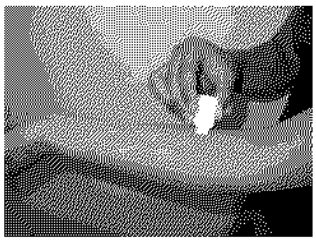
Acrux Limited (ASX: ACR)

Shareholder Update

March 2005



Acrux is a dynamic Australian specialty pharmaceutical company developing and commercialising a range of patient-preferred healthcare products for global markets, using innovative technology to deliver drugs through the skin

[1]Photo credit: Karen Tweedy-Holmes, Population Council

About Acrux (ASX: ACR)

- *Acrux is a specialty pharmaceutical company, developing and commercialising a range of patented, patient-preferred healthcare products for global markets, using its innovative technology to administer drugs through the skin.*

- *Acrux's product pipeline includes treatments of hormonal deficiencies, pain, central nervous system disorders and a contraceptive.*

- *20 human clinical trials have been completed with 8 different drugs and the lead product, Evamist™ (Estradiol MDTS®), is nearing the end of phase 3 clinical trials in the USA.*

- *Acrux has licensed USA rights for Evamist™ (Estradiol MDTS®) and Testosterone MDTS® to **VIVUS** and AUS/NZ distribution rights for Testosterone MDTS® and Fentanyl UDTS™ to **CSL Limited**. Acrux has also licensed its technology to **Eli Lilly** for veterinary healthcare products.*

3 March 2006

Dear Shareholder,

Acrux's first Shareholder Update since we published our Annual Report in October 2005 is attached. We trust that you will find it useful and informative. As you will see from the "Highlights" and from the "Milestones to watch out for", the Company has made sound progress. We remain in a strong financial position and are approaching a number of significant milestones in 2006. We will keep you and prospective shareholders well informed as we achieve these milestones.

We announced Board changes in January, as our products move closer to commercial release. Nuno D'Aquino decided to step down as non-executive Chairman due to private commitments. Nuno was instrumental in the transformation of Acrux to a listed company and we are pleased that he will continue as a non-executive director and will chair the Board's important Human Capital Committee. Ross Dobinson was appointed non-executive Chairman. Ross is a founder and former CEO of Acrux, has a comprehensive knowledge of the Company's operations and a strong interest in the Company's success. Ken Windle, a director since 2001, was appointed non-executive Deputy Chairman to support Ross and to provide complementary skills and independence. We also intend to introduce new skills onto the Board to enhance our international business development expansion.

Yours sincerely,

Ross Dobinson
Chairman

Igor Gonda
Chief Executive Officer

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Highlights since Annual Report:

- Licence agreement signed with Population Council[1], enabling Acrux to progress toward commercialisation of a unique contraceptive spray, containing the new-generation contraceptive drug Nestorone®

- Acrux's partner VIVUS completes enrolment in final US trial (Phase 3) with Evamist™ to treat menopausal symptoms and remains on track for US marketing application in mid-2006

- VIVUS and Acrux hold end of Phase 2 meeting with FDA on Testosterone MDTS® to treat decreased libido in women. VIVUS subsequently submitted proposal for Phase 3 trials to FDA for approval

- Two small clinical studies in preparation with Fentanyl MDTS® for chronic pain, to increase value of the product for commercial partnering

- Initiation of first of 3 remaining pharmacokinetic trials with Testosterone MD-Lotion™ to treat male testosterone deficiency in USA

- Acrux terminates licence to Napa Biosciences and recovers rights to dermatology products using Acrux's technology

- New patent for MDTS® delivery system granted in USA, extending protection out five more years to 2022. Two other patents granted in USA, bring total granted to nine

- 12% stake in Acrux acquired by Orbis Mutual Funds

- Cash reserves of $24.7 million at 31 December 2005

[1] The New York-based Population Council is one of the world's leading developers of reproductive health products, with a proven track record in the successful development of female contraceptives

Milestones to watch out for[1]:

- H1 2006 - European patent office decision on grant of key patent plus associated milestone payment from our partner Elanco (Eli Lilly's division of animal healthcare)
- H1 2006 - FDA decision on US Phase 3 trials design for Testosterone MDTS®
- Q2 2006 - Evamist™ US Phase 3 trial results
- Mid-2006 - US marketing application by VIVUS for Evamist™
- H2 2006 - Initiation by VIVUS of US Phase 3 trials with Testosterone MDTS® (pending FDA decision on trial design)
- H2 2006 - Initiation of Phase 2 trials with contraceptive spray
- H2 2006 - Initiation of second of three remaining trials with Testosterone MD-Lotion™

[1] calendar year

Product Development and Commercialisation

We are able to develop multiple products simultaneously at a relatively low cost because we use proven drugs and the same technology platform. Our key task for the major part of our product development is to show in human clinical trials that we obtain drug levels in the blood that are safe and effective ("pharmacokinetics"). This avoids (for most of our products) the lengthy, expensive and risky trials typically required for the development of new drugs.

