



NEUREN PHARMACEUTICALS (ASX:NEU)

CULPER'S REPORT IS EXAGGERATED

19 FEBRUARY 2024

On 15 February 2024, Culper Research published a short report [1] on ACADIA Pharmaceuticals Inc. (NASDAQ:ACAD), the distribution partner for Neuren's Rett Syndrome drug Daybue in the US. Culper's view is that there will be a significantly higher discontinuation rate of Daybue due to its side effects.

Neuren is one of PGF's largest positions. We find Culper's report refreshing as it provides an opportunity for us to challenge and test our thesis on why we should continue to hold the stock. After digesting Culper's report and conducting further due diligence, we have published this special report to showcase our findings.

Culper's key thesis is that from Facebook posts, physician feedbacks and FAERS data, the discontinuation rate for Daybue is dramatically higher than ACADIA's stated discontinuation rate as well as the consensus sell-side forecasts. Our report aims to critically evaluate the discontinuation rates of Daybue as presented by Culper, contrasting them with new estimates provided by PGF. Culper's analysis indicates a 72% discontinuation rate in 2024 and 2025, a figure we contend to be significantly overstated. Our findings support an estimated 35% and 25% discontinuation rate during the same two years.

Methodology

Physician feedback has been consistently offered by numerous high-quality sell-side analysts, including those from Australia focusing exclusively on Neuren [2]. The FAERS data has also been thoroughly elucidated by sell-side analysts and reputable sources on the day Culper's report was released. We won't replicate them here and will instead focus on the Facebook posts.

Our discontinuation rate estimation is based on the posts and comments from a total of 139 distinctive patient carers on the Facebook Daybue (Public) page [3], spanning from 1 October 2023 to 18 February 2024, a period for which Acadia has not yet provided actual sales data for the drug. We adopted this methodology as it was a central element in Culper's report, which cited numerous Facebook posts from carers deciding to discontinue the drug.

We followed the same approach to determine whether the Facebook posts align more closely with Culper's 72% discontinuation rate or with Acadia and Neuren's confirmed discontinuations of 24% [4]. We methodically analysed all posts and comments published in the Daybue Public forum since 1 October 2023. To ensure the accuracy and relevance of our data, we focused exclusively on distinctive posters. This means that if an individual posted multiple times with positive feedback about Daybue, they were counted as a single positive case. We also prioritised the most recent updates from posters to accurately reflect their current stance on the drug. For example, if a poster initially expressed struggles with Daybue but later confirmed discontinuation, we classified them as a discontinued case. This approach ensures our analysis dynamically aligns with patient experiences over time. Ambiguous posts or comments, as well as those expressing a desire to try the drug, whether in the US or internationally, were carefully excluded. This meticulous process enabled us to derive nuanced insights into the efficacy and tolerability of Daybue from a key source that Culper utilised.

The Result

The analysis of 139 distinctive carer posts and comments on Facebook indicates an adjusted, effective discontinuation rate of approximately 35%, which is significantly lower than Culper's estimated 72% and closer to Acadia and Neuren's reported discontinuation rate of 24%. While our study isn't scientific in nature, it offers a more comprehensive approach than choosing to report just the negative comments.



It's also crucial to acknowledge that online forums, particularly those concerning health and medication, typically become venues where individuals seek advice, share experiences, and seek solutions to their challenges [5]. This dynamic suggests that the discussions are more likely to highlight issues rather than positive outcomes, given that individuals with satisfactory treatment experiences might feel less compelled to post.

This skew towards problem-solving and seeking support for issues can lead to an overrepresentation of negative experiences or side effects in the data collected from these forums. It's important to acknowledge this bias when analysing and presenting findings from such sources. Recognising that posts are more likely from those experiencing problems provides valuable context for understanding the overall sentiment and experiences shared within the forum. It also underscores the importance of complementing this qualitative analysis with other data sources, such as clinical trials and surveys, to obtain a more balanced view of the drug's impact on its users.

