KerrisdaleCapital

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Adamas Pharmaceuticals, Inc. (ADMS)

4x Upside for a Misunderstood Drug Maker

We are long shares of Adamas Pharmaceuticals, a small-cap drug company on the eve of launching its first product: a treatment called Gocovri for patients with Parkinson's disease. The mainstay therapy for Parkinson's is a drug called levodopa, which usually works well but frequently causes involuntary and often painful movements called dyskinesias. High-quality Phase 3 studies have proven that Gocovri significantly reduces dyskinesias and improves patients' overall conditions, leading the FDA to designate Gocovri the one and only drug approved for levodopa-induced dyskinesia. With the potential to deeply penetrate a $3.5 billion addressable market, Gocovri is worth, by our estimates, $1.6 billion, or $65 per Adamas share.

However, Adamas trades at a 64% discount to that value – indeed, even at a discount to its prior high of ~$30, reached years before FDA approval. In addition, Adamas is heavily shorted, with short interest standing at 33% of shares outstanding, equivalent to 7 days' worth of recent trading volume. Clearly many investors have little faith that Adamas will be able to capitalize on the Gocovri opportunity.

We believe this skepticism is misplaced. Criticism of Gocovri stems from aesthetics more than economics: some find it distasteful to make money by "merely" repackaging existing drugs in improved forms. This is what Gocovri, a high-dose, extended-release formulation of a generic drug called amantadine, does, leading to suspicion that it's nothing more than an unsustainable cash grab. But this view fails to appreciate the fact that Gocovri's generic, immediate-release counterpart, which is not FDA-approved for dyskinesia, has never been convincingly shown to work, with studies pointing to rapidly vanishing benefits and high rates of patient abandonment. By contrast, Gocovri's efficacy, even over the long term, is well-documented. In addition, multiple lines of evidence strongly suggest that Gocovri works ~30-50% *better* than generic amantadine; for instance, patients that switch from generic to Gocovri improve just as much as patients who switch from placebo.

Gocovri is a good drug, not another poster child for pharmaceutical-industry misdeeds. Besides, even those misdeeds are often quite profitable. Multiple precedents point to the potential for repackaged versions of off-patent drugs to generate billions of dollars of value, even in cases of dubious efficacy or only modestly improved convenience; Gocovri, with a far more convincing story, should do even better.

Beyond Gocovri, Adamas has two little-noticed Phase 3-ready pipeline assets with massive upside; in one case, despite compelling data and obvious M&A potential, no sell-side analyst has quantified what we estimate to be a ~$300mm opportunity. Overall, we believe Adamas is realistically worth over $100 per share – more than 4x higher than its current price.

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I. Investment Highlights

Adamas Pharmaceuticals: Kerrisdale Valuation

	Value			
	Total ($mm)	Per share	Prob.	Exp. value per share
Gocovri (Parkinson's)	$ 1,641	$ 65		
Namenda-related royalties	95	$ 4		
Baseline total	$ 1,735	**$ 69**	100%	$ 69
% upside		178%		
Gocovri (MS)	$ 1,578	$ 62	50%	$ 31
"Vimpat XR"	$ 293	$ 12	50%	$ 6
Grand total	$ 3,606	$ 143		**$ 106**
% upside		478%		328%

Source: Kerrisdale analysis
Note: "Gocovri (Parkinson's)" value includes the impact of existing cash and debt, as well as assumed R&D necessary to carry the MS indication through Phase 3.

