

Cobra Therapeutics Limited  
(formerly known as Therexsys Limited)  
Annual report  
for the year ended 31 December 1997



**Cobra Therapeutics Limited**  
**(formerly known as Therexsys Limited)**

**Annual report**  
**for the year ended 31 December 1997**

	<b>Pages</b>
<b>Directors and advisers</b>	<b>1</b>
<b>Chairman's statement</b>	<b>2 - 3</b>
<b>Directors' report</b>	<b>4 - 6</b>
<b>Report of the auditors</b>	<b>7</b>
<b>Profit and loss account</b>	<b>8</b>
<b>Statement of total recognised gains and losses</b>	<b>9</b>
<b>Balance sheet</b>	<b>10</b>
<b>Notes to the financial statements</b>	<b>11 - 19</b>

**Cobra Therapeutics Limited**  
**(formerly known as Therexsys Limited)**

1

**Directors and advisers**

**Directors**

Mr D Gibbons  
Ms C Bingham  
Dr D Bloxham  
Dr S Bunting  
Dr M Carter  
Mr J Curnock Cook  
Dr P Harris  
Mr R Moulson  
Mr S Siddall

**Auditors**

Coopers & Lybrand  
Abacus House  
Castle Park  
Gloucester Street  
Cambridge  
CB3 0AN

**Secretary**

Mr R Moulson

**Bankers**

Barclays Bank Plc  
Crewe Business Park  
Lyme Building  
Westmere Drive  
Crewe  
CW1 1ZL

**Registered office**

10 Newhall Street  
Birmingham  
B3 3LX

J Henry Schroder & Co Ltd  
120 Cheapside  
London  
EC2V 6DS

# **Cobra Therapeutics Limited** **(formerly known as Therexsys Limited)**

2

## **Chairman's statement** **for the year ended 31 December 1997**

1997 was a year of scientific accomplishment for Therexsys which ended on a high note with the appointment of Dr David Bloxham, formerly Chief Operating Officer of Celltech, as Chief Executive and the partnership with Cobra Biosciences at Birmingham University. To reflect the importance of this partnership the name of the company has been changed to Cobra Therapeutics Limited.

At the beginning of the year we decided to focus the company's research efforts and academic collaborations on gene delivery to tumours and on DNA vaccines. In the light of advances in AIDs treatment using triple drug therapy and the resources which would have been required, the HIV programme was dropped. Substantial progress was made in understanding the natural barriers to non-viral mediated tumour transfection, and techniques for overcoming several of these were developed. However, the very high rates of *ex-vivo* gene delivery we achieved could not be repeated with *in-vivo* models, and accordingly, we do not expect to commence clinical trials using the GDEPT NTR/CB1954 system this year. Nevertheless, the potency of the system has been demonstrated in tumour models, and a full toxicology package for CB1954 developed. We are hopeful that, using the adenoviral vectors acquired under the Cobra transactions, we will enter the clinic in 1999.

We have also built a strong foundation in DNA vaccines focusing on transfection of dendritic cells. We have achieved state of the art rates of non-viral transfection *ex-vivo* in both mouse and human dendritic cells and we are now exploring targeting strategies for *in-vivo* delivery.

We continue to broaden our patent portfolio and had three patents granted during 1997, including one for the production of DNA which avoids the use of antibiotics. This provides an interesting opportunity to establish our technology in the market place via out-licencing and contract manufacturing.

We concluded the technology agreements with Birmingham University and the founders of Cobra Biosciences in December. This is already proving to be a close and fruitful relationship and it provides us with scientific know-how and creativity that would be difficult to achieve in a company of our size in any other way.

We ended the year with 57 employees, up from 49 in 1996. Dr Nowell Stebbing left the Board in July and I should like to thank him for his valuable contribution. Dr Michael Carter became a non-executive director towards the end of the year and brings considerable experience of the cancer market and the pharmaceutical industry which will benefit us greatly.

**Cobra Therapeutics Limited**  
**(formerly known as Therexsys Limited)**

3

Our cash position at the year end was healthy, at over £15 million, which puts us in a strong position to build on the scientific base developed in 1997 and I look forward to our future with much confidence.

A handwritten signature in black ink, consisting of a large, stylized 'D' followed by a long, sweeping horizontal line that tapers off to the right.

