Acrux Limited

ACR.AX – INITIATION OF COVERAGE

MST Access

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14 November 2023

This is a revised version of the note published 13 August 2023.

Diversified pipeline reaching critical mass – tipping point close

NEED TO KNOW

- Leveraging topical formulation expertise and focusing on complex generics
- Product launches, deep pipeline and robust portfolio build momentum
- Targeting niche market segments to leverage first-mover advantage

Generic topical prescription pharmaceuticals more complex – and Acrux has the know-how: Topical generic pharmaceuticals (creams, ointments, gels, solutions) present unique challenges for manufacturers in their formulation, stability over time and proof of bioequivalence. Acrux, given its know-how and track record over 25 years in the development and commercialisation of topical prescription pharmaceuticals, is well suited to meet these challenges.

7th ANDA submitted and accepted for FDA review; new product launches and submissions: The FDA dossier submission to market a generic version of nitroglycerin ointment, 0.4%, is the 7th ANDA accepted for review by the agency. Acrux currently has 16 products in its portfolio (6 are approved). This is the highest number of approved products in the generic business to date for Acrux.

Targeting niche segments: Acrux targets niche topical market segments that will only support a few manufacturers and attract few competitors. This allows Acrux to potentially lock in an early-mover advantage and dominant market share, both reducing the appeal for new entrants and lessening pricing erosion and earnings volatility.

Investment Thesis

Topical generic pharmaceuticals more complex and less competitive: Acrux's proprietary drug delivery technology comprises known skin penetration enhancers and excipients, as well as solvents comprising volatile/non-volatile liquids. Acrux patents cover technology for delivering drugs through the skin using proprietary delivery methods. The transdermal and topical generic market is generally less competitive than the much larger oral generic market.

Portfolio of approved products reaches critical mass: Acrux has 16 products in its portfolio, of which 6 have been approved by the FDA and 4 commercialised.

Consistent record of commercialisation: Since incorporating in 1998, Acrux has been successful in developing formulations and bringing them to market via licensee partners in Europe and the US. A key aspect of its business model is out-licensing of products to strategic partners, reducing commercialisation risk.

Valuation

We value Acrux at $0.25 per share using a DCF methodology using a 12.5% discount rate, shares on issue of 288.7m and AUD/USD exchange rate of 0.65.

Risks

Our valuation is most sensitive to timing of approvals, as well as the ultimate pricing achieved given the number of competitors in specific product markets.

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ACRUX

Acrux is a specialty pharmaceutical company focused on developing and commercialising generic versions of topically applied prescription pharmaceuticals primarily for the US market. Acrux leverages on-site laboratories, a GMP manufacturing suite, and its clinical and commercial experience and has been successful over 25 years in bringing products to market through licensee partners in the US and Europe. The company's 16-product portfolio includes 6 approved products (4 commercialised, 2 pending) and 10 other products at various stages of development.

https://www.acrux.com.au/

Valuation	**A$0.25**
Current price	**A$0.04**
Market cap	**A$12m**
Cash on hand	**A$3.3m** *(30 September 2023)*

Upcoming Catalysts and Newsflow

Period	
2HCY23	Launch of Dapsone gel, 5%
1QCY24	Sales update of Prilocaine/Lidocaine
1HCY24	Pipeline progress and ANDA filings

Share Price (A$)

Source: FactSet, MST Access.

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Financial Summary

Acrux Ltd — ACR-AU

Year end 30 June, AUD unless otherwise noted

MARKET DATA

Price	**$**	**0.04**
52 week high / low	$	0.04-0.08
Valuation	**$**	**0.25**
Market capitalisation	$m	12.0
Shares on issue (basic)	**m**	288.7
Options / rights	m	0.0
Other equity	m	0.0
Shares on issue (diluted)	**m**	**288.7**

12-MONTH SHARE PRICE PERFORMANCE (A$)

INVESTMENT FUNDAMENTALS		FY22A	FY23A	FY24E	FY25E	FY26E
Reported NPAT	$m	(9.8)	(0.0)	(0.0)	0.0	0.0
Underlying NPAT	**$m**	**(9.8)**	**(0.0)**	**(0.0)**	**0.0**	**0.0**
Reported EPS (diluted)	¢	(3.5)	(0.3)	(1.3)	0.8	3.6
Underlying EPS (diluted)	**¢**	**(3.5)**	**(0.3)**	**(1.3)**	**0.8**	**3.6**
Growth	%					
Underlying PER	x	**nm**	**nm**	**nm**	**5.0**	**1.2**
Operating cash flow per share	¢	(3.1)	0.2	(1.2)	0.9	3.7
Free cash flow per share	¢	(3.3)	0.2	(1.2)	0.9	3.7
Price to free cash flow per share	**x**	**nm**	**20.4**	**nm**	**4.4**	**1.1**
FCF Yield	%	nm	4.9%	nm	22.6%	88.9%
Dividend	**¢**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Payout	%	0.0%	0.0%	0.0%	0.0%	0.0%
Yield	**%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**
Franking	%	0.0%	0.0%	0.0%	0.0%	0.0%
Enterprise value	**$m**	**6.2**	**5.7**	**9.3**	**6.8**	**(3.7)**
EV/EBITDA	x	nm	nm	nm	3.3	nm
EV/EBIT	x	nm	nm	nm	2.9	nm
Price to book (NAV)	x	1.3	1.4	2.4	1.6	0.7
Price to NTA	x	1.6	1.8	4.2	2.3	0.8

KEY RATIOS		FY22A	FY23A	FY24E	FY25E	FY26E
ROE	%	nm	nm	nm	33.0	58.7
ROA	%	nm	nm	nm	20.0	46.2
Net tangible assets per share	$	0.0	0.0	0.0	0.0	0.1
Book value per share	$	0.0	0.0	0.0	0.0	0.0
Net debt/(cash)	$m	(5.8)	(6.2)	(2.7)	(5.2)	(15.7)

DUPONT ANALYSIS		FY22A	FY23A	FY24E	FY25E	FY26E
Return on Assets	%	nm	nm	nm	20.0	46.2
Leverage	x	1.6	1.5	2.0	1.6	1.3
Return on Equity	%	nm	nm	nm	33.0	58.7

KEY PERFORMANCE INDICATORS	FY22A	FY23A	FY24E	FY25E	FY26E
Commercialised	3	4			
Approved	5	6			
Under review by FDA	3	3			
Under development	8	7			

HALF YEARLY DATA		2H21	1H22	2H22	1H23	2H23
Revenue	$m	0.5	0.7	1.0	1.4	7.0
Other income	$m	3.4	1.4	2.0	1.8	1.5
Operating expenses	$m	9.2	7.1	7.6	6.0	6.1
EBITDA	$m	(5.6)	(5.3)	(4.9)	(3.1)	2.2
EBIT	$m	(5.2)	(5.0)	(4.6)	(2.8)	2.4
PBT	$m	(4.9)	(5.3)	(4.9)	(3.1)	2.9
Reported NPAT	$m	(4.8)	(5.5)	(5.0)	(3.3)	2.5

PROFIT AND LOSS		FY22A	FY23A	FY24E	FY25E	FY26E
Revenue	**$m**	**1.7**	**8.4**	**6.5**	**12.3**	**20.2**
Other income	**$m**	**3.4**	**3.4**	**2.9**	**3.2**	**3.2**
Operating expenses	$m	14.7	12.7	13.3	13.1	13.1
EBITDA	**$m**	**(10.3)**	**(0.9)**	**(4.3)**	**2.1**	**10.0**
Depreciation & Amortisation	$m	0.7	0.6	0.4	0.3	0.3
EBIT	**$m**	**(9.6)**	**(0.3)**	**(3.9)**	**2.4**	**10.3**
Net interest	$m	0.0	0.1	0.1	0.1	0.1
Pretax Profit	**$m**	**(9.6)**	**(0.2)**	**(3.8)**	**2.4**	**10.4**
Tax expense	$m	(0.3)	(0.6)	0.0	0.0	0.0
Reported NPAT	**$m**	**(9.8)**	**(0.8)**	**(3.8)**	**2.4**	**10.4**
Weighted average diluted shares	m	283.9	286.5	288.7	288.7	288.7

GROWTH PROFILE		FY22A	FY23A	FY24E	FY25E	FY26E
Other income	%	(11.1)	0.3	(15.3)	12.4	0.0
EBITDA	%	(23.0)	(96.5)	1,076.0	(159.9)	337.0
EBIT	%	(21.9)	(90.9)	367.9	(147.4)	386.3
Reported NPAT	%	(22.1)	(92.2)	397.1	(163.5)	331.4

BALANCE SHEET		FY22A	FY23A	FY24E	FY25E	FY26E
Cash	$m	5.8	6.2	2.7	5.2	15.7
Receivables	$m	0.4	0.4	0.4	0.4	0.4
Current assets	**$m**	**10.0**	**9.9**	**6.3**	**8.8**	**19.3**
Leased assets	$m	1.9	2.0	2.0	2.0	2.0
Non current assets	**$m**	**4.3**	**3.4**	**3.2**	**3.2**	**3.2**
Total assets	**$m**	**14.3**	**13.3**	**9.6**	**12.0**	**22.5**
Trade and other payables	$m	0.9	0.8	0.8	0.8	0.8
Other	$m	2.4	1.6	1.6	1.6	1.6
Current liabilities	**$m**	**3.3**	**2.4**	**2.4**	**2.4**	**2.4**
Total liabilities	**$m**	**5.2**	**4.6**	**4.7**	**4.7**	**4.8**
Net assets	**$m**	**9.1**	**8.7**	**4.9**	**7.3**	**17.7**
Share capital	$m	114.6	114.9	114.9	114.9	114.9
Retained earnings	$m	(113.7)	(114.5)	(118.3)	(115.9)	(105.5)
Other	$m	8.3	8.3	8.3	8.3	8.3
Total equity	**$m**	**9.1**	**8.7**	**4.9**	**7.3**	**17.7**

CASH FLOW		FY22A	FY23A	FY24E	FY25E	FY26E
Net loss for period	**$m**	**(9.8)**	**(0.8)**	**(3.8)**	**2.4**	**10.4**
Depreciation & Amortisation	$m	0.7	0.6	0.4	0.3	0.3
Changes in working capital	$m	(0.4)	(0.3)	0.0	0.0	0.0
Other	$m	0.8	1.2	0.0	0.0	(0.0)
Operating cash flow	**$m**	**(8.8)**	**0.7**	**(3.4)**	**2.7**	**10.7**
Payments for PPE	$m	0.0	0.0	0.0	0.0	0.0
Investing cash flow	**$m**	**(0.5)**	**(0.1)**	**0.0**	**0.0**	**0.0**
Capital raising costs	$m	0.0	0.0	0.0	0.0	0.0
Lease liability prinicipal repayments	$m	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)
Financing cash flow	**$m**	**(0.2)**	**(0.2)**	**(0.2)**	**(0.2)**	**(0.2)**
Cash year end	**$m**	**5.8**	**6.2**	**2.7**	**5.2**	**15.7**
Free cash flow	**$m**	**(9.3)**	**0.6**	**(3.4)**	**2.7**	**10.7**

