria for the trial were allowed to receive the vaccine.

Earlier in the year CancerVax brought in additional early stage product candidates for the treatment of solid tumour cancers through the acquisition of the private company Cell-Matrix.

These include several monoclonal antibodies that appear to inhibit angiogenesis, the blood vessel development necessary for tumour growth.

In May 2002 IBT invested £0.6m in the US based company **Genosis** in a financing round of £1.2m where the price of the financing was set by a new external investor. SVLS was involved in the founding of the company in April 1999 and Mike Carter of SVLS is on the Board of the company.

The company is developing an over-the-counter (“OTC”) screening kit for male and female infertility under the brand name Fertell. Fertell contains a male test capable of measuring the concentration of active sperm, an established marker of male infertility, and a female test which measures follicle stimulating hormone (FSH) as an indicator of ovarian reserve. It is intended that each of these tests will be performed concurrently, at home without prescription, supervision by a physician or laboratory involvement. To our knowledge there are currently no home use OTC products or devices available to diagnose infertility for couples.

There are currently over 500 million couples of reproductive age worldwide and one in six of these are infertile. The current screen for infertility is simply to wait and try to conceive for twelve months. By providing earlier diagnosis of male and female infertility, Fertell helps to identify couples likely to require medical intervention so they can be directed to the most appropriate form of treatment as early as possible.

In June 2002, IBT invested £0.7 million in the US-based company **Auxilium Pharmaceuticals** as part of a £10 million private placement. Another Fund advised by SVLS has an investment in Auxilium and invested in this round, in which the price was set by a new external investor.

Auxilium is a specialty pharmaceutical company focused on the development and commercialisation of medicines to maintain functionality in ageing individuals. The company’s lead product is a testosterone gel (Testim) that has successfully completed Phase III studies in the USA and Europe. The company has filed for approval in the USA and the UK for the use of Testim to normalise testosterone levels in testosterone deficient men. Auxilium anticipate the launch of Testim in early 2003.

Testosterone is a male sex hormone, the levels of which have been found to decline in men from about the age of 40 onwards. In a proportion of men this can result in clinical hypogonadism which is associated with osteoporosis, decreased sexual function and loss of body mass. Testim is a clear gel that is convenient to apply to the skin. The testosterone contained in the gel is very effectively absorbed through the skin, normalising testosterone levels.

Follow-on products will concentrate on male health, treatment of peri-menopausal disorders in women and pain management. Furthermore, the company is actively pursuing in-licensing opportunities for other interesting compounds as well as evaluating opportunities to purchase more mature products.

In August 2002 IBT invested £1.4m in a £30m financing round in UK-based **KuDOS Pharmaceuticals** where the price of the financing was set by a new external investor. SVLS was involved in the initial funding of the company in May 1999 and Mike Carter of SVLS is on the Board.

KuDOS is a leader in the discovery and development of novel small molecule drugs that inhibit DNA repair enzymes and signaling pathways for the treatment of cancer. The company retains strong links with the academic laboratory of Professor Stephen Jackson of the Wellcome/Cancer Research UK Institute in the University of Cambridge, a world-renowned authority in DNA repair, on whose initial work the KuDOS programs are based.

The two lead compounds are PaTrin-2 and AQ4N. PaTrin-2 is an inhibitor of the DNA repair enzyme AGT, and appears to enhance the efficacy of certain types of cytotoxics in treating cancer. Two Phase II trials will be conducted using PaTrin-2 in metastatic melanoma and colorectal cancer. AQ4N is a potent killer of cells for use in cancer therapy but is only activated in the hypoxic cells within solid tumours. These cells are not killed by radiotherapy or the chemotherapy regimens used today and are recognised as a major cause of resistance. AQ4N is currently in Phase I clinical trials.

KuDOS also has earlier drug discovery programs and has discovered several potent, highly selective, small molecule inhibitors of the DNA repair enzymes ATM, DNA-PK and PARP. KuDOS expects to be able to select lead candidate compounds from these programs to enter pre-clinical development in 2003.

### **Follow-on investments**

In October 2001 a follow-on investment of £0.3m was made in the German company, **Axxima Pharmaceuticals**, as part of a £21m financing round. This increased IBT's total investment in Axxima to £1.4m. Axxima is an infectious disease, drug discovery company focused on small molecule compounds to block critical signal transduction pathways required by pathogens for survival. Axxima is searching for drug candidates in the areas of HIV, Hepatitis B and C, influenza, human cytomegalovirus, and tuberculosis.

In August 2001, IBT made an investment of £1.8m in **Eyetech Pharmaceuticals** and a commitment to invest a further £1.6m in August 2002, subject to milestones. Eyetech's lead product, Macugen, is designed to inhibit the biological pathway that causes vision loss in age-related macular degeneration (AMD) and diabetic macular edema (DME), two of the leading causes of blindness in the adult population. Enrollment was completed in the pivotal Phase II/III trials for AMD in August 2002, enrolling 1,196 patients at 117 sites worldwide. This triggered the second installment of the financing agreed in August 2001. Eyetech is also conducting Phase II trials with Macugen for DME. Alternative delivery systems for Macugen are under development as it is currently administered via injection into the eye. Eyetech has also in-licensed other promising compounds for treating diseases of the back-of-the-eye.