**D Gibbons MBE**  
**Chairman**

# **Cobra Therapeutics Limited** **(formerly known as Therexsys Limited)**

4

## **Directors' report** **for the year ended 31 December 1997**

The directors present their report and the audited financial statements for the year ended 31 December 1997. Comparative figures are presented for the period 1 October 1995 to 31 December 1996.

### **Principal activity**

The profit and loss account for the year is set out on page 8.

The principal activity of the company is the scientific research and commercialisation of gene therapy.

### **Review of business and future developments**

A full review of the company's activities is incorporated in the Chairman's statement on page 2.

### **Dividends**

The directors do not recommend the payment of a dividend.

### **Directors**

The directors who served during the period are listed below:

Mr D Gibbons	
Ms C Bingham	
Dr S Bunting	
Dr R Craig	(Resigned 31 January 1997)
Mr J Curnock Cook	
Mr S Siddall	
Dr N Stebbing	(Resigned 30 July 1997)
Dr M Carter	(Appointed 9 October 1997)
Dr P Harris	(Appointed 26 November 1997)
Mr R Moulson	(Appointed 26 November 1997)

# Cobra Therapeutics Limited (formerly known as Therexsys Limited)

5

## Directors' interests

The interests of the directors of the company in the shares of the company at 31 December 1997, together with their interests on appointment were:

	1997		On appointment	
	Ordinary shares of 10p each Number	'A' Preferred ordinary shares of 10p each Number	Ordinary shares of 10p each Number	'A' Preferred ordinary shares of 10p each Number
P Harris	10,000	-	10,000	-
R Moulson	-	450	-	450

Details of the interests of directors in share options over ordinary shares of 10p each at 31 December 1997 are as follows:

	At 1 January 1997	Number of options granted in the year	At 31 December 1997	Exercise price per share £	Date from which exercisable	Expiry date
D Gibbons	70,000	50,000	120,000	1.20	15 March 1997	1 February 2004
M Carter	-	10,000	10,000	1.20	8 October 1998	7 October 2004
P Harris	37,000	35,000	72,000	1.20	1 January 1996	29 July 2004
	65,000	-	65,000	0.12	19 September 1995	18 September 2001
R Moulson	50,000	12,000	62,000	1.20	1 February 1997	1 January 2004
	25,000	-	25,000	0.12	1 February 1997	31 January 2003
S Siddall	10,000	-	10,000	1.20	14 December 1996	13 December 2002

## Directors' responsibilities

The directors are required by UK company law to prepare financial statements for each financial year that give a true and fair view of the state of affairs of the company as at the end of the financial year and of the profit or loss of the company for that period.

The directors confirm that suitable accounting policies have been used and applied consistently and reasonable and prudent judgements and estimates have been made in the preparation of the financial statements for the year ended 31 December 1997. The directors also confirm that applicable accounting standards have been followed and that the financial statements have been prepared on the going concern basis.

The directors are responsible for keeping proper accounting records, for safeguarding the assets of the company and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

**Cobra Therapeutics Limited**  
**(formerly known as Therexsys Limited)**

6

**Auditors**

A resolution to reappoint the auditors, Coopers & Lybrand, will be proposed at the annual general meeting.

**By order of the board**

A handwritten signature in black ink, appearing to read 'R Moulson', with a horizontal line underneath.

**R Moulson**  
**Company secretary**



**Cobra Therapeutics Limited**  
**(formerly known as Therexsys Limited)**

7

**Report of the auditors to the members of**  
**Cobra Therapeutics Limited**  
**(formerly Therexsys Limited)**

We have audited the financial statements on pages 8 to 19.

**Respective responsibilities of directors and auditors**

As described on page 5 the company's directors are responsible for the preparation of financial statements. It is our responsibility to form an independent opinion, based on our audit, on those statements and to report our opinion to you.

**Basis of opinion**

We conducted our audit in accordance with Auditing Standards issued by the Auditing Practices Board. An audit includes examination, on a test basis, of evidence relevant to the amounts and disclosures in the financial statements. It also includes an assessment of the significant estimates and judgements made by the directors in the preparation of the financial statements, and of whether the accounting policies are appropriate to the company's circumstances, consistently applied and adequately disclosed.