Gocovri is a good drug. While some modified-release drugs differ little in effect from their immediate-release counterparts, Gocovri's pharmacokinetics are clearly differentiated, delivering high, smooth levels of amantadine throughout patients' waking hours, rather than the spikes and plunges associated with side effects. Generic immediate-release amantadine has been long been criticized in the medical literature for the weakness of the evidence supporting its use in levodopa-induced dyskinesia, mainly from small, brief, and poorly controlled trials; moreover, some evidence suggests that its benefits fade away rapidly. Gocovri, however, clearly continues to work for years. In addition, while no ideal head-to-head studies have directly compared Gocovri to generic immediate-release amantadine, looking at previous trials strongly suggests that Gocovri works better, while Adamas has shown that patients switching from generic to Gocovri improve to the same degree as patients switching from placebo to Gocovri, underscoring the weakness of the generic and the strength of Gocovri. Finally, Gocovri has at least one benefit that the generic has never been claimed to have – reducing "off" time, i.e. the periods during which Parkinson's symptoms elude the control of levodopa. In sum, Gocovri is not some indefensible exploitative dud; it presents a compelling value proposition for patients and doctors.

Gocovri will be a commercial success. Despite purists' doubts, many drugs that repackage old, off-patent molecules have done well commercially in recent years. For instance, Raptor Pharmaceutical was acquired for ~5x consensus peak revenue even though its main asset was just a delayed-release version of a competing therapy. Despite a huge price premium, this delayed-release drug achieved 66% US market share in only three years. Similarly, Acorda Therapeutics has achieved high market share and ~$500mm of annual revenue with an extended-release version of an old drug that the vast majority of patients don't even respond to.

Additional examples abound. Overall, even mediocre repackaged drugs have generated strong financial results when they offer improved convenience and especially when they boast an FDA approval that competitors lack – two advantages that Gocovri, an FDA-approved once-a-day version of an off-label two-or-three-times-a-day drug – clearly possesses. We thus believe that Gocovri can realistically achieve significant market share within the $3.5 billion addressable market of US patients with levodopa-induced dyskinesia, giving rise to a $1.6 billion present value even when assuming a slow, eight-year-long trajectory toward peak penetration.

Applying Gocovri to multiple sclerosis is a billion-dollar opportunity. One of Adamas's two major pipeline assets – a program to use Gocovri to treat walking-related difficulties caused by multiple sclerosis – could easily generate as much value as Gocovri in Parkinson's disease. Our analysis of Gocovri's Phase 2 results in MS strongly suggests that the drug works better than Acorda's drug Ampyra (already discussed above as an example of a commercially successful yet mediocre repackaged drug); assuming that Gocovri achieved a similar level of success after completing pivot trials, we estimate incremental value of $1.6 billion or $62 per share. While some sell-side analysts have incorporated some estimate of this value into their existing target prices, they have been needlessly conservative.

"Vimpat XR" could be worth ~$300 million. Adamas's other pipeline asset is a high-dose, extended-release formulation of Vimpat, a blockbuster epilepsy drug manufactured by the large pharmaceutical firm UCB and valued by the market at ~$3 billion. Vimpat goes off patent in 2022, putting UCB's earnings at risk – but "Vimpat XR," if licensed from Adamas, could keep UCB's highly successful franchise going till 2036. Such a transaction would mirror Adamas's successful licensing deal for a different extended-release drug with Forest Laboratories in 2012, which generated hundreds of millions of dollars for Adamas and clearly demonstrated the strength of its intellectual property. Even assuming that most of the economics of "Vimpat XR" go to UCB, a deal could produce major gains relative to Adamas's current market cap and is not, to our knowledge, reflected in current sell-side target prices.

II. Company Overview

Adamas Pharmaceuticals: Capitalization and Financial Results

Capitalization	
Share price ($)	$24.66
Fully diluted shares (mm):	
Shares outstanding	22.5
Dilutive impact of options/RSUs*	3.4
Total	25.9
(*in $mm*)	
Fully diluted market cap	$ 640
Royalty-backed loan at face	35
Less: cash and securities	(128)
Enterprise value	$ 546

Financial results ($ mm)	2015	2016	2017†
Revenue	$ 2	$ 1	$ 0
Net income	(52)	(60)	(74)
Free cash flow	(49)	(50)	(54)

**Based on 12/31/16 disclosures (not updated in subsequent 10-Qs).*
†Represents 2017 H1 values annualized.
Source: company filings, Kerrisdale analysis