Source: Company reports, MST Access estimates

Investment Thesis: Pivotal Year Ahead

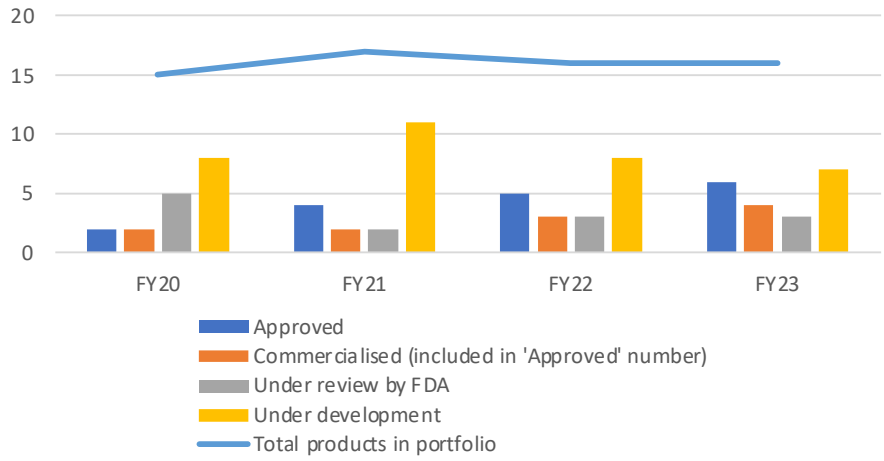
Acrux Limited, incorporated in 1998 and listed on the ASX in 2003, is a specialty pharmaceutical company focused on developing and commercialising generic versions of topically applied prescription pharmaceuticals for the US market. Acrux has 16 generic topical pharmaceutical products at various stages of development and commercialisation. The company has focused on identifying niche products and markets with high entry barriers, looking for opportunities that provide efficient scale for only a small number of players to create a defensible position. This diversified product portfolio is now fast approaching a tipping point in revenue/profitability. Acrux uses on-site laboratories, a GMP manufacturing suite, and clinical and commercial experience garnered over 25 years in bringing products to market through licensee partners in the US and Europe.

Overview: a full pipeline of complex generics for the US market

While Acrux previously applied proprietary technology to create new branded products, the company decided to shift its strategic focus to developing generic versions of complex topical pharmaceuticals specifically for the US market in 2015. This decision, based on the relatively lower development costs and opportunity to achieve a sustainable commercial advantage and recurring revenues in more niche market segments, is now bearing fruit.

Acrux submitted its first generic product to the FDA during FY2018. Its July 2023 submission for nitroglycerine ointment, 0.4%, was its seventh such application to the FDA. Figure 1 summarises the company's 16 products, with 6 currently approved. Of the approved products, 4 are commercialised, and the other 2 predate the company's move into generics.

Figure 1: Acrux product portfolio and pipeline:
16 products currently at various stages of development and commercialisation



Source: Acrux. Note that 'Commercialised' products are a sub-set of the 'Approved' category.

Industry background: understanding topical generic pharmaceuticals

Generic topicals treat a range of conditions, such as infections, inflammatory disorders and localised pain.

Topical pharmaceuticals are applied directly to the skin or mucous membranes. They come in various forms (creams, ointments, gels, lotions, patches, sprays) and are most commonly designed for local treatment of skin conditions or to deliver medication through the skin into the bloodstream. Topical medications have several advantages over other modes of application, including more targeted delivery to affected areas, reduced systemic side effects compared to oral medications, and easier application. Notably, Acrux focuses on topical dermatological products that act primarily on the surface of the skin.

Generic pharmaceuticals have the same active ingredient as a branded drug, but may contain different non-active ingredients and/or look different. Generics are as effective, safe and flexible as the branded drug (with various forms allowing healthcare providers to choose the best formulation for a patient). They are more cost effective for patients and the health system and more widely available to a larger population.

Commercial strategy: how Acrux has chosen its target segment

Acrux is targeting niche, complex generic pharmaceutical market segments within the topical category. This is a strategically attractive space for the company, and is aligned with its knowledge base and technical skills, for a number of reasons.

Not every company can create complex topical generics – Acrux has the skills and know-how

Generics can be characterised as simple or complex. Simple generics are generally copies of a small-molecule reference drug, chemically identical to their branded counterparts (typically, oral formulations). By contrast, the FDA has defined 'complex generics' as those with any of several characteristics including complex formulations and complex dosage forms – both of which apply to many of the products in Acrux's portfolio and pipeline.

Pharmacokinetic (PK) parameters of topically applied drugs can be challenging, as topical products are typically applied in multiple doses over repeated applications, making measures of bioavailability technically more difficult. Measuring PK is also difficult as there is limited absorption, making measurement of levels in the blood level less relevant than for orals. This complexity of development increases when creating generic versions of approved topically applied products. Acrux's focus on topically applied formulations goes back to the origins of the company's transdermal drug delivery platform which predates its foray into generic drugs. As such, we think Acrux's technical and regulatory know-how, built over 25 years, positions the company well to pursue these markets.

Topical generics can only sustain a few players in a quickly saturated space – Acrux is poised to strike fast

The challenges inherent in developing topical generic pharmaceuticals result in a smaller number of manufacturers and lower competition relative to generic oral formulations, which provides opportunities for those players that can gain a first-mover advantage or be early entrants into a market. Further, given the impact on discount to brand pricing of additional generic competitors, these smaller markets typically reach a natural point of economic equilibrium that support only a limited number of players but for longer periods of time. Diminishing returns on investment for late comers can therefore discourage competitors from entering the market, highlighting the importance of speed to market.

Once in the market, early entrants have a sustainable advantage – Acrux knows how to leverage it

The challenges can create significant barriers to entry and include technical complexity of development which can have a direct impact on cost of development and discourage new entrants. This first-mover advantage is further compounded by the fact that FDA Priority Review is given to ANDA applications with three or fewer approved generics, rewarding the companies that act fast. Acrux's demonstrated ability to identify and establish marketing/distribution partnerships ahead of ANDA approvals bodes well for being an early entrant into a target market and potentially gaining a first-mover advantage.

Recent events

Dec 22 - Launch of Prilocaine/Lidocaine

Accepted by FDA for review:

- July 23 -Nitroglycerin ointment, 0.4%: a treatment for moderate to severe pain caused by chronic anal fissure
- August 22 - Acyclovir cream, 5%: a treatment for cold sores
- March 21 - Dapsone gel, 7.5%: a treatment for acne vulgaris

Potential near-term catalysts

2HCY23 - Launch of Dapsone gel, 5%

1QCY24 - Sales update of Prilocaine/Lidocaine

1HCY24 - FDA approvals of ANDA filed for review

Valuation

We value Acrux at $0.25 per share, using a DCF methodology on free cash flow (see Figure 17). Key DCF inputs are a beta of 1.22, WACC of 12.3% and a conservative terminal growth rate of 0%.

Sensitivities and risks

Our valuation is most sensitive to timing of approvals, as well as the ultimate pricing achieved given the number of competitors in specific product markets. Please refer to page 17 for a more detailed discussion.

Company Overview: Building a Diversified Product Pipeline Across Development Stages

The Acrux story – from 1998 to today

Beginnings – seeking new patents with novel technology for proven drugs: Acrux Limited was incorporated in 1998 and listed on the ASX in 2003. Its goal was to develop new products using novel technology discovered at Monash University, Melbourne, for delivery of pharmaceuticals via the skin. Acrux initially focused on adapting proven drugs to create new patentable pharmaceuticals. This generated a range of applications and products, which were licensed to and commercialised by various partners.

The Axiron era – ups and downs: Acrux's most successful product in the early years – when the company's focus was on adapting proven drugs to create new patentable pharmaceuticals – was Axiron, a testosterone replacement therapy approved for male hypogonadism (low testosterone levels) and out-licensed to Eli Lilly. Axiron was the first testosterone replacement product approved for administration via the armpit (underarm) using Acrux's then-proprietary MDTS® drug delivery system. This product brought Acrux significant success, with peak annual sales in the US of US$179m in 2014. However, sales slumped when the FDA raised safety concerns regarding the entire testosterone replacement therapy category. Furthermore, generic competitors successfully challenged Acrux's Axiron patents. These challenges culminated in the termination of Acrux's licensing agreement with Eli Lilly in September 2017.

Today – a new focus; filling the pipeline with lots of possibilities: In 2018, Acrux refocused the company's efforts on expanding and advancing its burgeoning generic topically applied pharmaceutical pipeline. Since 2017, the company has submitted 7 generic dossiers[1] with the FDA for review under an Abbreviated New Drug Application (ANDA), a process whereby a generic company must demonstrate the generic product's substitutability with the reference (branded) product. This includes the most recent ANDA in July 2023 for a generic version of nitroglycerin ointment, 0.4%. Overall, Acrux now has 16 products in its portfolio at various stages of development and commercialisation (see Figure 2).

Figure 2: Overview of the Acrux product pipeline

		Development phase					
Acrux product	**Branded equivalent**	***Formulation development***	***Process development***	***Bioequivalence/ clinical***	***Regulatory submission***	***Approval/ launch***	***On market***
		Determine product formulation in in-house laboratory	Scale up to commercial manufacturing	Demonstrate equivalence to brand-name product	Submit dossier and data for FDA approval	Obtain FDA approval	Launch by partner
Approved and commercialised							
Prilocaine/Lidocaine 2.5% cream		✓	✓	✓	✓	✓	✓
Estradiol solution (Lenzetto® ex-US)	Lenzetto® ex-US	✓	✓	✓	✓	✓	✓
Estradiol solution (Evamist® in US)	Evamist® in US	✓	✓	✓	✓	✓	✓
ACR108 Testosterone 30mg/1.5ml solution		✓	✓	✓	✓	✓	✓
Approved and not commercialised							
Dapsone 5% gel		✓	✓	✓	✓	✓	
Efinaconazole 10% solution		✓	✓	✓	✓	✓	
Under review by FDA							
Nitroglycerin 0.4% ointment		✓	✓	✓	✓		
Dapsone 7.5% gel		✓	✓	✓	✓		
Acyclovir 5% cream		✓	✓	✓	✓		
Development projects							
Not publicly disclosed		✓	✓				
Not publicly disclosed		✓	✓				
Not publicly disclosed		✓	✓				
Not publicly disclosed		✓					
Not publicly disclosed		✓					
Not publicly disclosed		✓					
Not publicly disclosed		✓					

Source: Acrux.

[1] Dossier: a document that contains all the technical data (administrative, quality, nonclinical and clinical) of a pharmaceutical product to be approved/registered/marketed in a country.

Asset overview: product portfolio – 16 products across stages and drug types

Acrux has a total of 16 products across its portfolio and pipeline. Figures 3–5 break down the details across each category in the pipeline – drugs that are:

- approved and commercialised
- approved but not yet commercialised
- currently under FDA review.

In addition, Acrux has several drug candidates which are in development, but not yet submitted to the FDA. Details for these drug candidates are not disclosed for competitive reasons.