We planned and performed our audit so as to obtain all the information and explanations which we considered necessary in order to provide us with sufficient evidence to give reasonable assurance that the financial statements are free from material misstatement, whether caused by fraud or other irregularity or error. In forming our opinion we also evaluated the overall adequacy of the presentation of information in the financial statements.

**Opinion**

In our opinion the financial statements give a true and fair view of the state of the company's affairs at 31 December 1997 and of its loss and total recognised gains and losses for the year then ended and have been properly prepared in accordance with the Companies Act 1985.

*Coopers & Lybrand*

**Coopers & Lybrand**  
**Chartered Accountants and Registered Auditors**  
**Cambridge**

*28 April 1998*

**Cobra Therapeutics Limited**  
**(formerly known as Therexsys Limited)**

8

**Profit and loss account**  
**for the year ended 31 December 1997**

	Notes	Year ended 31 December 1997 £	Period ended 31 December 1996 as restated £
Revenue	2	7,500	-
Staff costs	4	(2,007,997)	(1,938,548)
Depreciation		(917,030)	(645,570)
Other operating charges		(3,221,408)	(3,352,834)
Exceptional other operating charges	3	(847,195)	166,934
		<hr/>	<hr/>
Operating loss		(6,986,130)	(5,770,018)
Interest receivable		1,074,928	1,011,149
		<hr/>	<hr/>
Loss on ordinary activities			
before taxation	6	(5,911,202)	(4,758,869)
Taxation	7	-	-
		<hr/>	<hr/>
Loss for the financial year	16	(5,911,202)	(4,758,869)
		<hr/>	<hr/>

All amounts relate to continuing operations.

**Cobra Therapeutics Limited**  
**(formerly known as Therexsys Limited)**

9

**Statement of total recognised gains and losses**

	Notes	Year ended 31 December 1997 £	Period ended 31 December 1996 as restated £
Loss for the financial year		(5,911,202)	(4,758,869)
Prior year adjustment	8	(806,383)	-
<b>Total recognised losses since last annual report</b>		<b>(6,717,585)</b>	<b>(4,758,869)</b>

The introduction of UITF Abstract 17 ("Employee share schemes") has necessitated a further prior year adjustment relating to the granting of options in 1996 (see note 8). The cumulative effect on opening reserves is £Nil, comprising a credit to the prior year profit and loss account of £166,934, offset by a corresponding charge to reserves.

**Cobra Therapeutics Limited**  
**(formerly known as Therexsys Limited)**

10

**Balance sheet**  
**at 31 December 1997**

	Notes	1997 £	1996 as restated £
<b>Fixed assets</b>			
Tangible assets	9	1,868,547	2,221,596
<b>Current assets</b>			
Stocks	10	-	30,638
Debtors	11	99,467	217,524
Investments	12	14,490,073	19,486,078
Cash at bank and in hand		677,698	-
		15,267,238	19,734,240
<b>Creditors: amounts falling due within one year</b>	13	(1,090,049)	(1,002,144)
<b>Net current assets</b>		14,177,189	18,732,096
<b>Total assets less current liabilities</b>		16,045,736	20,953,692
<b>Capital and reserves</b>			
Called up share capital	14	1,387,513	1,352,848
Share premium account	16	28,930,479	28,809,093
Profit and loss account	16	(14,272,256)	(9,208,249)
<b>Equity shareholders' funds</b>	17	16,045,736	20,953,692

The financial statements on pages 8 to 19 were approved by the board of directors on 7th April, 1998 and were signed on its behalf by:



Director

# **Cobra Therapeutics Limited** **(formerly known as Therexsys Limited)**

11

## **Notes to the financial statements** **for the year ended 31 December 1997**

### **1 Principal accounting policies**

The financial statements have been prepared in accordance with applicable Accounting Standards in the United Kingdom. A summary of the more important accounting policies, which have been applied consistently, is set out below.

#### **Changes in accounting policies**

UITF Abstract 17 ("Employee share schemes") was introduced in 1997 and applies to accounting periods ending on or after 22 June 1997. In accordance with its provisions, the company has made a charge to the profit and loss account when options are granted being the market value of the shares at the date of grant less the exercise price of the options. The charge is then credited back to reserves in accordance with the Abstract.