Evamist™ (Estradiol MDTS®) for the treatment of symptoms of menopause

Hot flushes and night-sweats are symptoms which profoundly affect quality-of-life for many menopausal women. Transdermal estradiol is a well-accepted treatment of these and other symptoms associated with menopause.

In October, our partner (VIVUS) reported that it had completed enrolment of patients in their US Phase 3 trial. Before starting the trial, VIVUS secured a "Special Protocol Assessment" agreement from the FDA to confirm that this trial could provide the basis for a marketing application in the USA. The results of the trial are expected to be available in the second quarter of 2006 and VIVUS remains on track to file the marketing application with the FDA in mid-2006. If Evamist™ is approved by the FDA on a typical timescale this would mean approval to market the product in 2007.

VIVUS is due to pay Acrux a total of US$4 million on achievement of the two milestones of filing and approval of the marketing application. VIVUS will then pay Acrux royalties on US sales of the product. Annual sales of estrogen therapies in the USA are currently estimated as approximately US$1.4 billion, of which transdermal patches and gels comprise approximately US$250 million. Rodman & Renshaw predict that peak sales of Evamist™ by VIVUS will be US$160 million. Our published market research in post-menopausal women reported that 100% of women using patches or implants and 88% of women using tablet therapy would prefer to use our metered dose spray.

Acrux retains the rights over this product for the rest of the world and is seeking partners to distribute the product in other major markets.

Testosterone MDTS® for the treatment of decreased libido in women

Testosterone and other androgens are sex hormones that have major physiological significance in women. Androgen insufficiency in women is associated with a variety of symptoms which affect their quality-of-life, including fatigue, depression, low libido, muscle weakness and bone loss. There are currently no approved testosterone products for women in USA, Australia, Europe or Japan.

Using information gained from an end of Phase 2 meeting with FDA that Acrux and our US partner (VIVUS) attended, VIVUS has submitted a proposal to FDA on the size and length of Phase 3 trials to demonstrate the pivotal safety and efficacy of our testosterone product. VIVUS is again seeking a Special Protocol Assessment agreement from FDA to confirm that the trials can provide the basis for a marketing application. We expect a decision from FDA on the trials design in the first half of 2006 and expect VIVUS to start the trials in the second half of the year. VIVUS will fund all Phase 3 development and manufacturing expenditure for the USA.

VIVUS is due to pay Acrux a total of US$5.5 million on achievement of the three milestones of starting a Phase 3 trial, filing a marketing application and receiving approval of that application. VIVUS will then pay Acrux royalties on US sales of the product. In October, Rodman & Renshaw published a detailed review of this new market and products currently in development. The report predicted peak sales of Testosterone MDTS® of approximately $500 million in the USA alone. Our market research suggests that, when approved, many women will prefer our metered dose spray over a testosterone patch being developed by Procter & Gamble and testosterone gels being developed by Biosante and Cellegy. As far as we are aware, other companies developing testosterone products are all awaiting guidance from FDA on the Phase 3 trial requirements.

We retain the rights to license the distribution rights for Testosterone MDTS® outside the USA, Australia and New Zealand and we are actively seeking commercial partners for other major territories. We have consulted with European regulatory authorities on the remaining development requirements for Europe, and we are helping our Australian distributor (CSL) to prepare for commercialisation of the product in Australia and New Zealand.

Nestorone® MDTS®, the contraceptive spray

Nestorone® (which cannot be taken orally) is a versatile, fourth-generation synthetic progestin contraceptive. It closely resembles the natural hormone (progesterone) and has a good safety profile, with no undesirable androgenic hormonal effects.

