Gene Therapy (1998) 5, 861–862

GT News

Finding funding fast

The first half of 1998 gives the impression it will be a record breaking year for gene therapy companies to find money. Up to the start of June these companies raised just over $119 million. This compares to $44 million by the same time in 1997 and around $83 million in 1996. The trend of increasing investment into the sector, which can be seen over the past four years, looks set to continue this year (chart 1).

The way firms are raising this money has not changed much either. Initial public offerings (IPO), where companies first offer shares on stock exchanges, remains the most lucrative method of raising capital. Indeed 37% of the money invested in gene therapy firms since the start of 1994 has come through this route (chart 2). This year is no exception to that strategy. Transgene's (Strasbourg, France) IPO in March, with dual listings on the French Nouveau Marché and US Nasdaq stock exchanges, raised around $66 million, which makes up over half of this year's total investments. This is the largest IPO ever for a gene therapy company, with the next closest being Transkaryotic Therapies (TKT, Cambridge, MA, USA) which raised $37.5 million back in August 1996. The result is that these two companies come first and second in the top-ten money raising gene therapy companies over the last four years (table 1).

Having gone public on one of the stock exchanges, it is possible to make follow-on share issues at a later date. One company to have utilised this money source is Targeted Genetics (Seattle, WA, USA) which has raised nearly $25 million in two follow-ons in 1995 and 1996. In total nearly $83 million has come through this route since 1994, but interestingly none in the last two years.

There are several reasons why this route is least frequently used as a source of funding. Clearly this option is not open to private companies, which rules out more than 50% of gene therapy firms. Additionally, if companies go for the massive IPO, like Transgene and TKT, where a larger proportion of the company is sold in the first round, there is less need to make follow-on share issues as these firms already have enough money. This is illustrated by

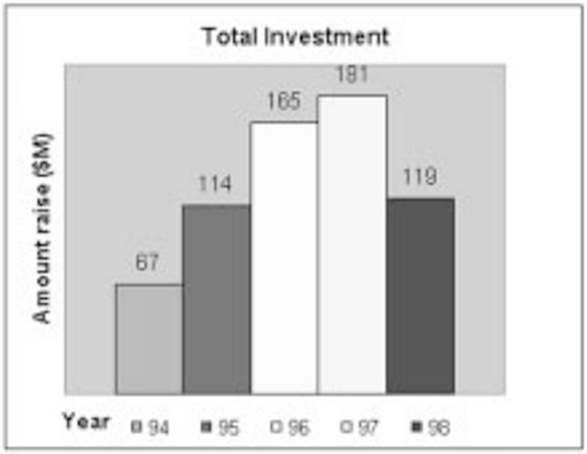

Chart 1 source: BioCentury

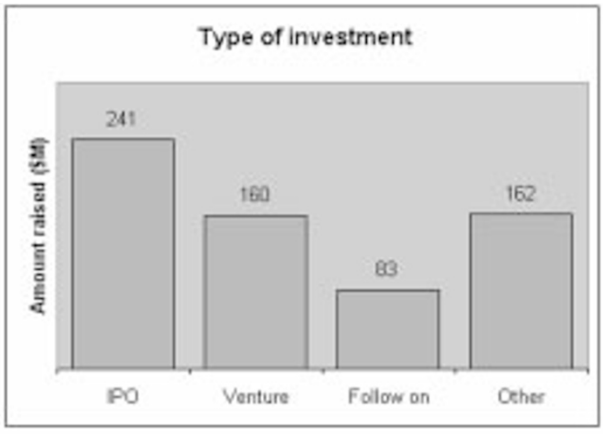

Chart 2 source: BioCentury

Table 1 source: BioCentury

Top ten money raisers

Company	Amount raised ($M)
TKT	93
Transgene	65.8
Megabois	54
Targeted Genetics	51
Aastrom	42
Ariad	38
GeneMedicine	34
Cobra (Therexsys)	34
Vical	30.6
Diacrin	29.5

Targeted Genetics, GeneMedicine (The Woodlands, TX, USA), which raised nearly $20 million in follow-on share offering in 1995, and Vical (San Diego, CA, USA) which raised $30 million in the same year. When these firms went public they only raised modest amounts, necessitating later follow-ons. Targeted Genetics raised $12 million, GeneMedicine raised $14.5 million, and Vical around $10 million. Although these firms have had a different fund raising strategy they are equally successful and all three appear in the top-ten money raising companies.

All the companies in this top-ten group have used public markets for investments, except Cobra (Keele, UK). Formerly called Therexsys, the firm raised a staggering $34 million in venture capital in 1996 from a host of leading institutional investors including 3i Group (London, UK), Biotechnology Investments (London), and Schroders Ventures (London). This level of venture capital is unique in gene therapy, the next closest is Megabios (Burlingame, CA, USA), which raised around $23 million in venture capital; although not even in one sitting but over two years from 1995 to 1996. Megabios also raised $30 million in its IPO last August, which places it in third place in the top-ten fundraisers.

Total venture capital put forward for gene therapy in 1998 so far stands at $20.6 million, which compares favourably with 1997 figures of $45 million for the whole year. Over the last four years $160 million of venture capital has gone into gene therapy, this amounts to almost a quarter of all investments.

The remaining 25% of the investments have come from a range of other money sources; these can vary in nature and size. They fall predominantly into the category of private placements, where companies offer institutional investors and individuals stock in exchange for cash. The largest private placement so far in 1998 has gone to Targeted Genetics, which raised $13 million primarily through GeneChem Technologies Venture Fund (Toronto, Canada), but also a handful of others. These private placements are the one area of investment that, so far in 1998, does not look set to increase substantially. Only $43 million has been raised this year which compares to $84 million for the whole of 1997.

RESEARCH

Researchers at the **University of Bristol** (Bristol, UK) have developed a technique that allows expression of a transfected gene to be switched on and off. The tetracycline-regulatable adenoviral transfection system allows long-term transfer of genes to neuronal cells *in vivo*. The activation and deactivation of expression is controlled by removing doxycycline from the animals' drinking water. **James Uney** and his team believe the technique could be valuable in behavioural and *in vivo* studies of neuronal gene function. Ultimately this could be used for gene therapies to treat brain disorders.
Nature Biotechnology **16**(6):5

Researchers at the INSERM institute (Paris, France) believe they have found a target which causes allergic asthma. A sub-group of T-cells, the gamma-delta group, produce IL-4, which triggers the asthmatic symptoms. **Marina Pretolani** and her team bred mice that had an allergic response to ovalbumin, and from this stock of mice bred more which lacked the gamma-delta cells. This last set of mice should have had an allergic response to ovalbumin but they only regained allergy when given IL-4.
Science **280** (5367):1265

A new treatment for haemophilia has corrected the mutation in liver cells which causes the disease. The technique called chimeraplasty used direct injection of RNA/DNA oligonucleotides into haemophiliac dog hepatocytes. This complex induces sequence mutation in the defective rat factor IX gene, resulting in prolonged blood coagulation. This latest research, conducted by **Clifford Steer** of the **University of Minnesota Medical Center**, builds on the principle work published in March.
Nature Medicine **4**(3):285

Sickle cell anaemia has so far shown difficult to treat with gene therapy. However, researchers at **Duke University Medical Center** (Durham, NC, USA) have developed a technique that uses RNA repair to address the problem. A ribozyme was used to alter sickle cell patients' mutant β-globin RNA transcripts. These transcripts were converted to mRNA encoding the anti-sickling protein γ-globin. The researchers, led by **Bruce Sullenger**, believe the technique could be used to treat other genetic disorders.
Science **280**(5369):1593-1596