With effect from 1 January 1997 the company changed its accounting policy for licence fees and intellectual property. The company now writes off such costs to the profit and loss account as incurred, previously these amounts were capitalised and amortised.

The effects of these changes in accounting policies are disclosed in note 8.

#### **Basis of accounting**

The financial statements are prepared in accordance with the historical cost convention.

#### **Tangible fixed assets**

The cost of tangible fixed assets is their purchase cost, together with any incidental costs of acquisition.

Depreciation is calculated so as to write off the cost of tangible fixed assets, less their estimated residual values, on a straight line basis over the expected useful economic lives of the assets concerned. The principal annual rates used for this purpose are:

	%
Short leasehold building improvements	25
Computers and office equipment	25
Laboratory equipment	25

# **Cobra Therapeutics Limited** **(formerly known as Therexsys Limited)**

12

## **Operating leases**

Costs in respect of operating leases are charged on a straight line basis over the lease term.

## **Pensions**

The company contributes to a defined contribution pension scheme providing benefits for employees. The pension cost charge represents contributions payable by the company to the fund in respect of the year.

## **Revenue recognition**

Amounts received or receivable in respect of licence fees are recognised as revenue when the licence rights are granted or the specific conditions stipulated in the contract or agreement have been satisfied.

## **Deferred taxation**

Provision is made for deferred taxation, using the liability method, on all material timing differences to the extent that it is possible that a liability or asset will crystallise.

## **Foreign currencies**

Assets and liabilities expressed in foreign currencies are translated into sterling at rates of exchange ruling at the end of the financial year. All foreign exchange differences are taken to the profit and loss account in the year in which they arise.

## **Cash flow statement**

The company has taken advantage of the exemption available under Financial Reporting Standard No. 1 (revised 1996) not to prepare a cash flow statement as it was a small company in 1996 and therefore qualifies for the financial reporting exemptions available to small companies for the current year.

## **Research and development**

All research and development costs are written off as incurred.

## **Intellectual property**

The cost of acquiring rights to intellectual property is written off to the profit and loss account as it is incurred.

# Cobra Therapeutics Limited (formerly known as Therexsys Limited)

13

## Government grants

Revenue grants are credited to the profit and loss account when received. Capital grants are included in deferred income and amortised in the profit and loss account over the expected useful life of the qualifying assets.

## 2 Revenues

Revenues consist of amounts receivable under collaborative research licence agreements in the United States.

## 3 Exceptional other operating charges

The exceptional operating charges of £847,195 (1996: credit £166,934) arise from the charge made on granting of share options. The charge is the difference between the market value of the shares at the date of grant and the exercise price of the options.

## 4 Employee information

The average monthly number of persons (including executive directors) employed by the company during the year was:

	Year ended 31 December 1997 Number	Period ended 31 December 1996 Number
Research	47	37
Administration	7	6
	—	—
	54	43
	==	==

Staff costs for the above persons:

	Year ended 31 December 1997 £	Period ended 31 December 1996 £
Wages and salaries	1,715,176	1,729,100
Social security costs	161,200	147,104
Other pension costs	131,621	62,344
	—	—
	2,007,997	1,938,548
	==	==

# Cobra Therapeutics Limited (formerly known as Therexsys Limited)

14

## 5 Directors' emoluments

	Year ended 31 December 1997 £	Period ended 31 December 1996 £
Aggregate emoluments:		
Emoluments and benefits	152,036	352,574
Compensation for loss of office	112,000	272,500
Pension contributions	1,905	19,131
	<u>265,941</u>	<u>644,205</u>
Highest paid director:		
Emoluments and benefits	28,958	127,395
Compensation for loss of office	112,000	272,500
Pension contributions	792	12,500
	<u>141,750</u>	<u>412,395</u>

Three directors had retirement benefits accruing to them from money purchase pension schemes, in respect of qualifying services.

No directors have exercised share options in the period. No directors have benefits accruing to them under long term incentive plans.