Figure 3: FDA approved and commercialised: 4 products

Generic name and approval date	Brand name product	Commercial partners	Use and addressable markets	Addressable market size	Orange Book ANDAs	Marketed
Lidocaine 2.5%/Prilocaine 2.5%	EMLA	Padagis	Topical anaesthetic for use on normal intact skin for local analgesia, genital mucous membranes for superficial minor surgery and as a pre-treatment for infiltration anaesthesia	US$38m	5	3
Estradiol solution	Lenzetto® ex-US	Gedeon Richter	Used to treat moderate to severe hot flushes commonly associated with menopause	n/a	n/a	n/a
Estradiol solution	Evamist® in US	Padagis	Used to treat moderate to severe hot flushes commonly associated with menopause	n/a	0	0
Testosterone 30mg/15ml solution	Generic (Perrigo)	Dash Pharmaceuticals	Testosterone replacement therapy	US$3m	6	6

Source: Acrux.

Figure 4: FDA approved but not yet commercialised: 2 products

Generic name and approval date	Brand name product	Commercial partners	Use and addressable markets	Addressable market size	Orange Book ANDAs	Marketed
Dapsone 5% gel	Aczone	undisclosed	Treatment for acne vulgaris	US$19m	3	2
Efinaconozole 10% solution	Jublia	n/a	Treatment for fungal infection of toenails	US$274m	2	0

Source: Acrux.

Figure 5: Submitted to FDA and currently under review: 3 products

Generic name and approval date	Brand name product	Commercial partners	Use and addressable markets	Addressable market size	Orange Book ANDAs	Marketed
Nitroglycerin ointment, 0.4%	Rectiv	undisclosed	Treatment for moderate to severe pain caused by chronic anal fissure	US$20m	0	0
Dapsone gel, 7.5%	Aczone	undisclosed	Treatment for acne vulgaris	US$47m	4	3
Acyclovir cream, 5%	Zovirax	undisclosed	Treatment for cold sores	US$15m	3	3

Source: Acrux.

Industry Backdrop: Generics Grow in Importance

Pharmaceutical product life cycle: where generics come in

The research and drug development phase

Pharmaceutical companies invest heavily in research and development to create new drugs that can be patent protected. During this phase, the focus is on discovering and developing new active pharmaceutical ingredients (APIs) and formulations, testing for safety/toxicity and proving clinical efficacy.

Brand-name drugs must demonstrate their safety and effectiveness through expensive and time-consuming research and development programs, including clinical studies. This phase typically lasts 10–15 years until FDA approval is obtained.

The branded drug phase

Patent protection for products is a critical component of new product development in the pharmaceutical industry. Patents give companies which generate the 'branded'/'originator' drug a set period of time to recoup their investment. The typical patent protection period is 20 years when the patent is not challenged.

The generic introductions phase

On average, however, branded drugs are only on the market for 12.5 years before generic forms are launched, given successful challenges to patents under paragraph IV certification (see information later on this section for a brief description of the various frameworks under which generics may be brought to market, as well as Appendix 1 for a detailed outline of the process).

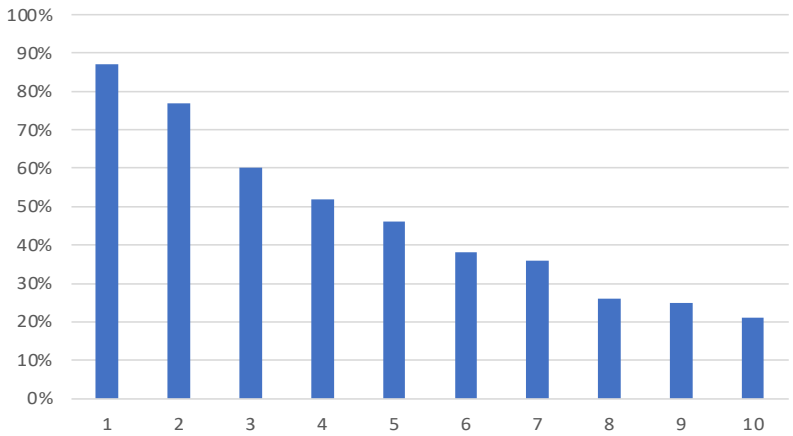
After a patent expires or is successfully challenged, multiple generic forms of the drug may enter the market, after which time the price of the drug typically falls significantly for both the branded and generic forms. This level of discount to branded pricing, or price erosion, is highly correlated to the number of generic competitors for the branded drug (see Figure 7).

Generic pharmaceuticals play a key role in the pharmaceutical product life cycle by increasing competition and improving access to essential medications as patents expire or become unenforceable. The key advantage of generic medicines, however, is their substantially lower cost – up to 85% less than that of a brand-name drug. This in turn may improve access and availability to medicine and support treatment adherence.

Figure 6: Pharmaceutical product life cycle

Source: Pharmaceutical Research and Manufacturers of America (PhRMA). Drug Discovery and Development: Understanding the R&D Process. Washington, DC: PhRMA; 2014. Grabowksi et al.

Figure 7: Relative generic-to-brand price per dose falls as number of manufacturers goes up



Source: Dave C, Hartzema A, Kesselheim A 2017, 'Prices of Generic Drugs Associated with Numbers of Manufacturers', N Engl J Med 377;26, pp. 2597-2598.

Understanding generics – a primer on key characteristics of generic pharmaceuticals

What is a generic drug?

A generic pharmaceutical is therapeutically equivalent to a 'branded' (also known as an 'innovator' or 'originator') drug, with the same risks and benefits. Generics are drugs for which the initial patent protection for the active ingredient has either expired or been successfully challenged by a generic company ahead of its expiration (under a paragraph IV action). The generic must provide the same quality, safety and efficacy as the original branded product, undergoing strict scrutiny before it is approved by regulators. However, a generic drug may look different from the branded version and contain different non-active ingredients. Generic drugs account for about 90% of prescriptions filled in the US.

How do generics compare with brand-name drugs? They are just as good – and in some ways, better

Compared with brand-name drugs, generic drugs are:

- **equally effective:** Generic pharmaceuticals must meet the same rigorous quality and efficacy standards as brand-name drugs to ensure that they work just as effectively. Regulatory authorities (such as the FDA) require generic versions to be bioequivalent to the brand-name drug, with the same active ingredient, strength, dosage form, and route of administration.
- **equally safe:** Generic pharmaceuticals undergo rigorous testing for safety and quality, just like brand-name drugs. Patients can trust that generics are safe and well-tolerated.
- **equally flexible:** Generics come in various forms, including creams, ointments, gels, lotions, sprays, and patches. This allows healthcare providers to choose the most appropriate formulation for a patient's specific needs.
- **more cost-effective:** The introduction of generics into the market creates competition, which often leads to reduced prices for both generic and brand-name versions. This can lead to significant cost savings for patients, especially those without insurance coverage or with high co-pays, and can contribute to overall healthcare cost savings across the system.
- **more widely available:** Because of their lower cost, generics are more widely available at pharmacies and healthcare facilities than brand-name drugs, enhancing patient access to necessary treatments.
- **eligible, in some cases, for market exclusivity**: For some generic products, which are first to market, exclusivity for the first 180 days post commercial launch can be granted under the FDA's Competitive Generic Therapies (CGT) guidance, published in March 2020.

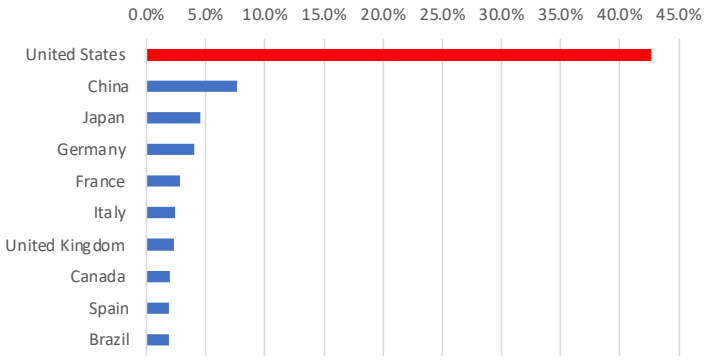
The market for generics

Geography: focusing on the US

According to Statista, the global pharmaceutical industry had annual revenues of US$1.42 trillion in 2021, of which the US pharmaceutical sector accounted for US$550 bn (billion dollars).

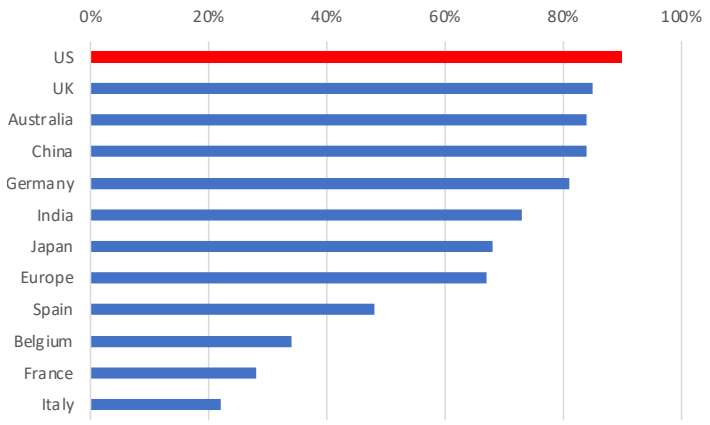
Figures 8 and 9 clearly illustrate why the US is such an attractive market for generic pharmaceuticals, with around 44% market share of the global pharmaceuticals industry in 2023 and 90% of the US pharmaceutical market comprising generics.

Figure 8: Pharmaceuticals market share by country (as % of global market)



Source: 'Generics 2030: Three strategies to curb the downward spiral', KPMG 2020.

Figure 9: Generics market share (as % of country's overall pharmaceuticals market)

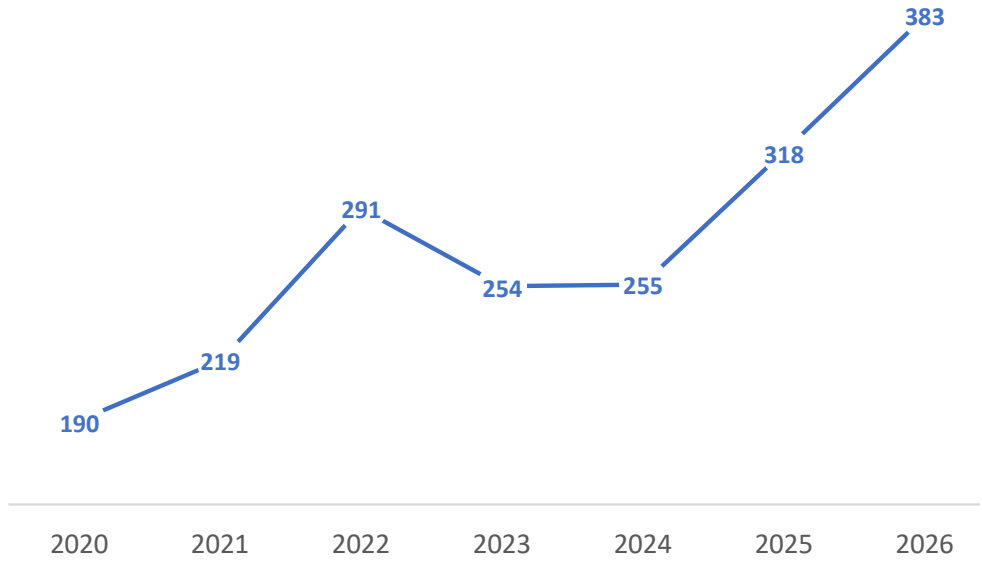


Source: https://www.statista.com/statistics/245473/market-share-of-the-leading-10-global-pharmaceutical-markets/.