Category/Segment	1. Staying on Daybue	2. Staying on Daybue	3. Staying on Daybue	4. Currently Struggling	5. Discontinued
Definition	Stated that drug is working and/or happy with the experience, with no to very minimal side effects	Stated that they are on the drug, but did not state whether there are improvements. Likely to have little to no impact from managing side effects	Stated that they are on the drug, but specifically stated that they did not see any observed improvements so far. Have little to moderate impact from managing side effects	Stated that they are struggling with managing side effect that are moderate to extreme.	Stated that they have come off the drug completely.
Number of Observations	33	40	7	34	21
Percentage	24.4%	29.6%	5.2%	25.2%	15.6%
Estimated Discontinuation Rate	5%	15%	30%	50%	100%
Weighted Average Discontinuation Rate	48 observations or 35.4% in 2024, but ratcheting down to 17.0% in 2030 (see following explanation)				

We have applied discontinuation rates ranging from 10% to 100% across five distinct categories, resulting in a weighted average discontinuation rate of 35.4%, which is significantly lower than Culper's estimate of 72%. Our methodology differs notably in that we segment patients and apply specific discontinuation rates based on categorisation.

Our approach introduces a nuanced understanding of patient retention, contrasting sharply with Culper's broad application of a 72% discontinuation rate. For example, in Segment 1 of the above table, representing patients who continue using Daybue, is expected to grow over time due to its lower discontinuation rate and the addition of new patients to this segment. This growth can be likened to the compounding interest in a bank account, indicating that a simple, uniform discontinuation rate cannot accurately model patient behaviour over future periods.

By segmenting the cohort into groups with distinct discontinuation rates (5% for those in Segment 1 and 100% for those who discontinued in Segment 5), we present a more realistic projection of patient adherence over time. This methodology reveals that the discontinuation base across the entire patient cohort is not linear in future years, allowing for the potential cumulative growth of Daybue's user base even with an initial high discontinuation level.



Here we present a comparison between our modelled numbers and Culper's estimates. For consistency, we assumed the same number of new patients in each period as Culper's report suggests. This comparison highlights the significant impact our study of potential discontinuation rates, derived from the Facebook group page, has on long-term projections when we apply a segmented approach to the patient cohort.

Culper Assumptions							
Monthly Discontinuation	10%	10%	5%	5%	5%	5%	5%
Annual Discontinuation	72%	72%	46%	46%	46%	46%	46%
Year	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Start of Period Patients	956	1006	755	730	717	710	706
Added in Period	1150	750	400	400	400	400	400
Discontinued in Period	1100	1001	425	413	407	404	402
End of Period Patients	1006	755	730	717	710	706	704
Average Patient in Period	981	881	743	724	714	708	705
List Price	\$575,000	\$575,000	\$575,000	\$575,000	\$575,000	\$575,000	\$575,000
Gross to net (average)	80%	80%	80%	80%	80%	80%	80%
Titration level (average)	80%	80%	80%	80%	80%	80%	80%
Neuren royalty rate	12.50%	12.50%	12.50%	12.50%	12.50%	12.50%	12.50%
Net Revenues - Acadia	\$316	\$284	\$239	\$233	\$230	\$228	\$227
Consensus - Acadia	\$369	\$471	\$567	\$645	\$721	\$782	\$827
Difference - Acadia	-14%	-40%	-58%	-64%	-68%	-71%	-73%

PGF Assumptions							
Monthly Discontinuation	2.6%	1.9%	1.6%	1.5%	1.4%	1.3%	1.3%
Annual Discontinuation	35.4%	24.9%	20.5%	19.0%	18.1%	17.4%	17.0%
Year	2024E	2025E	2026E	2027E	2028E	2029E	2030E
Start of Period Patients	956	1361	1586	1579	1603	1641	1685
1. Staying on Daybue	234	489	639	700	758	813	865
2. Staying on Daybue	283	530	640	645	649	652	655
3. Staying on Daybue	50	76	81	71	64	59	56
4. Currently Struggling	241	265	227	164	132	117	109
5. Discontinued	149	0	0	0	0	0	0
Added in Period	1150	750	400	400	400	400	400
1. Staying on Daybue	281	183	98	98	98	98	98
2. Staying on Daybue	341	222	119	119	119	119	119
3. Staying on Daybue	60	39	21	21	21	21	21
4. Currently Struggling	290	189	101	101	101	101	101
5. Discontinued	179	117	62	62	62	62	62
Discontinued in Period	745	525	407	376	362	356	354
1. Staying on Daybue	26	34	37	40	43	46	48
2. Staying on Daybue	94	113	114	114	115	116	116
3. Staying on Daybue	33	35	30	28	25	24	23
4. Currently Struggling	265	227	164	132	117	109	105
5. Discontinued	328	117	62	62	62	62	62
End of Period Patients	1361	1586	1579	1603	1641	1685	1731
Average patient in period	1159	1474	1583	1591	1622	1663	1708
List Price	\$575,000	\$575,000	\$575,000	\$575,000	\$575,000	\$575,000	\$575,000
Gross to net (average)	80%	80%	80%	80%	80%	80%	80%
Titration level (average)	80%	80%	80%	80%	80%	80%	80%
Neuren royalty rate	10.83%	11.23%	11.42%	11.44%	11.49%	11.55%	11.61%
Net Revenues - Acadia	\$380	\$481	\$516	\$519	\$528	\$541	\$555
Consensus - Acadia	\$369	\$471	\$567	\$645	\$721	\$782	\$827
Difference - Acadia	16%	15%	3%	-9%	-17%	-22%	-24%