## 6 Loss on ordinary activities before taxation

The operating loss is stated after charging:

	Year ended 31 December 1997 £	Period ended 31 December 1996 £
Depreciation of tangible fixed assets:		
- owned by the company	917,030	647,308
Auditors' remuneration	8,000	6,250
Hire of plant and machinery - operating leases	1,972	2,234
Hire of other assets - operating leases	151,554	124,031
Research and development expenditure	<u>1,765,813</u>	<u>2,579,596</u>



# Cobra Therapeutics Limited (formerly known as Therexsys Limited)

15

## 7 Taxation

Due to the incidence of tax losses there is no taxation charge for the year. At the year end tax losses of £12,700,000 were carried forward subject to agreement with the Inland Revenue.

## 8 Changes in accounting policies

The prior year adjustments totalling £639,449 are made as a result of the changes in accounting policies for share options (£166,934) and licence fees (£806,383) discussed in note 1. The adjustment is reported in the statement of total recognised gains and losses and reserves (see note 16).

The effect of the change in accounting policy for licence fees is to reduce the current year's loss before taxation by £196,945. The effect on the comparative profit and loss account is to decrease the loss before taxation by £95,949.

The effect of the change in accounting policy for share options is to increase the current year's loss before taxation by £847,195. The effect on the comparative profit and loss account is to decrease the loss before taxation by £166,934.

## 9 Tangible fixed assets

	Short leasehold building improvements £	Computers and office equipment £	Laboratory equipment £	Total £
<b>Cost</b>				
At 1 January 1997	1,590,170	211,445	1,482,924	3,284,539
Additions	172,419	32,737	358,825	563,981
<b>At 31 December 1997</b>	<b>1,762,589</b>	<b>244,182</b>	<b>1,841,749</b>	<b>3,848,520</b>
<b>Depreciation</b>				
At 1 January 1997	547,979	57,275	457,689	1,062,943
Charge for year	430,376	55,751	430,903	917,030
<b>At 31 December 1997</b>	<b>978,355</b>	<b>113,026</b>	<b>888,592</b>	<b>1,979,973</b>
<b>Net book value</b>				
At 31 December 1997	784,234	131,156	953,157	1,868,547
At 31 December 1996	1,042,191	154,170	1,025,235	2,221,596

## 10 Stocks

	1997 £	1996 £
Consumables	-	30,638

# Cobra Therapeutics Limited (formerly known as Therexsys Limited)

16

## 11 Debtors

	1997 £	1996 £
Amounts falling due within one year		
VAT recoverable	37,552	168,583
Other debtors	46,716	-
Prepayments and accrued income	15,199	48,941
	<u>99,467</u>	<u>217,524</u>

## 12 Short term investments

Short term investments comprise certificates of deposit, bank deposits, commercial paper and fixed return deposits which are not repayable on demand.

## 13 Creditors: amounts falling due within one year

	1997 £	1996 £
Bank loans and overdrafts	-	161,964
Trade creditors	144,765	389,851
Taxation and social security	-	100,522
Other creditors	462,371	12,051
Accruals and deferred income	482,913	337,756
	<u>1,090,049</u>	<u>1,002,144</u>

Other creditors includes an amount of £177,970 (1996: £Nil) in respect of outstanding pension contributions.

## 14 Called up share capital

	1997 £	1996 £
<b>Authorised</b>		
5,015,900 (1996: 3,586,080) ordinary shares of 10p each	501,590	358,608
5,950,000 preferred ordinary shares of 10p each	595,000	595,000
6,666,667 "A" preferred ordinary shares of 10p each	666,667	666,667
	<u>1,763,257</u>	<u>1,620,275</u>
<b>Allotted, called up and fully paid</b>		
1,514,058 (1996: 1,167,410) ordinary shares of 10p each	151,406	116,741
5,941,666 preferred ordinary shares of 10p each	594,167	594,167
6,419,404 "A" preferred ordinary shares of 10p each	641,940	641,940
	<u>1,387,513</u>	<u>1,352,848</u>

# **Cobra Therapeutics Limited** **(formerly known as Therexsys Limited)**

17

## **Rights attached to each class of share**

### **Income and capital distribution**

Dividends shall be applied pari passu amongst all the issued ordinary, preferred ordinary and 'A' preferred ordinary shareholders of the company when they are declared.