Opportunity for generics vs. brand names: generics potential climbing

An increasing number of pharmaceutical patents are set to expire over the next few years worldwide (see Figure 10). This creates a growing opportunity for nimble generics manufacturers who can capitalise on new potential openings for generic drugs.

Figure 10: A growing number of small-molecule drugs are going off patent each year globally



Source: 'Generics 2030: Three strategies to curb the downward spiral', KPMG 2020.

The regulatory process for generics

Regulatory pathway[2] – getting generics approved

Although generic drugs (and modern generic firms) emerged in the mid-1960s, it was not until 1984 that Congress passed the Drug Price Competition and Patent Term Restoration Act ('the Hatch-Waxman Act'). This act was effectively the regulatory framework for branded and generic companies.

The act aimed to strike a balance between protecting innovation and increasing competition by using exclusivities and patent extensions to protect innovation and creating the modern Abbreviated New Drug Application (ANDA) approval pathway to facilitate the market entry of lower-cost generics.

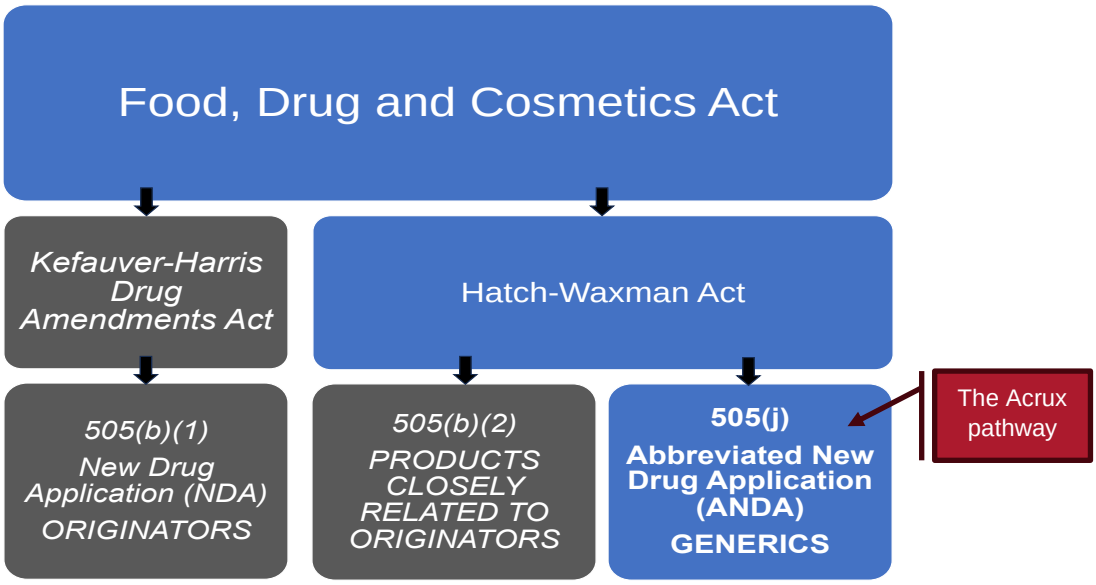
Under this framework, novel products are evaluated through the NDA (New Drug Application) regulatory pathway, also called 505(b)(1), while generics or copies are authorised through the ANDA (Abbreviated New Drug Application) pathway, also called 505(j) – the key pathway for Acrux (see Figure 11).

When a generic company wants to sell its generic version of a branded product, it usually does so through the ANDA pathway, by filing an application containing evidence that the generic has achieved bioequivalence.

The 505(b)(2) pathway is a hybrid between the ANDA and NDA pathways, and caters to manufacturers who seek approval for a new indication for an already-approved drug. The 505(b)(2) submission contains full safety and effectiveness reports but allows at least some of the information required for NDA approval, such as safety and efficacy information on the active ingredient.

[2] https://www.fda.gov/drugs/development-approval-process-drugs/orange-book-preface/
https://www.fr.com/insights/ip-law-essentials/orange-book-101/

Figure 11: Regulatory pathways to approval of originator and generic drugs



Source: Utilizing 505(b)(2) Regulatory Pathway for New Drug Applications: An Overview on the Advanced Formulation Approach and Challenges: Chen et al (2023).

The Orange Book – the portal to the competitive landscape for generic companies

Once approved by the FDA, all products (prescription and over-the-counter drugs; innovator and generic versions) are listed in the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations*, also known as the Orange Book. It lists all approved drugs along with their official and proprietary names.

The Orange Book is designed as a comprehensive resource that provides public information to state health agencies, prescribers, and pharmacists in order to promote public education in the area of drug product selection and foster the containment of healthcare costs.

Challenging patents prior to patent expiry

Four types of patent certifications allow challenges: The Hatch-Waxman Act also created a way for generic applicants to challenge patents on a branded product via litigation prior to ANDA approval. As such, a company can seek FDA approval to market a generic drug before the expiration of patents related to the brand-name drug that the generic seeks to copy.

Under the law, a generic applicant challenging an existing patent must provide in its application a 'certification' that a patent submitted to FDA by the brand-name drug's sponsor and listed in the Orange Book is, in the generic applicant's opinion and to the best of its knowledge, invalid, unenforceable, or will not be infringed by the generic product.

There are four types of patent certifications, referred to as Paragraph I, II, III and IV certifications.

- Paragraph I certification – No patents listed for the NDA
- Paragraph II certification – Patents on the NDA have expired
- Paragraph III certification – Patents on the NDA still exist at the application submission, and generic drug will be marketed only after patent expiration
- Paragraph IV certification – Patents on the NDA still exist, and generic applicant, in its opinion, asserts that patents will not be infringed, or are invalid or unenforceable

Paragraph IV certification – the most commercially attractive option, with market exclusivity for the first past the post: Paragraph IV certification allows a successful challenger the opportunity to market its generic well before the patent expires on the branded drug it seeks to copy. Further, the challenger that is first to file its ANDA with a Paragraph IV certification and that is successful in the subsequent lawsuit is granted a period of 180-day market exclusivity. About 15% of the time, the branded drug's company will not file a suit against the generic company.

Acrux's efinaconazole 10% solution is an example of a successful Paragraph IV challenge.

Strategy: Focus on Higher-Value Complex Generics – an Area of Strength for Acrux

Understanding Acrux's focus area of 'complex generics'

What are complex generics?

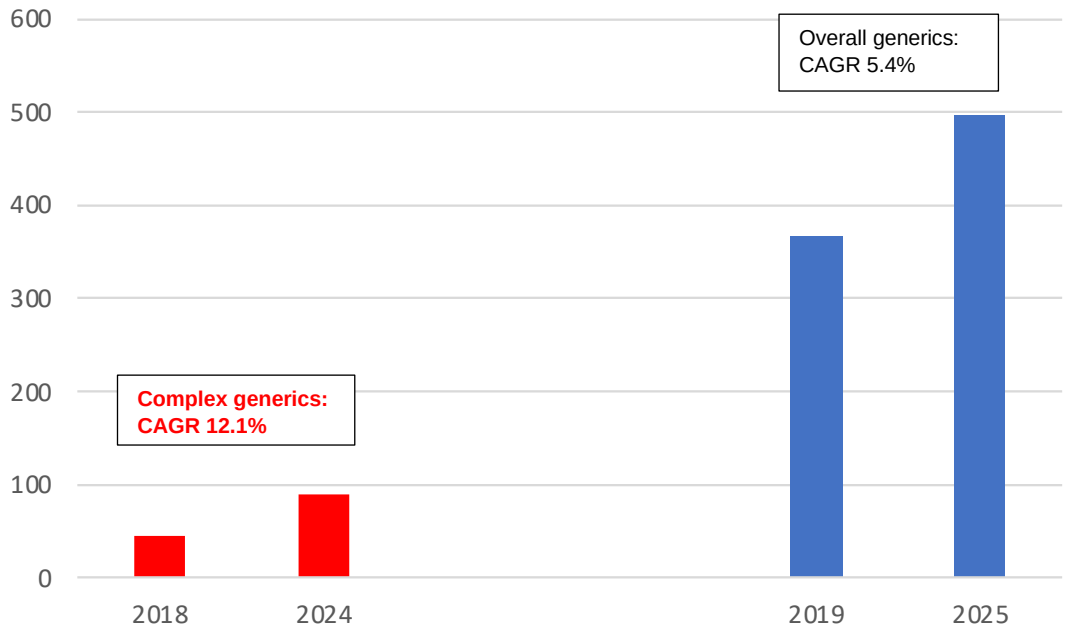
Generics can be characterised as simple or complex. Simple generics are generally copies of a small-molecule reference drug, chemically identical to their branded counterparts. By contrast, the FDA (in the Generic Drug User Fee Act [GDUFA] III commitment letter[3]) has defined 'complex generics' as those with one or more of the following characteristics:

- **complex active ingredients** (e.g., peptides, polymeric compounds, complex mixtures of active pharmaceutical ingredients, naturally sourced ingredients)
- **complex formulations** (e.g., liposomes, colloids)
- **complex routes of delivery** (e.g., locally acting drugs such as dermatological products, complex ophthalmological products, and otic dosage forms that are formulated as suspensions, emulsions or gels)
- **complex dosage forms** (e.g., transdermal systems, metered dose inhalers, extended-release injectables).

Complex generics also include **complex drug-device combination products** (e.g., pre-filled auto-injector products, metered dose inhalers) and other products where **complexity or uncertainty concerning the approval pathway or possible alternative approach** would benefit from early scientific engagement.

What are the growth dynamics of the 'complex generics' market?

Figure 12: The global generics market is growing – but this is supercharged for complex generics (in US$ bn)



Source: 'Generics 2030: Three strategies to curb the downward spiral', KPMG 2020.

Identifying specific opportunities – targeting the right topically applied complex generics

Identifying the target market segment: Complex generics, and topical generics in particular, are typically more challenging to develop – and to demonstrate therapeutic equivalence for – compared to simple generics. Further, the market for topically applied pharmaceuticals is smaller than that for oral pharmaceuticals; thus, fewer companies develop topical generics, making this space less competitive than the oral generic market. For example, oral generics generate over US$200 bn in annual sales in the US, compared with topically applied pharmaceuticals generics that generate around US$16 bn.

[3] https://www.fda.gov/media/153631/download?attachment

This combination (relatively tricky development for a relatively small market) provides nimble players with relevant development capability with a significant opportunity: to gain economically meaningful market share in product markets often deemed too small to attract larger players. Further, given the impact on discount to brand pricing of additional generic competitors, these smaller markets typically reach a natural point of economic equilibrium where they support only a limited number of players but for a longer time.