Nestorone MDTS® is the third product in our "trilogy" of women's health sprays. On 14 February we announced that we had acquired the rights to commercialise a unique contraceptive spray, containing the new generation contraceptive Nestorone®. Under the agreement, Acrux has a worldwide licence from the Population Council (one of the world's leading developers of reproductive health products) to intellectual property covering the use of Nestorone® with Acrux's patented metered-dose skin spray delivery technology (MDTS®). Acrux will develop and commercialise Nestorone® MDTS® and has the right to sub-license distribution rights to the product to commercial partners. In addition to commercial distribution of the product, Acrux (or its sub-licensees) will make Nestorone® MDTS® available at reduced prices to public sector organisations that provide human reproductive health products to disadvantaged people.

Results of a Phase 1 clinical trial conducted by Acrux last year under a development agreement with the Population Council showed that a once-daily application of Nestorone® MDTS® provides the level of Nestorone® in the blood known to be effective for contraception. A Phase 2 trial, scheduled to start in the second half of 2006, aims to demonstrate that Nestorone® MDTS® controls ovulation. We will seek commercial partners for the remaining steps required for global commercialisation of the product.

The global market for hormonal contraceptives is more than US$5 billion per annum. The first transdermal patch, marketed by Johnson & Johnson, has sales of more than US$500 million per annum. The advantages of Nestorone® MDTS® include a convenient daily spray onto the arm, which is more discreet and less irritating to the skin than a patch, and we anticipate a better safety profile than other hormonal contraceptives. We expect that many women will prefer the ease and convenience of the spray to either ingesting pills or wearing patches.

Under the financial terms of the agreement, we will pay the Population Council 20% of licence fees, milestone payments and royalties that we receive from commercial partners for Nestorone® MDTS®. If we market the product ourselves in any territory, we will pay the Population Council 5% of our net sales. We have paid a licence fee of US$0.1m and will make milestone payments of US$0.1m for each of three milestones in the Phase 3 clinical and regulatory approval process. We also have the right to develop Nestorone® with our technology for uses other than contraception.

Fentanyl UDTS™ for the treatment of chronic pain

Fentanyl is a potent narcotic analgesic that is commonly used for the treatment of chronic pain. Transdermal fentanyl (in the form of patches) is a popular option for controlling chronic, moderate-to-severe pain associated with cancer, osteoarthritis, back injury and other chronic pain conditions.

In parallel with finalising the commercial product design, we are currently preparing for two small pharmacokinetic clinical trials in healthy volunteers. These trials will increase the value of the product by providing information on certain characteristics. We expect this information to be very useful in our ongoing discussions with potential commercial partners, and we are seeking partners to conduct and fund Phase 3 trials and marketing in major markets including the USA, Japan and Europe. Last year, we confirmed in a meeting with FDA that Fentanyl UDTS™ will follow an abbreviated path to approval in the USA, similar to the path followed by Evamist™.

Transdermal fentanyl patches, led by Johnson & Johnson's Duragesic® currently sell more than US$2 billion per annum worldwide. We are aiming for a product that has little or no skin irritation, is continuously effective and has high flexibility in dosing (and therefore pain control). Our market research indicates that with these competitive advantages over patches, sales could be very substantial.

Testosterone MD-Lotion® for the treatment of testosterone deficiency in men

Testosterone deficiency in men is associated with a number of symptoms including lethargy, depression and reduced libido. It is estimated that four to five million men suffer from testosterone deficiency in the USA alone, with this figure predicted to increase in future years. With an aging demographic in all developed countries, the worldwide market for this product is expected to grow rapidly.

Our development and commercialisation strategy for this product is based on guidance from FDA which shows that all the trials required for US marketing approval will only involve measuring the amount of drug delivered to the bloodstream ("pharmacokinetics"), rather than needing to measure the clinical effects of the drug. This means that our trial programme is more straightforward and has lower risk and lower cost than a traditional Phase 2 and Phase 3 clinical trials programme. We therefore intend to fund and complete the entire programme before licensing distribution rights for Testosterone MD-Lotion® to a commercial partner. A licence for a product with development completed and all technical risks removed would achieve significantly higher licence fees, milestone payments and royalty rates than a licence after either Phase 1 or Phase 2.

There are three remaining trials required, the first of which has just been initiated in 16 subjects. The remaining two larger trials will be completed during 2006 and 2007 under a US Investigational New Drug Application (IND). A New Drug Application is targeted for the second half of 2008 to obtain FDA approval to market the product in the USA.

The target profile for our product is a convenient, no-mess lotion which is faster drying and which has better dose control and a smaller application area than the existing transdermal gels. The target market of US$0.4 billion is currently dominated by Solvay's Androgel®.