Also in August 2001, IBT invested £1.3m in the Swedish company **Affibody** and committed to invest a further £1.4m a year later. This second tranche was invested in September 2002, following the end of the reporting period. Affibody uses cutting-edge combinatorial protein technology to create Affibodies. These are small, novel, robust ligands, which can be engineered to bind to any desired protein. Affibodies mimic monoclonal antibodies in many ways and their unique properties make them a preferred choice for a number of diagnostic, proteomic and therapeutic applications. Since the initial investment was made there have been significant advances in the production and characterisation of Affibodies and the library of these ligands has increased in size to around three billion variants. The strategic partnership with Amersham Biosciences in the area of separations has been broadened and lengthened. In addition Dr Hakan Mogren, the former CEO of Astra has joined as Chairman. Preclinical experiments are ongoing to test the possibility of using Affibodies as therapeutics; much of this data should be gathered by the end of the year.

### **Sales**

As outlined in the interim report, two of the unquoted US-based companies in the portfolio were sold to trade buyers during the year, however the returns on both investments were disappointing. Elan announced that **Delsys Pharmaceuticals** would merge with one of its subsidiaries, realising £1.2m for IBT (cost £6.3m). This resulted in a write-up for IBT of £1.2m during the period under review as the holding had previously been written down to nil.

**Netgenics** was sold to the German company Lion Bioscience, and IBT received stock worth £1.1m at the time of the transaction (write-down £3.7m, cost £3.6m).

## **PORTFOLIO SUMMARY AT 31 AUGUST 2002**

IBT has investments in 36 companies - 24 quoted companies (making up 48% of NAV) and 12 unquoted companies (making up 43% of NAV). The remaining 9% of NAV is made up of cash, money market instruments and other net current assets.

The new investments and follow-ons in unquoted companies have increased the weighting of the unquoted portion of the portfolio. The correction in the public markets has also meant that the percentage in unquoted companies has increased due to the falling share prices in the quoted portion of the portfolio.

A member of SVLS sits on the Board of 10 of the 36 portfolio companies – Aderis Pharmaceuticals, Affibody, Auxilium, CancerVax, Epimmune, Essential Therapeutics, Eyetech Pharmaceuticals, Genosis, KuDOS and Micromet.

As planned, the concentration in the top ten quoted stocks has been reduced in order to increase the diversification within the portfolio and they now account for 31% of NAV in comparison with 45% a year ago.

In terms of the geographical split of the portfolio, 60% of NAV is invested in the US, 3% in Canada, 8% in the UK/Ireland and 20% in Continental Europe. By sub-sector, 73% of NAV is invested in biopharmaceuticals, 7% in drug delivery, 3% in medical technology and 8% in other areas. The remaining 9% of NAV is made up of cash, money market instruments and other net current assets.

Analysing the 36 investments by the stage of their most advanced product in drug development; four companies have products on the market, one has filed for approval, nine are in Phase III trials, four are in Phase II, eight are in Phase I, one is in pre-clinical development and two have been written off. Of the remaining seven, one is commercialising an anaesthesia monitoring device, another is about to enter late stage testing for a diagnostic device, four are platform technology companies and one is focused on drug delivery.

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, cardiovascular complications, rheumatoid arthritis, asthma, blindness, low testosterone levels and management of the side effects of opioids for pain relief.

## **VALUATION**

During the reporting period the net effect of the change in the Directors valuations of unquoted companies was a reduction in net assets for the year of £6.1m. This included a write up of Delsys Pharmaceuticals following a sale for £1.2m, after a write-down to nil at the last year end. Axxima and Micromet were written up following financing rounds with prices set by new external investors. Entigen and ValiGen were written off resulting in write-downs of £1.7m and £2.4m respectively. Netgenics was acquired and IBT received shares in Lion Bioscience resulting in a write-down of £3.7m. The remaining unquoted companies in the portfolio are held at cost – Aderis, Affibody, Auxilium, CancerVax, Eyetech, Genosis, KuDOS and Sunesis.

Within the quoted portfolio, five holdings are held at a discount to their mid market prices – Essential Therapeutics and Epimmune due to restrictions on sale due to SVLS presence on the Board; Targeted Genetics and Inflazyme due to liquidity constraints given the size of the holdings; and, in the case of Lion Bioscience, a portion of the shares are to be held in

ESCROW for a year following the acquisition of Netgenics. The effect of these discounts is to reduce the valuation of quoted investments by £1.3m at 31 August 2002.

## **OUTLOOK**

The biotech sector is strongly underpinned but a sustained series of positive news events is needed for a broad-based recovery in the market. The nomination of an FDA commissioner is positive, and should go some way to allay fears about the regulatory climate. However a lasting improvement in confidence is likely to require strong clinical data as well as new product approvals and successful launches of new blockbuster drugs. An increase in M&A activity and further signings of large biotech collaborations may also help sentiment.