As such, Acrux is seeking niche opportunities for its generic versions of topical pharmaceuticals in indications where it can gain significant market share that can be maintained over the long term. The company plans to do this by leveraging its know-how in developing formulations and its ability to navigate the challenging product testing protocols required.

Choosing the best opportunities: Acrux's strategy of identifying suitable targets and building a business case has several key inputs and steps. Some of these are detailed below.

- **Finding drugs with few generic competitors:** The company can use information sources such as IQVIA[4] data to determine market sizes and the number of approved and marketed competitor generic products – the fewer competitors, the better the opportunity. This process includes determining the market size of the target drug, alternatives in different dosage forms of the same drug, and other products in the category.
- **Finding off-patent but still uncontested products:** If a product has been off patent for some time, but has very limited competition from generics, this generally implies a level of technical difficulty – an opportunity that Acrux is poised to exploit.
- **Assessing at the IP status for the branded drug:** The expiry dates and enforceability of IP attached to the branded products will usually be listed in the FDA Orange Book. An IP assessment allows Acrux to assess barriers to entry and investigate the drug's formulation.
- **Assessing the technical complexity of development:** The FDA provides Product Specific Guidance for many products, allowing generic companies to assess the bioequivalence of their products to the reference product (Reference Listed Drug – RLD). The technical complexity of drug development will also determine the likely cost of development and number of competitors.
- **Assessing the optimal scale:** The company evaluates manufacturing volumes to assess whether cost advantages from economies of scale exist and whether the cost of goods is sensitive to large scale or niche scale.

Regulatory considerations for complex generics – Acrux is strong in the necessary testing protocols

How the FDA generally defines equivalence

Generics are subject to rigorous regulations and approval processes that parallel their brand-name counterparts. Equivalence to the reference listed drug (RLD or on-market brand) is a major requirement and is defined by the FDA in three ways as shown in Figure 13.

Figure 13: How the FDA defines equivalence

Pharmaceutical equivalence	A drug with the same active ingredients and dosage form that is identical in strength, quality, purity, and identity as the brand-name product. The drug may differ in characteristics such as shape, packaging, and excipients (e.g., colours, flavours, and preservatives).
Bioequivalence	The generic's rate and extent of absorption is not significantly different from the brand-name drug. Bioequivalence also includes the concept of bioavailability (the amount of active drug that a product delivers to the site of drug action).
Therapeutic equivalence	The generic is safe and effective, pharmaceutically equivalent to the original, bioequivalent, adequately labelled, and manufactured in compliance with current regulations. The concept of therapeutic equivalence, as used in the Orange Book, applies only to drug products containing the same active ingredient(s) and does not encompass a comparison of different therapeutic agents used for the same condition.

Source: FDA.

Testing bioequivalence – a more complex process for Acrux's area of focus

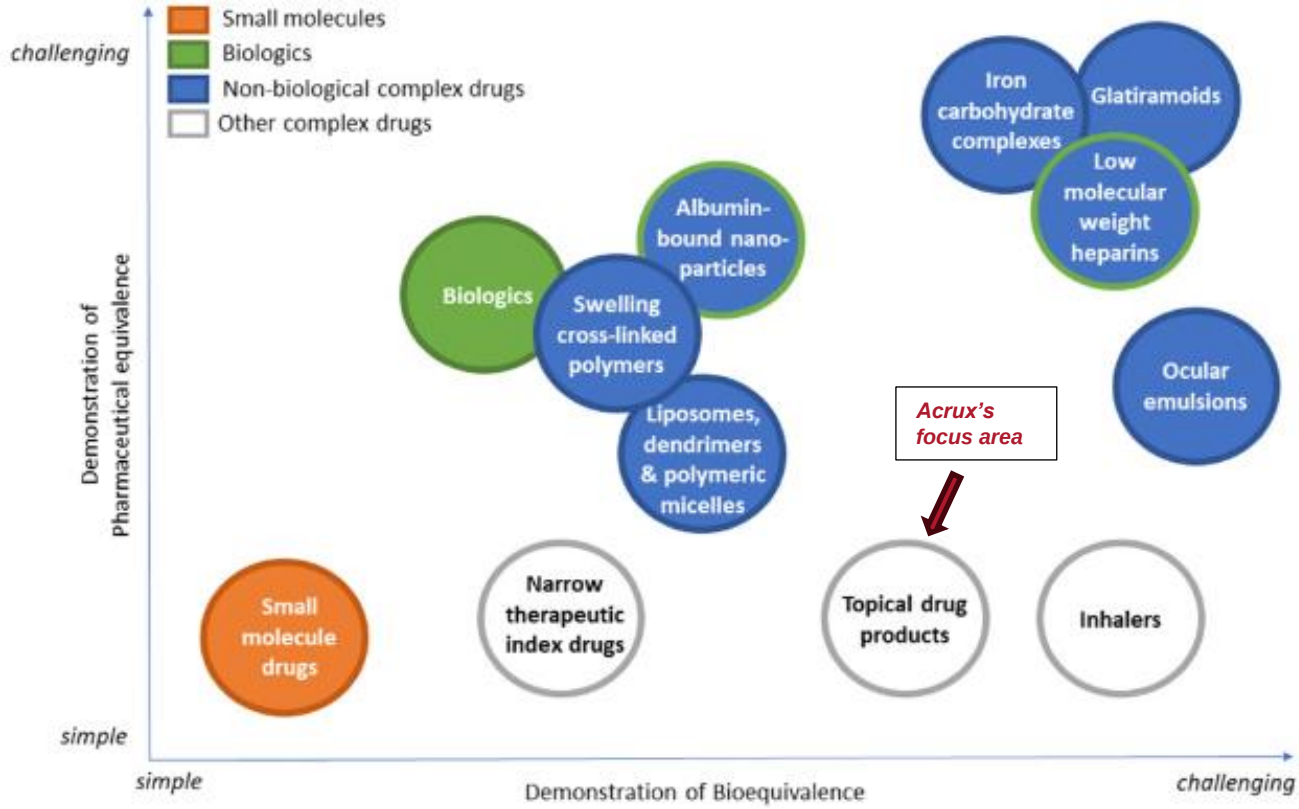
Challenges for complex topical generics: Acrux's primary complex generic focus is on topical dermatological formulations. Typically, these products act locally and therefore require more complex methods (see descriptions below of IVRT and IVPT) to be used to assess bioequivalence, rather than the standard procedure of measuring for the drug in the blood. Further, topical dermatological formulations may be used infrequently and therefore need to remain stable over extended periods of time.

These challenges arise due to variations in:

- excipient, viscosity, or solubility which can impact both stability and degree of skin penetration
- therapeutic activity, which can vary with different skin types
- potential for local irritation, which can vary with different skin types.

[4] IQVIA is a leading healthcare data and analytics provider

Figure 14: Determining bioequivalence is the key challenge for manufacturers of complex topical generics



Source: Regulatory framework and disparities of complex generics in United States, European Union & Latin America; Bhatt et al (2023).

Competitive advantage – Acrux adept at navigating more complex testing protocols

Demonstrating bioequivalence in oral generic drugs is often based on pharmacokinetic studies in the blood that compare the generic product to the branded product. However, for the reasons cited above, similar approaches are not appropriate for topical drugs.

The FDA has recognised the need for more sensitive and efficient surrogate approaches to demonstrate bioequivalence for topical dermatological products, and new approaches have been developed to demonstrate bioequivalence for these types of drugs. Two of these new approaches, detailed below, use a collective weight of evidence from in-vitro studies and are considered challenging to master. Acrux has considerable experience in both techniques with its products successfully brought to market to date.

- **In-vitro release test (IVRT):** This is a test designed to determine product quality. It is primarily used for quality control of semisolids in the product development stage. The FDA states that a IVRT study 'may be used to assess the rate of drug release (i.e., release of an active ingredient) from a topical product. Once validated, an IVRT study may also be useful in controlling product quality and/or establishing the acceptability of post-approval manufacturing changes.'
- **In-vitro permeation test (IVPT):** This is a test designed to mimic biological conditions. The FDA states that applicants may use an IVPT study to 'assess the rate and extent to which a drug (i.e., an active ingredient) from a topical product becomes available at or near a site of action in the skin'. It further states that such a study can be used to compare test topical products and reference standards.

Intellectual property, proprietary technology, and know-how

Acrux's generic product focus leverages its know-how and specialised expertise, accumulated over 25 years through its focus on topically applied pharmaceutical products, to develop its generic portfolio of products. This includes a TGA-approved good manufacturing practice (GMP) facility with 25 specialised scientists. It also includes an experienced management team with a proven record of coordinating contract manufacturers, sourcing of raw materials and bringing new products to market through commercial licencing partnerships.

Intellectual property owned by Acrux, for its transdermal drug delivery technology platform now more relevant to the company's earlier strategy of developing specialty pharmaceuticals or branded products, has largely expired or is not currently used. As such, the company does not rely on any of its prior granted patents for the current business model.

Case study: the process for launching the generic version of EMLA® (Lidocaine/Prilocaine cream, 2.5%)

Acrux's generic version of EMLA® (Lidocaine 2.5% and Prilocaine 2.5%), launched in December 2022, is a good example of the generic drug development process.

Identifying the target

In the case of this drug, the innovator, EMLA®, was in a late lifecycle phase in an established generic market that was maturing and rationalising. Acrux conducted a market screening process and identified this drug as an opportunity for a well-timed and cost-competitive market entrant.

Developing the generic and submitting it for approval

Acrux's structured development process progressed through a series of core milestones over several years to

- characterise the innovator
- develop a pilot product
- establish at-scale manufacturing capability
- manufacture exhibit batches
- compile a comprehensive dossier with the US FDA incorporating IVRT/IVPT.