Assumptions on Segments	1. Staying on Daybue	2. Staying on Daybue	3. Staying on Daybue	4. Currently Struggling	5. Discontinued
Percentage	24.4%	29.6%	5.2%	25.2%	15.6%
Estimated Discontinuation Rate	5%	15%	30%	50%	100%

Concluding Remarks

Our analysis, based on collecting all data from the (Public) Facebook comments and posts and applying a segmented approach, yields a materially different outcome from Culper's report. While our study is not scientific or comprehensive in nature, we have demonstrated that using Culper's own approach yields a completely different result when all data points are represented.

Daybue is not a miracle drug and affects individuals differently. Some experience significant benefits without side effects, while others are adversely impacted by gastrointestinal issues (GI). Our analysis excludes important factors like ongoing efforts to address the GI side effects and the innovative strategies developed by carers and physicians to manage them. There is also potential for Daybue to be reformulated to better accommodate those affected by GI issues in future years.

We also note that Neuren is not by Daybue. Neuren's ongoing trial involving a separate drug NNZ-2591 for a number of neurodevelopment disorders appear to be very promising with less side effects, with a potential valuation that is 2 to 4 times higher than Daybue if commercialised. [6]

Investor reactions to negative reports are often quick and irrational. An evidence-based examination of the data in question is essential. We're closely watching for Acadia's upcoming quarterly results on 27 February, which should provide further insights.



References

- [1] Culper Research *15 February 2024 - ACADIA Pharmaceuticals Inc. (ACAD): Daybue in the Rearview (pdf)*.
- [2] Petra Capital Note 16 February 2024 - ACADIA short report - We do not concur and think this is a great Buying opportunity for NEU.
- Canaccord Genuity ASX:NEU Research 16 February 2024 - The Brains Trust
- [3] *Daybue (PUBLIC GROUP) Facebook Tips, Tricks, & Support for Rett Families*
- [4] *Neuren Pharmaceuticals Q4 2023 Activity Report ASX Release 31 January 2024*
- [5] *Shaw, E. K. (2020). The use of online discussion forums and communities for health research. Family Practice, 37(4), 574-577.*
- Montgomery, A. J., Powell, J. S., & Murray, L. E. (2020). Using online forums for health research: Three methodological approaches and key ethical considerations. Qualitative Health Research, 30(6), 899-912.*
- [6] Petra Capital ASX:NEU Research 6 November 2023 Another Daybue beat on Stellar Execution.
- Evans and Partners ASX:NEU Research 5 November 2023 DAYBUE Launch Ramp Continues to Impress.
- Canaccord Genuity ASX:NEU Research 16 February 2024 - The Brains Trust
- [Others]
- Trofinetide Clinical Review - FDA 10 March 2023*
- Neul, J. L., Percy, A. K., Benke, T. A., Berry-Kravis, E. M., Glaze, D. G., Marsh, E. D., Lin, T., Stankovic, S., Bishop, K. M., & Youakim, J. M. (2023). Trofinetide for the treatment of Rett syndrome: A randomized phase 3 study. Nature Medicine, 29(12), 1468-1475.*

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**The fund is currently open for
new applications
for Wholesale Investors.**

Portfolio Manager

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Responsible Manager

Benjamin Peters | ben@pgf.net.au

Fund Guideline

- Maximum Single Holding Size: 20% at Cost
- Maximum Unlisted Holdings: 30% at Cost
- Buy Sell Spreads: Nil
- Distribution Frequency: Annually
- Minimum Investment: \$100,000

Application and Redemptions

<https://www.registrydirect.com.au/offer/phoenix-growth-fund/>

Website

<https://www.pgf.net.au/>

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