Other Products

During the quarter, we began to increase investment into the systematic search for additional proven drugs that can be combined with our technology to create valuable new products. Our recently appointed Chief Scientific Officer, Adam Watkinson, is leading this initiative. We expect to be able to announce new products resulting from this initiative during 2006.

In November, we announced that we had terminated our licence to the US company Napa Biosciences Inc., which was to develop dermatology products using our technology for topical delivery of drugs. Napa Biosciences did not complete the capital raising that was a condition of the licence agreement. The licence was not material to our business, but we are seeking alternative means to generate value from our intellectual property in this non-core area. All intellectual property rights under the licence have returned to Acrux.

Personnel

During the quarter, Andrew Humberstone transitioned from full time Director of Clinical and Regulatory to part time Clinical & Regulatory Advisor. Andrew now focuses solely on providing his extensive expertise and experience to our project teams, rather than participating in managing the Company.

Investor Relations

The three principle milestones announced since the Annual Report were the contraceptive spray agreement with the Population Council on 14 February, the completion by VIVUS of enrolment of patients in the US Phase 3 trial of Evamist™ in October and the investment of $9.6m by the Bermuda-based fund manager Orbis to acquire 12% of Acrux's shares, also in October. The market reacted very positively to both October announcements, with the share price rising to 79 cents. The price has since fallen back to around 70 cents.

We are encouraged by the level of interest shown in Acrux so far in 2006, including a number of meetings with current or potential investors. The contraceptive spray announcement received excellent coverage in the Australian press, including the Age, Herald Sun, Australian Financial Review and the Australian. The announcement was also distributed in the USA and the UK, and was the first of a number of important value-adding business milestones expected to be achieved during 2006. On 8 December, a Business Review Weekly review of the biotech sector included Acrux in the 10 stocks to watch in 2006.

Acrux continues to be invited to take part in important investor conferences. In the fourth quarter of 2005, CEO Igor Gonda presented at the Wilson HTM Biotechnology and Medical Device Investment Conference, the BBY Life Sciences Conference and the Ausbiotech 2005 Conference. CFO Jon Pilcher presented at the Australasian Life Sciences investor forum in London. Igor, Jon and CSO Adam Watkinson also met with a number of institutions and brokers in Melbourne and Sydney in October and in Perth in November.

The UK specialist broker Rodman & Renshaw-Elixir published an analyst report on Acrux for the London Forum. This report and reports by some of the Australian analysts that cover us are now available in the Investor section of our website. Rodman & Renshaw in the USA also initiated analyst coverage of our partner VIVUS, as well as publishing a comprehensive review of the potential market which our Testosterone spray for women will enter.

Acrux and one other biotech company were selected by the Victorian government to give a private briefing to overseas venture capital intermediaries and investors as part of the Melbourne International Venture Capital Conference on 25 January.

Igor recently presented in a "Cure the Pain" experts panel at the annual "BIO CEO and Investors" conference in New York on 14 February. This is a reflection of the interest in our Fentanyl UDTS™ product for chronic pain. At the same conference, Nina Wilkins (Senior Manager Business Development & Intellectual Property) presented in a panel entitled "What's new in Gender/Sexual Health?", which was further evidence of the interest in our three women's health products. Acrux was the only company invited to be represented on two panels at the conference. Both panels gave Acrux good exposure in the USA for business development and investor relations.

Finance

Our financial results for the half-year to 31 December 2005 were released on 16 February:

Summary of financial results ($ million):

	6 months ended 31 Dec 2005	6 months ended 31 Dec 2004	Year ended 30 June 2005
Licensing and R&D revenues	-	0.9	2.7
Grant income	0.2	0.4	0.8
Interest and other income	0.7	0.5	1.3
Total revenue	**0.9**	**1.8**	**4.8**
Total expenditure	**(4.6)**	**(5.5)**	**(10.8)**
Loss before share options amortisation	**(3.7)**	**(3.7)**	**(6.0)**
Share options amortisation	(0.4)	(0.6)	(1.3)
Net loss	**(4.1)**	**(4.3)**	**(7.3)**
Net cash outflow before new capital	**(3.8)**	**(3.7)**	**(6.4)**
New share capital net proceeds	0.5	27.8	27.9
Net cash inflow/(outflow)	**(3.3)**	**24.1**	**21.5**
Net cash	**24.7**	**30.7**	**28.1**

We expect to receive three milestone payments in 2006 under our existing commercial agreements with Eli Lilly and VIVUS, subject to milestone achievement. Under the agreement with Eli Lilly, we will receive $0.5m on grant of a patent in Europe, and we expect a decision from the European patent office in the first half of 2006. Under the agreements with VIVUS, we will receive a payment upon filing of the US marketing application for Evamist™ and a payment upon first dosing in a Phase 3 trial with Testosterone MDTS®.