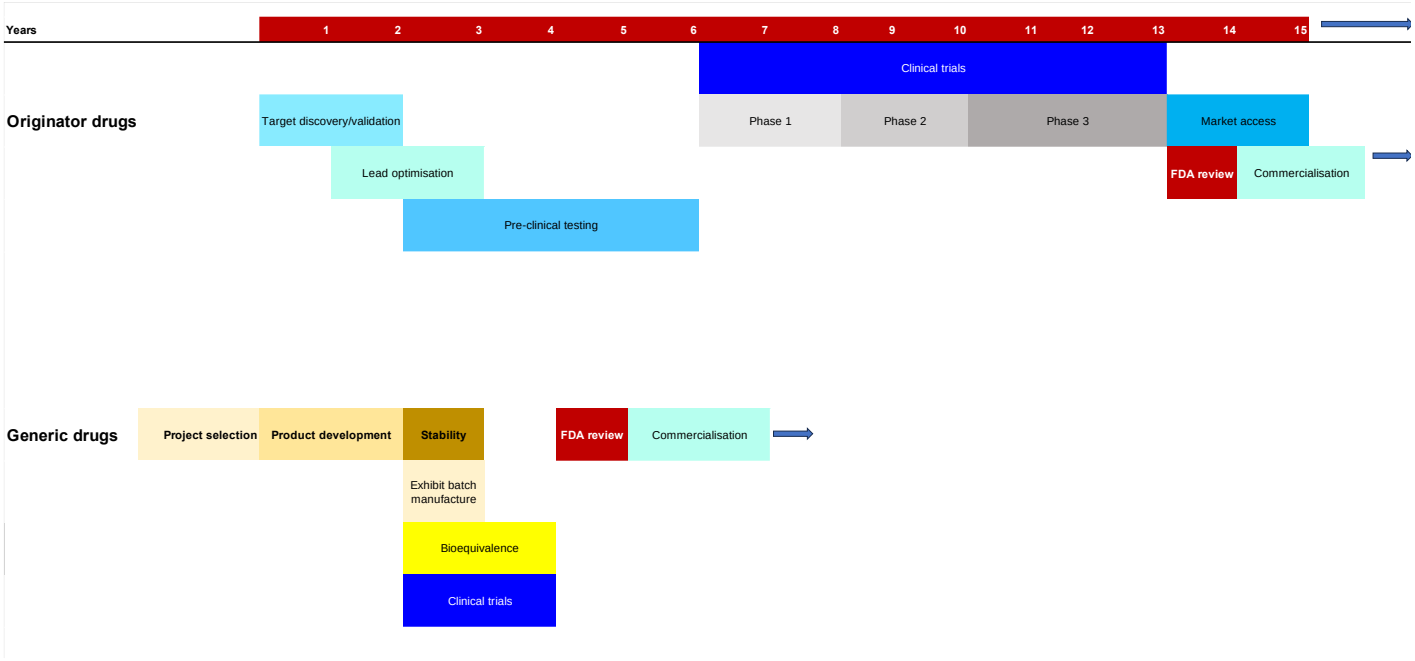
This process resulted in an approval to market Acrux's product as a bioequivalent generic.

Commercialising the generic

In line with the Acrux business model, Acrux entered into a commercial licensing arrangement with Padagis, an established and proven entity, to launch the product. Padagis' strong market engagement and ability to capitalise on an evolving mature generic market have resulted in a very successful launch and market-leading position. This should drive strong returns to Acrux.

Figure 15 compares the typical timelines for originator and brand-name timelines from inception to commercialisation.

Figure 15: Timelines for generics are significantly compressed compared with those for originator drugs



Source: Acrux, FDA, MST Access

Financials: 2023 a Landmark Year as Revenues Start to Flow

FY2023 was a landmark year for Acrux with the launch of Prilocaine 2.5% and Lidocaine 2.5%, cream in December 2022, approval of Dapsone 5%, gel in June 2023, and filing in July 2023 of its ANDA for Nitroglycerine 0.4%, ointment – its seventh ANDA in 5 years, bringing the total to 3 ANDAs currently under review by the FDA. In addition, Acrux has another 7 undisclosed products in development.

As such, we think Acrux has reached an important milestone in its strategic objective of building a substantially diversified portfolio of marketed generic topical products targeting the US market.

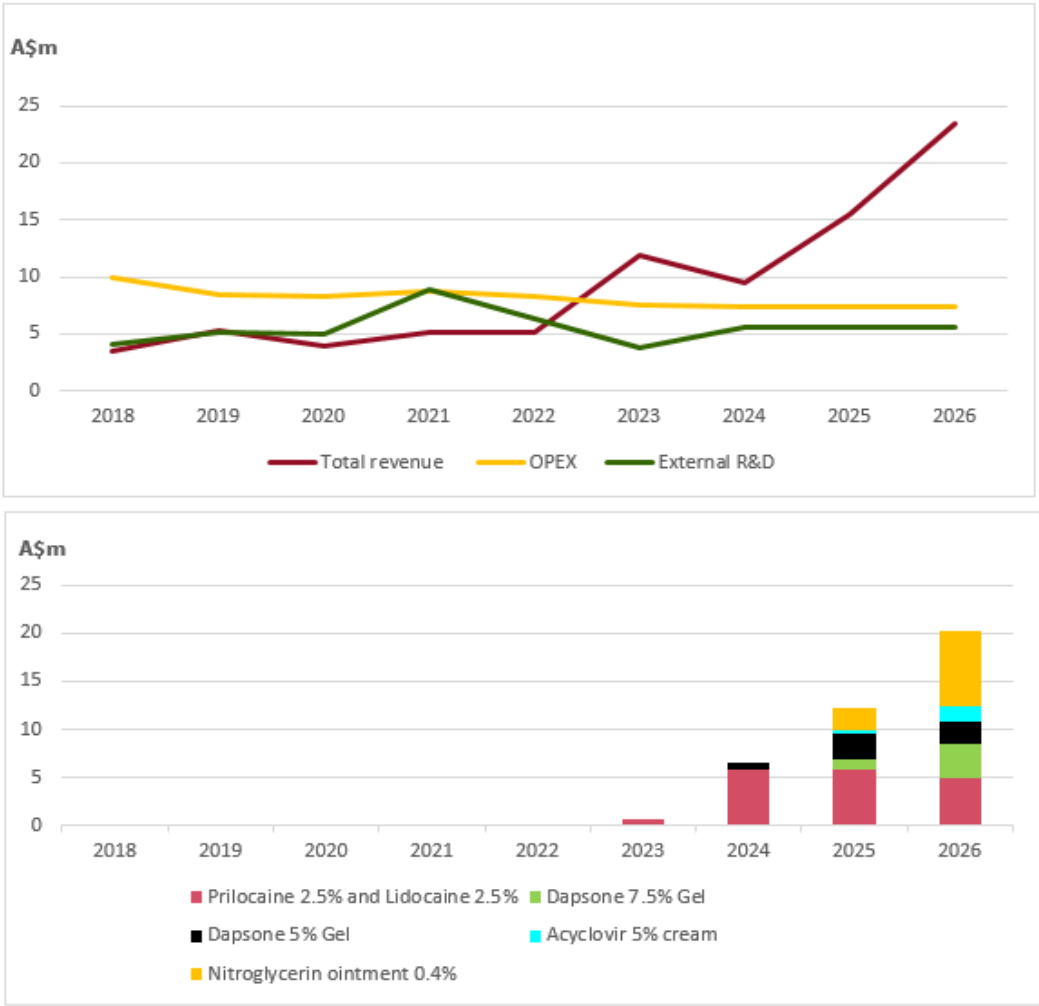
With the imminent launch of Dapsone 5%, gel and potential approval of the 3 dossiers currently under FDA review, Acrux is on the cusp of a significant period of revenue growth based on a growing number of marketed products. Separately Acrux monetised its Lenzetto® royalty stream for EUR4.1m or A$6.4m, streamlining its legacy offering.

FY23 result

Acrux reported FY23 total revenue of A$11.9m, which included a Research and Development Tax Incentive payment of A$3.4m for FY22 and A$6.4m (EUR4.1m) from the sale of the Lenzetto® royalty stream to Gedeon Richter Plc. Excluding the Lenzetto® transaction, the underlying growth of Acrux's total revenue was 10% for the year.

Expenses for the year totalled A$12.1m, down 17% year on year, compared with A$14.7m in FY22. Adjusting for the one-time impairment charge for Estradiol® of A$0.3m, following the Lenzetto® royalty buyout, and purchases relating to the sale of ingredients required for the manufacture of Prilocaine 2.5% and Lidocaine 2.5% cream of A$0.6m, the reduction in total expenses was approximately 23% year on year. Cash on hand at 30 June 2023 totalled A$6.2m, representing an increase of A$0.4m vs. end-FY22.

Figure 16: Key financials (FY18–FY23 actual and FY24–FY26 forecast)



Source: Company reports, MST Access estimates.

Valuation

We value Acrux at $0.25 per share, using a DCF methodology on free cash flow (see Figure 17). Key DCF inputs are a beta of 1.22, WACC of 12.3% and a conservative terminal growth rate of 0%. We think DCF methodology allows for granular modelling of accumulated tax losses and best captures the cash flow generation potential of the business over time.

Our revenue forecasts reflect the growing contribution of existing products on the market and anticipated approvals and launches of new generic products that are in the public domain.

- Prilocaine 2.5% and Lidocaine 2.5% – on the market
- Dapsone 7.5% gel – under review by FDA
- Dapsone 5% gel – imminent launch
- Acyclovir 5% cream – under review by FDA
- Nitroglycerin ointment 0.4% – under review by FDA

We assume each product partner will absorb of cost of goods, resulting in a 60% gross margin for all products commercialised. Further, we assume each product will be partnered with net profits shared equally with Acrux. We do not include the 7 products currently in development given they remain undisclosed at this point, which limits our ability to assess the end target market, potential market share and relative pricing dynamics. Nonetheless, based on average revenue contribution of around $3m per product per annum and development timelines of around 5 years, we note that the contribution to total revenue of these currently undisclosed products could be material and could represent further upside over the medium term.

Figure 17: DCF valuation and key assumptions

		Jun-23	Jun-24	Jun-25	Jun-26	Jun-27	Jun-28	Jun-29	Jun-30	Jun-31	Jun-32	Jun-33
EBIT	A$m	(0.3)	(3.9)	2.4	10.3	10.3	10.3	10.3	10.3	10.3	10.3	10.3
Tax at standard rate	A$m	**(0.6)**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
Post-tax EBIT	A$m	**0.2**	**(3.9)**	**2.4**	**10.3**	**10.3**	**10.3**	**10.3**	**10.3**	**10.3**	**10.3**	**10.3**
Depreciation & Amortization	A$m	0.7	0.7	0.6	0.4	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Post-tax cash flow	A$m	**0.9**	**(3.3)**	**2.9**	**10.7**	**10.6**	**10.6**	**10.6**	**10.5**	**10.5**	**10.5**	**10.5**
Less capex	A$m	(0.5)	(0.1)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)
Less change in working capital	A$m	(0.3)	(0.4)	(0.3)	-	-	-	-	-	-	-	-
Free cash flow	A$m	**0.1**	**(3.8)**	**2.4**	**10.5**	**10.3**	**10.3**	**10.3**	**10.3**	**10.3**	**10.3**	**10.3**
Discount coefficient	years	0.0	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0	9.0	10.0
Discounted cash flow	A$m		**(3.4)**	**1.9**	**7.4**	**6.5**	**5.8**	**5.1**	**4.6**	**4.1**	**3.6**	**3.2**

Sum of discount streams	A$m	38.7	**CAPM**			
Terminal growth	%	0.0%	Risk free rate	%	5.0%	5.0%
Future value into perpetuity	A$m	83.6	Equity beta	x	1.22	1.22
NPV of terminal value	A$m	26.2	Equity risk premium	%	6.0%	6.0%
PV of cash flows	A$m	64.9	Cost of equity	%	12.3%	12.3%
PLUS: Value of investments	A$m	-	Debt	%	0%	0%
LESS: Net debt	A$m	(6.2)	Equity	%	100%	100%
Equity value	**A$m**	**71.1**	Interest rate	%	3.0%	3.0%
Ordinary shares	m	288.7	Tax rate	%	30%	30%
Value per share	**A$**	**0.25**	WACC	%	12.3%	12.3%

Source: MST Access.