Valuations in the biotech sector are at an attractive level and it is a good time to be making investments for the long term. However volatility looks set to continue and it is difficult to see how the biotech market will stage a significant recovery without a pick up in the overall markets, which will require a marked improvement in the macroeconomic picture.

## International Biotechnology Trust plc

### Unaudited Preliminary Results

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

	For the year end 31 August 2002			For the year end 31 August 2001		
	Revenue £'000	Capital £'000	Total £'000	Revenue £'000	Capital £'000	Total £'000
Realised (losses)/ gains on investments	–	(16,865)	(16,865)	–	50,942	50,942
Performance fee and termination costs	–	–	–	–	(2,160)	(2,160)
Increase in unrealised depreciation on investments	–	(32,667)	(32,667)	–	(173,782)	(173,782)
Exchange loss on currency balances	–	(28)	(28)	–	(1,359)	(1,359)
Income	278	–	278	2,700	–	2,700
Management fees	(804)	–	(804)	(2,171)	–	(2,171)
Administrative expenses	(758)	–	(758)	(1,690)	–	(1,690)
<b>Net deficit on ordinary activities before finance costs and taxation</b>	<b>(1,284)</b>	<b>(49,560)</b>	<b>(50,844)</b>	<b>(1,161)</b>	<b>(126,359)</b>	<b>(127,520)</b>
Interest payable and similar charges	–	–	–	(15)	–	(15)
<b>Net deficit on ordinary activities before taxation</b>	<b>(1,284)</b>	<b>(49,560)</b>	<b>(50,844)</b>	<b>(1,176)</b>	<b>(126,359)</b>	<b>(127,535)</b>
Tax on ordinary activities	–	–	–	–	–	–
<b>Net deficit on ordinary activities after taxation</b>	<b>(1,284)</b>	<b>(49,560)</b>	<b>(50,844)</b>	<b>(1,176)</b>	<b>(126,359)</b>	<b>(127,535)</b>
<b>Transfer from reserves</b>	<b>(1,284)</b>	<b>(49,560)</b>	<b>(50,844)</b>	<b>(1,176)</b>	<b>(126,359)</b>	<b>(127,535)</b>
<b>Deficit per share</b>	<b>(2.64)p</b>	<b>(101.94)p</b>	<b>(104.58)p</b>	<b>(1.86)p</b>	<b>(199.60)p</b>	<b>(201.46)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

	2002 £'000	2002 £'000	2001 £'000	2001 £'000
<b>Fixed assets</b>				
Investments		43,584		88,524
<b>Current assets</b>				
Debtors	153		219	
Investments	1,889		4,677	
Cash at bank	2,912		7,157	
	4,954		12,053	
<b>Creditors: amounts falling due within one year</b>	643		1,838	
<b>Net current assets</b>		4,311		10,215
<b>Net assets</b>		47,895		98,739
<b>Capital and reserves</b>				
Called up share capital		12,154		12,154
Capital redemption reserve		10,843		10,843
Share premium account		67,083		67,083
Capital reserve		(34,178)		15,382
Revenue reserve		(8,007)		(6,723)
<b>Equity shareholders' funds</b>		47,895		98,739
<b>Net asset value per share</b>		98.52p		203.10p

## International Biotechnology Trust plc

### Unaudited Cash Flow Statement

	For the year ended 31 August 2002 £'000	For the year ended 31 August 2001 £'000
<b>Operating activities</b>		
Dividend income received	–	2
Current asset investment income received	256	2,639
Deposit interest received	27	504
Management fee paid	(852)	(3,043)
Performance fee	–	(4,440)
Other cash payments	(729)	(2,138)
<b>Net cash outflow from operating activities</b>	<b>(1,298)</b>	<b>(6,476)</b>
<b>Servicing of finance</b>		
Interest paid	–	(15)
<b>Cash outflow from servicing of finance</b>	<b>–</b>	<b>(15)</b>
<b>Taxation</b>		
UK income tax recovered/(suffered)	67	(67)
<b>Tax recovered/(paid)</b>	<b>67</b>	<b>(67)</b>
<b>Capital expenditure and financial investment</b>		
Purchase of investments	(25,579)	(49,124)
Disposal of investments	19,816	101,152
<b>Net cash (outflow)/inflow from capital expenditure and financial investment</b>	<b>(5,763)</b>	<b>52,028</b>
<b>Net cash (outflow)/inflow before management of liquid resources and financing</b>	<b>(6,994)</b>	<b>45,470</b>
<b>Management of liquid resources</b>	<b>2,777</b>	<b>85,319</b>
<b>Financing</b>		
Repurchase of shares following Tender Offer	–	(121,828)
Stamp duty	–	(609)
<b>Net cash outflow from financing</b>	<b>–</b>	<b>(122,437)</b>
<b>Net cash (outflow)/inflow in the year</b>	<b>(4,217)</b>	<b>8,352</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 2002 or 31 August 2001. The financial information for the year ended 31 August 2001 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 2002 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 12.00 noon on Thursday 19 December 2002 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 November 2002 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.