Our expenditure will be higher in the second half of the current financial year than in the first half, as we invest in further clinical trials of Fentanyl UDTS™, Testosterone MD-Lotion® and Nestorone

MDTS®. Our cash position remains strong and sufficient to fund our programmes until they start to generate revenue, whilst maintaining appropriate levels of working capital.

Intellectual Property

Since the Annual Report, three new patents have been granted in the USA. The most important, announced on 1 March, is patent number 6,978,945, which covers our Metered Dose Transdermal Spray (MDTS®) applicator. Importantly, the new patent does not expire until 2022, which is five years later than our other granted US patents. The patent provides very broad protection for the familiar part of our products that the patient sees and uses. It means that copies of our unique transdermal spray devices that provide a precise and convenient means of drug delivery are now kept out of the market until 2022 at the earliest. The applicator is currently used in our three women's health products – the contraceptive spray Nestorone® MDTS®, Testosterone MDTS® to treat decreased libido and Evamist™ to treat menopause symptoms.

Two other patents were granted in the USA, expiring in 2017, which provide an additional layer of patent protection for delivery of anti-anxiety drugs and anti-alopecia (baldness) drugs using Acrux's delivery technology.

Many of our patents are pending in other major markets; we expect a decision from the European patent office during the first half of 2006 on the grant of our first key patent in Europe. Two patents have been granted in Korea since the Annual Report.

The table on the next page shows our patent portfolio, with changes since the Annual Report shown in bold.

Acrux's current patent portfolio

	Family member	USA	Europe	Australia	ROW
Patent Family 1	Enhancer Patent i	G	P	G	P/G
	Enhancer Patent ii	G	n/a	n/a	n/a
	Enhancer Patent iii	G	n/a	n/a	n/a
	Enhancer Patent iv	G	n/a	n/a	n/a
	Enhancer Patent v	G	n/a	n/a	n/a
	Enhancer Patent vi	G	n/a	n/a	n/a
	Enhancer Patent vii	**G**	n/a	n/a	n/a
	Enhancer Patent viii	**G**	n/a	n/a	n/a
	Enhancer Patent ix	A	n/a	n/a	n/a
	Enhancer Patent x	P	n/a	n/a	n/a
	Enhancer Patent xi	P	n/a	n/a	n/a
	Enhancer Patent xii	n/a	**P**	n/a	n/a
Patent Family 2	**Dispensing Device i**	**G**	P	P	**P/G**
	Dispensing Device ii	n/a	n/a	n/a	**A**
	Dispensing Device iii	n/a	n/a	**P**	n/a
Patent Family 3	Delivery Patent	P	n/a	n/a	P
Patent Family 4	**Delivery Patent**	P	P	P	**P/G**
Patent Family 5	Delivery Patent	P	P	P	P
Patent Family 6	Delivery Patent	P	P	P	**P/G**
Patent Family 7	Dispensing Device	P	n/a	P	P
Patent Family 8	Dispensing Device	P	n/a	P	P
Patent Family 9	**Dispensing Device**	**PCT**	**PCT**	**PCT**	**PCT**
Patent Family 10	**Delivery Patent**	-	-	**Prov**	-
Patent Family 11	Delivery Patent	PCT	PCT	PCT	PCT
Patent Family 12	Delivery Patent	PCT	PCT	PCT	PCT
Patent Family 13	Method and Device	PCT	PCT	PCT	PCT
Patent Family 14	**Delivery Patent**	**PCT**	**PCT**	**PCT**	**PCT**
Patent Family 15	**Dispensing Device**	**PCT**	**PCT**	**PCT**	**PCT**
Patent Family 16	Dispensing Device	PCT	PCT	PCT	PCT
Patent Family 17	**Delivery Patent**	-	-	**Prov**	-
Patent Family 18	Delivery Patent	-	-	Prov	-
Patent Family 19	Method and Device	-	-	Prov	-
Patent Family 20	**Delivery Patent**	-	-	**Prov**	-
Patent Family 21	**Delivery Patent**	**Prov**	-	-	-
Design Family 1	Dispensing Device	G	G	G	G

G = granted; A = accepted; P = pending; Prov = provisional; PCT = Patent Cooperation Treaty