Notwithstanding pricing dynamics in each product market, our valuation is most sensitive to assumptions relating to gross margin and discount rate used in our DCF methodology. Figure 18 shows the impact of varying these two elements to our valuation.

Figure 18: Senstitivity matrix

0.25	50.0%	60.0%	70.0%	80.0%	90.0%
12.0%	0.18	0.25	0.33	0.36	0.42
12.3%	0.17	0.25	0.32	0.35	0.40
13.0%	0.16	0.23	0.30	0.33	0.38

Source: MST Access estimates.

Sensitivities and risks to our view

New product development: A key commercial objective in generics development is the early introduction of products to the market in order to gain commercial advantages over competitors, and ideally secure 180-day market exclusivity for those situations where it is first to file with the FDA.

As such, Acrux has demonstrated an ability to identify niche product targets for development of its generic versions and built a diversified portfolio of products, including those approved and others pending FDA review, where this potential for first-mover advantage is within reach. The challenge therefore is to maintain momentum in this evaluation process, given the opaque nature of competitor development pipelines and changes to the FDA's -specific product guidelines.

Drug pricing relative to branded product and level of competition: The entry and ultimate number of generics has a direct impact on pricing for all market participants, and the branded drug in particular. Branded drugs have been known to lose more than 80% of their price in the first six months after going off patent. As such, the discount to brand pricing is highly correlated with how many competitors are targeting the same branded product market.

Competition can come from both the innovator (branded product originator) through an authorised generic or from other generic manufacturers.

A lack of patent protection inherent in generic drug development and the commercial advantage of being first to market results makes it difficult to assess competitor pipelines prior to submission of dossiers to the FDA for review.

In addition to these sources of competition, challenges to existing patents of branded drugs under Paragraph IV can also allow entry of generic manufacturers and also disrupt pricing dynamics of product target markets.

Lastly, Indian and Chinese generic manufacturers often compete on the basis of price given their access to cheaper labour, further eroding prices for product markets that they enter.

Purchasing power of integrated buyer groups, evolving drug channels, and impact to generics pricing: The bargaining power of large buyer groups can also impact pricing given their strategic position in the US pharmaceutical supply chain. Buyers of generic drugs include both the wholesale distributors and large intermediary customer groups such as pharmacy benefit managers (PBMs) and group purchasing organisations (GPOs). A number of these have consolidated in recent years in the US, either through acquisition or joint ventures, to form wholesale buying consortia. The three largest wholesale buying consortia together represent about 90% of all generics purchases by volume, equating to significant purchasing power.

Commercial partnering/licensing: A key aspect of the Acrux business model is out-licensing of products developed to strategic development partners with distribution capabilities. However, appropriate licensee partners for product candidates might not be found, or commercially attractive licensing agreements established, despite progress on the R&D pipeline.

Technological issues: Other drug delivery technologies are under development, one or more of which could displace Acrux's products. In addition, Acrux relies on third-party contract manufacturing organisations (CMOs) to scale production. This involves a technical transfer of the Acrux-developed formulations of generic products and the associated methods of manufacture to a CMO that will scale up manufacturing to commercial batch sizes for both regulatory submission and commercial purposes. As such, there is a risk of failing to replicate formulations or maintain batch quality at scale.

Pooled development fund structure and shareholder risk considerations: Acrux is structured as a Pooled Development Fund. Under the Pooled Development Fund Act 1992, shareholders are entitled to concessionary tax treatment in Australia for income and capital gains derived in connection with their shareholding. Gains realised on the disposal of shares will not be included in an investor's assessable income in Australia. An investor will not be entitled to any deduction or capital loss on the sale of shares. Unfranked dividends received by an Australian resident will be exempt from tax. Franked dividends will also be exempt from tax unless the shareholder elects to be taxed.

While this structure benefits shareholders by not taxing capital gains if the share price increases, it conversely prevents any capital losses incurred through a decline in the share price to be used as a tax offset for the shareholder.

Funding: Notwithstanding cash of A$3.2m as of 30 September 2023, growing revenues from the launch of new products and R&D tax incentive rebate, Acrux remains exposed to funding risk should near-term commercialisation of new products fall short of expectations and not cover operating expenses. However, this is also contingent on the terms of commercialisation agreements with partners and sharing of costs. Exchange rate considerations should also be noted given the company's emphasis on the US market,

Board of Directors and Management Team

Board of Directors

Ross Dobinson (Chairman, Independent Non-executive Director), a director since 1998, became Chairman in 2006, serving as Executive Chairman from 2012 to 2014. He is a founder and former CEO of Acrux. Mr Dobinson has a background in investment banking and stockbroking, serving on boards including Reliance Worldwide (ASX: RWC), Starpharma (ASX: SPL), Hexima (ASX: HXL), Roc Oil (ASX: ROC) and Racing Victoria, and as Chairman of TPI Enterprises (now Palla Pharma – ASX: PAL).

Michael Kotsanis (Managing Director, CEO) has over 30 years' global pharma experience, including significant senior leadership roles. He was previously CCO and a board member of Synthon, a Dutch pharma company with global revenue of over EUR250m. He served as President (Europe, Middle East and Africa) for Hospira (the global leader in generic injectable pharmaceuticals before it was acquired by Pfizer), overseeing the delivery of annual revenue of over US$500m. He joined Hospira after it acquired Mayne Pharma in 2007. He holds a Bachelor of Science (Monash University), a Graduate Diploma in Business (Edith Cowan University) and a Master of Business (University of Technology, Sydney).

Geoff Brooke (Independent Non-executive Director) founded GBS Venture Partners in 1996 and has more than 30 years of venture capital (VC) experience. Dr Brooke was formally President of Medvest, a US-based early-stage VC group. His experience includes company formation, acquisitions, and NYSE, NASDAQ and ASX listings. He became Chairman of Actinogen Medical (ASX: ACW) in 2017. In 2020 Dr Brooke became Chairman of Cynata Therapeutics (ASX: CYP) and was an independent director of the Victoria WorkCover Authority in 2009–2015. He is licensed in clinical medicine by the Medical Board of Australia and has a Bachelor of Medicine/Surgery (University of Melbourne) and MBA (IMEDE, now IMD, Switzerland). He is a member of the Audit & Risk and the Human Capital & Nomination Committees.

Don Brumley (Independent Non-executive Director) spent 30 years as a senior partner of Ernst & Young (E&Y). He has extensive experience in IPOs, transactions and audit and has advised and worked with boards of organisations ranging from some of the largest in Australia to fast-growing entrepreneurial and medium-sized organisations. Mr Brumley was the Oceania IPO Leader at E&Y and worked with clients listing on Australian, US, UK and Asian exchanges. He is a Fellow of Chartered Accountants Australia & New Zealand and is a member of the Australian Institute of Company Directors. He was previously Chairman and Non-executive Director, Bio-Gene Technology (ASX: BGT). He is Chair of Acrux's Audit and Risk Committee and member of the Human Capital and Nomination Committee.

Tim Oldham (Independent Non-executive Director) has 20 years' experience in life sciences business development, alliance management and sales and marketing in Europe, Asia and Australia. He is CEO and MD of AdAlta Ltd (ASX: 1AD), a clinical-stage biotech developing innovative antibody-like drugs. He previously led Tijan Ventures, a life sciences business focused on strategic advisory and leadership services and acquiring cell and gene therapy assets and has been CEO & MD of Cell Therapies and President – Asia Pacific for Hospira. He is a Non-executive Director of BioMelbourne Network and has chaired the European Generic Medicines Association Biosimilars and Biotechnology Committee. Mr Oldham is on the Audit and Risk Committee and Chair of its Human Capital and Nomination Committee.

Joanna Johnson (CFO, Company Secretary) is a member of the Institute of Chartered Accountants Australia and New Zealand. She has over 25 years' experience in the pharmaceuticals industry, having held senior financial leadership positions at IDT Australia, Generic Health, Hospira, Mayne Pharma and FH Faulding. She has led finance teams of all sizes across the reporting, business planning, budgeting, forecasting and analysis, equity raising, tax, risk management, corporate compliance and IR functions.

Senior Management

Felicia Colagrande (Product Development, Technical Affairs Director) has a broad background in pharma operations, topical drug development, analytical development and production. She leads all technical aspects of Acrux's product development, focused on generic topical product development and exploiting Acrux's drug delivery technology. She has over 25 years' pharma/biotech experience (joining Acrux in 2001) and has worked at Faulding Pharmaceuticals, the Department of Clinical Pharmacology and Therapeutics – Austin Hospital, and Silliker-Microtech Laboratories, and was Adjunct Appointee Lecturer at the Faculty of Pharmacy and Pharmaceutical Sciences, Monash University. She has a Bachelor of Science with Honours (La Trobe University) and MBA (Australian Institute of Business).

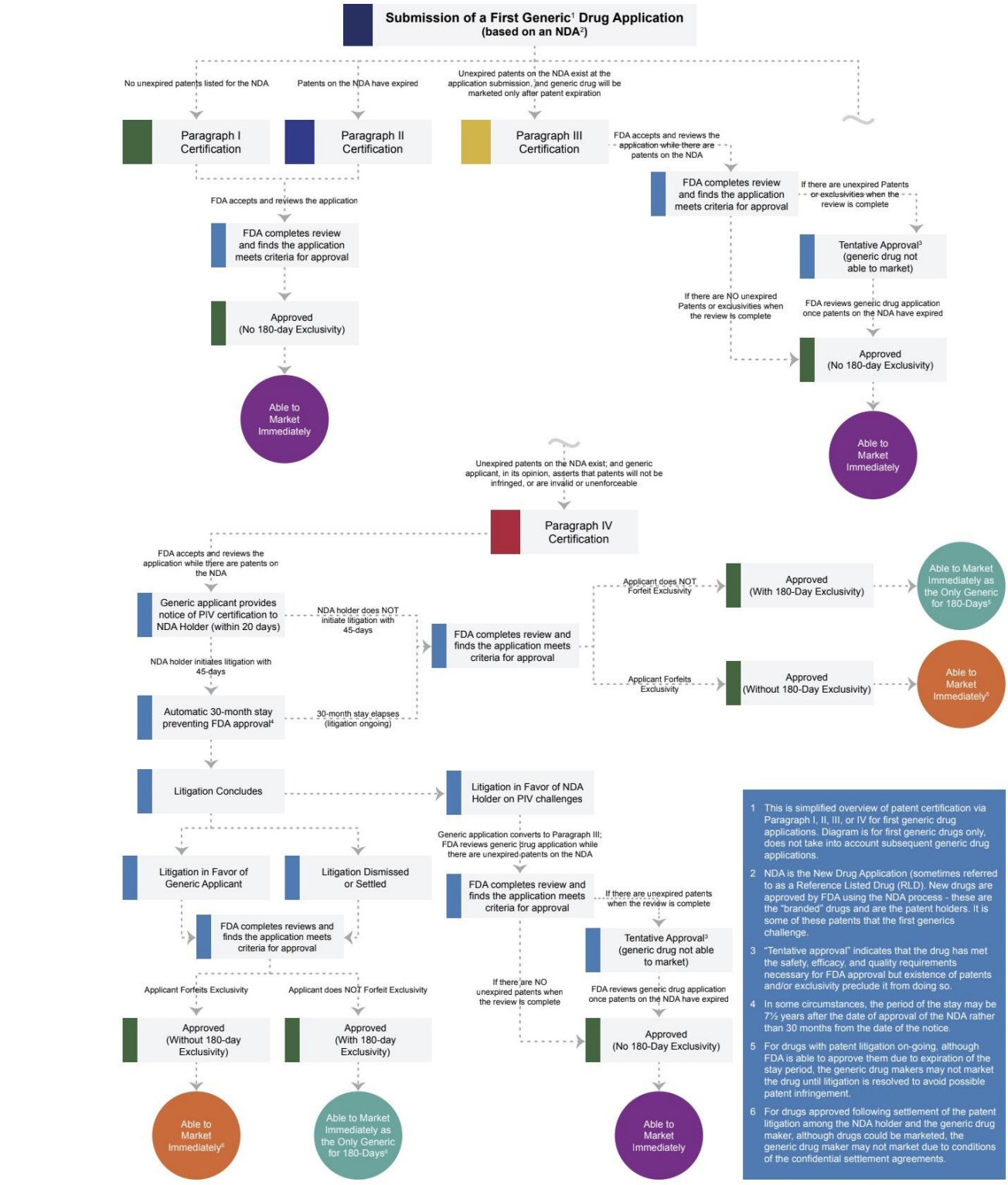
Mark Hyman (Project and Technical Development Director) has spent over 30 years in the pharma and medical device industries, with leadership positions in quality, manufacturing, logistics & operations, product development, project management and commercial development. His experience spans prescription and consumer health, proprietary and generic products across topical, oral and injectable dose forms and drug infusion systems, with expertise in project and technical management. Mr Hyman has a Bachelor of Science in Chemistry and Pharmacology (Monash University).