In the event of a return of capital the preferred ordinary and 'A' preferred ordinary shareholders take priority over the ordinary shareholders. The preferred ordinary and 'A' preferred ordinary are entitled to receive, in respect of each share held, a sum equal to the amount subscribed for each share. Amounts paid up on each share are then returned to the ordinary shareholders. The balance of the company's assets are then divided amongst the preferred ordinary, 'A' preferred ordinary and ordinary shareholders.

### **Voting rights**

Holders of all classes of share have one vote per share held.

### **Transfer of shares**

Save as may otherwise be agreed between the members, or as authorised by the Articles of Association of the Company, no transfer, sale or disposal of ordinary and preferred ordinary shares of the company may be made without the written consent of a majority of the preferred ordinary shareholders. The 'A' preferred ordinary shares are freely transferable at any price to any person.

### **Increase in authorised share capital**

The company's authorised share capital was increased during the year by ordinary resolution from £1,620,275 to £1,763,257 by the creation of 1,429,820 new ordinary shares of 10p each.

### **Issue of share capital**

8,230 ordinary shares of 10p each (with an aggregate nominal value of £823) were issued in the year for total cash consideration of £6,052. The issues of shares occurred on the exercise of share options at various times during the year.

338,418 ordinary shares of 10p each (with an aggregate nominal value of £33,842) were issued in the year. The consideration for these shares was settled by the assignment of intellectual property which the directors have valued at £150,000. This has been written off to the profit and loss account in accordance with the company's accounting policy.

# Cobra Therapeutics Limited (formerly known as Therexsys Limited)

18

## 15 Options in shares of Cobra Therapeutics Limited

Options have been granted for 10p ordinary shares as follows:

Number of shares	Subscription price per share £	Period within which options exercisable
186,453	0.12	Before July 1999
18,860	0.63	Before August 2000
625	0.12	Before December 2000
124,297	0.12	Before October 2001
42,792	1.20	Before December 2001
48,250	1.20	Before December 2002
25,000	0.12	Before January 2003
25,000	0.12	Before July 2003
272,675	1.20	Before October 2003
142,250	1.20	Before March 2004
76,500	1.20	Between April 1998 and December 2004
744,519	0.10	Between December 1998 and December 2004
<u>1,707,221</u>		

## 16 Share premium account and reserves

	Share premium £	Profit and loss account £
At 1 January 1997 as previously stated	28,809,093	(8,401,866)
Prior year adjustment (see note 8)	-	(639,449)
Reversal of prior year adjustment (see note 8)	-	(166,934)
At 1 January 1997 as restated	28,809,093	(9,208,249)
Loss for the year	-	(5,911,202)
Reversal of share option charge (see note 1)	-	847,195
Premium arising on share issues	121,386	-
	<u>28,930,479</u>	<u>(14,272,256)</u>

# Cobra Therapeutics Limited (formerly known as Therexsys Limited)

19

## 17 Reconciliation of movements in shareholders' funds

	Year ended 31 December 1997 £	Period ended 31 December 1996 £
Loss for the year	(5,911,202)	(4,758,869)
Reversal of share option charge/(credit) (see note 1)	847,195	(166,934)
Share capital issued	34,665	655,436
Premium arising on share issues	121,386	21,786,756
	<u>(4,907,956)</u>	<u>17,516,389</u>
Opening shareholders' funds (previously £21,760,075 before deducting the prior year adjustment of £806,383)	20,953,692	3,437,303
Closing shareholders' funds	<u>16,045,736</u>	<u>20,953,692</u>

## 18 Capital commitments

	1997 £	1996 £
Capital expenditure that has been contracted for but has not been provided for in the financial statements	-	282,709
	<u>-</u>	<u>282,709</u>

## 19 Financial commitments

At 31 December 1997 the company had annual commitments under non-cancellable operating leases as follows:

	1997		1996	
	Land and buildings £	Other £	Land and buildings £	Other £
Expiring between two and five years inclusive	137,853	4,668	127,667	4,468
	<u>137,853</u>	<u>4,668</u>	<u>127,667</u>	<u>4,468</u>

## 20 Contingent liabilities

The Inland Revenue are challenging the company's treatment for tax purposes of its interest income, which could give rise to a taxation liability of the order of £660,000. The directors are of the opinion that the challenge is without foundation and intend to resist it strongly.

## 21 Post balance sheet event

On 20 February 1998 the company changed its name to Cobra Therapeutics Limited.