Appendices

Appendix 1: The generic drug approval process

The FDA's process to approve generics differs from the process for new drugs. The approval process requires that a generic company file an Abbreviated New Drug Application (ANDA) demonstrating the generic product's substitutability with the reference (or branded) product. The process flows as shown in Figure 19, with the path taken depending on whether patents have expired or not, as well as on the original branded manufacturer's response to the prospect of a generic competitor.

Figure 19: Generic drug approval process flowchart



Source: Chahal HS, Patel R, Shimer M. Marketing of First Generic Drugs Approved by U.S. FDA from January 2010 to June 2017. 2021. U.S. Food and Drug Administration. Retrieved from: https://www.fda.gov/about-fda/reports/reports-agency-policies-and-initiatives.

Appendix 2: Glossary

Figure 20: Glossary

Term	Abbreviation	Description
Abbreviated New Drug Application	ANDA	An application for a generic drug approval for an existing approved drug, submitted for review to the FDA's Center for Drug Evaluation and Research, Office of Generic Drugs. In order to achieve approval, applicants must demonstrate bioequivalence to the innovator drug. Once approved, an applicant may manufacture and market the generic drug product in the US. All approved products are listed in FDA's Orange Book.
Active pharmaceutical ingredient	API	The therapeutically active component in a medicine's final formulation which is responsible for its physiological action. Also known as active drug substance.
Acyclovir 5%, cream		Indicated in the US for the topical treatment of cold sores.
Addressable market		Total market sales value and volume of a pharmaceutical product in a specific dosage form. This market data is purchased from IQVIA.
Authorized generic drugs		Typically marketed by the brand-name drug company or company with the brand's permission but as a generic at a lower cost, considered a tactic to address generic competition in the first instance.
Bioequivalence/ Bioavailability		Bioequivalence studies compare the bioavailability of the proposed drug product with the Reference Listed Drug (RLD) containing the same active ingredient. Bioavailability is the rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of drug action. As such, bioequivalence is the absence of a significant difference in the rate and extent to which the drug substance becomes available at the site of drug action when administered at the same dose under similar conditions.
Contract Manufacturing Organisation	CMO or CDMO	Serves other companies in the pharmaceutical industry on a contract basis to provide services that may range from drug development services to commercial manufacturing.
Contract Research Organisation	CRO	Provides support to the pharmaceutical, biotechnology, and medical device industries in the form of research services outsourced on a contract basis. CROs may be involved in all aspects of the clinical development process, from initial drug discovery through preclinical and clinical trials and regulatory approval.
Dapsone gel		Indicated in the US for the topical treatment of acne vulgaris.
Estradiol		A form of estrogen (a female sex hormone produced by the ovaries); used to treat symptoms of menopause.
Evamist®		Brand name for Acrux's unique Estradiol spray product in the US. The Evamist® trademark is owned by Lumara Health and sublicensed to Padagis.
Food and Drug Administration	FDA	The government body that ensures safe and effective drugs are available to improve the health of people in the US. It regulates and supervises prescription, over-the-counter pharmaceutical drugs (medications), vaccines, biopharmaceuticals and veterinary products.
Generic Drug User Fee Act	GDUFA	Introduced in 2012 to create an evidence-, research-, and science-based standards-setting program for the FDA. In the first few years of GDUFA, approximately 800 Product-Specific Guidances (PSGs) were published. These documents 'identify the methodology for developing generic drugs and generating evidence needed to support generic approval.' PSGs contain recommendations on complex in-vitro and in-vivo release testing, among other topics.
Gedeon Richter		Acrux's licensee for Lenzetto®; a major international pharmaceutical company headquartered in Hungary.
Good Manufacturing Practice	GM or cGMP (current Good Manufacturing Practice)	The aspect of quality assurance that ensures medicinal products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the product specification.
In-vitro permeation testing	IVPT	In-vitro permeation testing studies across biological membranes for formulations that are applied to the skin are vital to guide product development and establish product bioequivalence. IVPT is a critical tool for understanding drug delivery into the various layers of skin and can aid in formulation selection.
In-vitro release testing	IVRT	Measurement of drug release from dosage forms applied topically for the purpose of bioequivalence testing. IVRT allows for targeted and systematic drug development and guides the establishment of therapeutic equivalence. IVRT involves subjecting the drug formulation to conditions that will induce drug release across a membrane and quantifying the amount of drug released under those conditions.
IQVIA		A US-based multinational company which provides, on a subscription basis, pharmaceutical industry-leading sales data.
Lenzetto®		Brand name for Acrux's unique Estradiol Spray in the European Union and other countries. The Lenzetto® trademark is owned by Gedeon Richter.
Nitroglycerin 0.4% ointment		Indicated in the US for moderate to severe pain associated with chronic anal fissure.
Orange Book		The publication Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book, identifies drug products approved on the basis of safety and effectiveness by the FDA and related patent and exclusivity information.
Padagis		A pharmaceutical manufacturer that offers high-quality generic and specialised pharmaceutical and OTC products that meet strict standards of quality and safety. Padagis' line of extended topicals includes prescription creams, ointments, suspensions, gels, foams, sprays, patches, nasal, and suppositories and is a market leader in that segment in the US.
Paragraph IV		Under this section of the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Amendments, a company can seek FDA approval to market a generic drug before the expiration of patents related to the brand-name drug that the generic seeks to copy.

Pooled Development Fund	PDF	The Pooled Development Fund Act 1992 was established by the Australian Government to increase the supply of capital to small and medium-sized Australian enterprises to enable them to grow and develop their own markets, creating industry and jobs for Australia. To incentivise investors, a concessional tax regime was established for those companies that were registered as Pooled Development Funds (PDFs).
Prilocaine 2.5% and Lidocaine 2.5%, Cream		Indicated in the US as a topical anaesthetic for use on normal, intact skin for local analgesia or genital mucous membranes for superficial minor surgery and as pre-treatment for infiltration anaesthesia.
Product-Specific Guidance	PSG	To facilitate generic drug product availability and identify the most appropriate methodology for developing drugs and generating evidence to support ANDA approval, the FDA publishes product-specific guidance describing its current thinking and expectations on how to develop generic drug products therapeutically equivalent to specific reference-listed drugs.
Route of administration – enteral		Includes oral, sublingual, buccal and rectal administration
Route of administration – parenteral		All injections which Includes intravenous, intramuscular, subcutaneous, and intraarterial administration
Route of administration – other		Includes trans-nasal, inhalation, vaginal, transdermal and topical administration. Note that Acrux's focus is on transdermal and topical drugs (including the under-arm route)
Transdermal		A route of administration wherein active pharmaceutical ingredients are delivered across the skin for systemic distribution.
Topical		A route of administration wherein active pharmaceutical ingredients are applied to or affect a localised area of the body.

Source: Acrux, MST Access.

Appendix 3: Shareholder registry

Figure 21: Top 25 shareholders

		Number of Fully Paid Ordinary Shares	Percentage of issued Capital
1	PHILLIP ASSET MANAGEMENT LIMITED	31,847,134	11.05
2	DDH GRAHAM LIMITED	3,927,347	1.36
3	CITICORP NOMINEES PTY LIMITED	4,831,059	1.68
4	HISHENK PTY LTD	4,500,000	1.56
5	DR THOMAS VUI CHUNG CHAI	4,460,560	1.55
6	MR ROSS DOBINSON	4,355,174	1.51
7	PACIFIC CUSTODIANS PTY LIMITED	3,849,912	1.34
8	ASHWOOD RIVER PTY LTD	3,800,000	1.32
9	MR PAUL COZZI	3,159,121	1.10
10	MR CHRISTOPHER MURRAY ABBOTT	3,000,000	1.04
11	MR DONALD CHARLES BRUMLEY	2,853,998	0.99
12	TSO PTY LTD	2,625,734	0.91
13	THE POOLE FAMILY SUPERANNUATION FUND PTY LTD	3,000,000	1.04
14	MR ALAN JEBB & MRS SANDRA JEBB	2,430,707	0.84
15	MR IAN VICTOR LANCINI & MRS DEBRA ANN LANCINI	2,045,000	0.71
16	ADAM JAMAL	1,905,719	0.66
17	MR BIKASH KAJI BANIYA	2,012,119	0.70
18	DURBIN SUPERANNUATION PTY LTD	1,727,640	0.60
19	ASIA UNION INVESTMENTS PTY LIMITED	1,691,083	0.59
20	MR MICHAEL JOHN KOTSANIS	1,511,083	0.52
21	MS HUI TAN	1,500,000	0.52
22	NEWECONOMY COM AU NOMINEES PTY LIMITED	1,511,799	0.52
23	MORGAN STANLEY AUSTRALIA SECURITIES (NOMINEE) PTY LIMITED	1,304,426	0.45
24	MR DAVID ANDREW SLOBOM & MRS LINDA JANE SLOBOM	1,409,596	0.49
25	MR STEPHEN EDWARD MAHNKEN & MRS DIOR LEONE MAHNKEN	1,319,986	0.46
Total of Top 25 shareholders		**96,579,197**	**33.51**

Source: Acrux.

Methodology & Disclosures

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