Adamas's recent success has been a long time coming. Founded in 2000, Adamas, then called NeuroMolecular Inc., brought together Greg Went, a co-founder of the pioneering genomics firm CuraGen, and several scientific advisors, including the main inventor of the blockbuster Alzheimer's drug Namenda. The company focused its research on a class of neuroactive molecules called aminoadamantanes, including Namenda and a more obscure generic drug called amantadine. But rather than gamble on novel molecules, Adamas took a more hard-headed approach. As the company wrote in 2010:

> Adamas was founded to approach drug development in an extremely practical way. … Adamas scientists work with well-characterized and widely studied drugs, which helps reduce the uncertainties typically associated with the development of new chemical entities. The Company's resulting product candidates hold advantages in efficacy, tolerability and compliance over other offerings in their markets.

In other words, Adamas specializes in the unglamorous, underrated, but nonetheless valuable enterprise of making existing treatments work better.

This approach clearly bore fruit by 2012, when Adamas struck a deal with Forest Laboratories to give the multi-billion-dollar pharma company – the manufacturer of Namenda – access to Adamas's patents relating to extended-release and combination-therapy versions of the drug. In exchange, Adamas would go on to receive $160 million in cash, along with a portion of future sales of both extended-release Namenda and Namzaric (a combination of extended-release Namenda and another Alzheimer's drug). This transaction allowed Forest's successors (first Actavis and then Allergan) to dramatically extend the lifespan of their Namenda revenue at a time when the original version of the drug was on the verge of losing patent protection; indeed,

as we describe in further detail below, Namenda XR has succeeded far beyond Forest's initial expectations.

For Adamas, the deal powerfully demonstrated the strength – both substantive and legal – of its intellectual property. Interestingly, Forest agreed to give up a percentage of its extended-release Namenda sales in the "low to mid-single digits"[1] even though it had already announced plans to bring such a product to market using only its own patents.[2] Evidently Forest concluded that coming to terms with Adamas made more sense than fighting in court – a striking validation of Adamas's commercial savvy and negotiating ability, skills that will likely come in handy as it seeks to strike deals with big pharma in the future.

Having monetized its Namenda research, Adamas focused on amantadine, an old drug originally used to treat the flu but later found to modestly improve the symptoms of Parkinson's disease. In particular, published research and real-world experience suggested that amantadine can ameliorate the condition known as dyskinesia – involuntary and often painful movements, including flailing and writhing, that arise as a side effect of the main Parkinson's treatment, levodopa. (A video created by one dyskinesia sufferer helps illustrate how difficult the condition can be.) Despite these hints of efficacy, though, only a small minority of Parkinson's patients with levodopa-induced dyskinesia take amantadine, and many who try it can't tolerate it and give up. Moreover, the clinical studies supporting the drug's use were weak, and multiple studies suggested that its benefits wore off quickly. Indeed, amantadine is not actually FDA-approved for the treatment of levodopa-induced dyskinesia, contributing to its limited adoption.

By creating (and patenting) a high-dose, extended-release version of amantadine, Adamas, in keeping with its philosophy, hoped to develop "advantages in efficacy, tolerability and" – thanks to the ease of once-a-day dosing – "compliance." The resulting drug, now branded Gocovri, significantly outperformed placebo in two Phase 3 trials, leading to FDA approval in August. The drug is now set to make its commercial debut in January 2018. Meanwhile, Adamas has made progress on two promising new opportunities: first, the use of Gocovri to treat the walking impairment associated with multiple sclerosis, and second, a high-dose, extended-release version of the blockbuster epilepsy drug Vimpat.

For a small company, Adamas has racked up several major victories. However, doubts linger. The knee-jerk reaction among some casual observers is that Gocovri exemplifies the pharmaceutical industry's usual bad behavior: repackaging an old, generic drug as a patent-protected "innovation" for the sake of a quick buck. From an investment perspective, such tactics have often served shareholders well, even as critics decried them as unsustainable all along the way. In the case of Gocovri, however, we believe the criticism is misplaced: Gocovri represents a genuine advance for Parkinson's patients, with superior efficacy and tolerability,

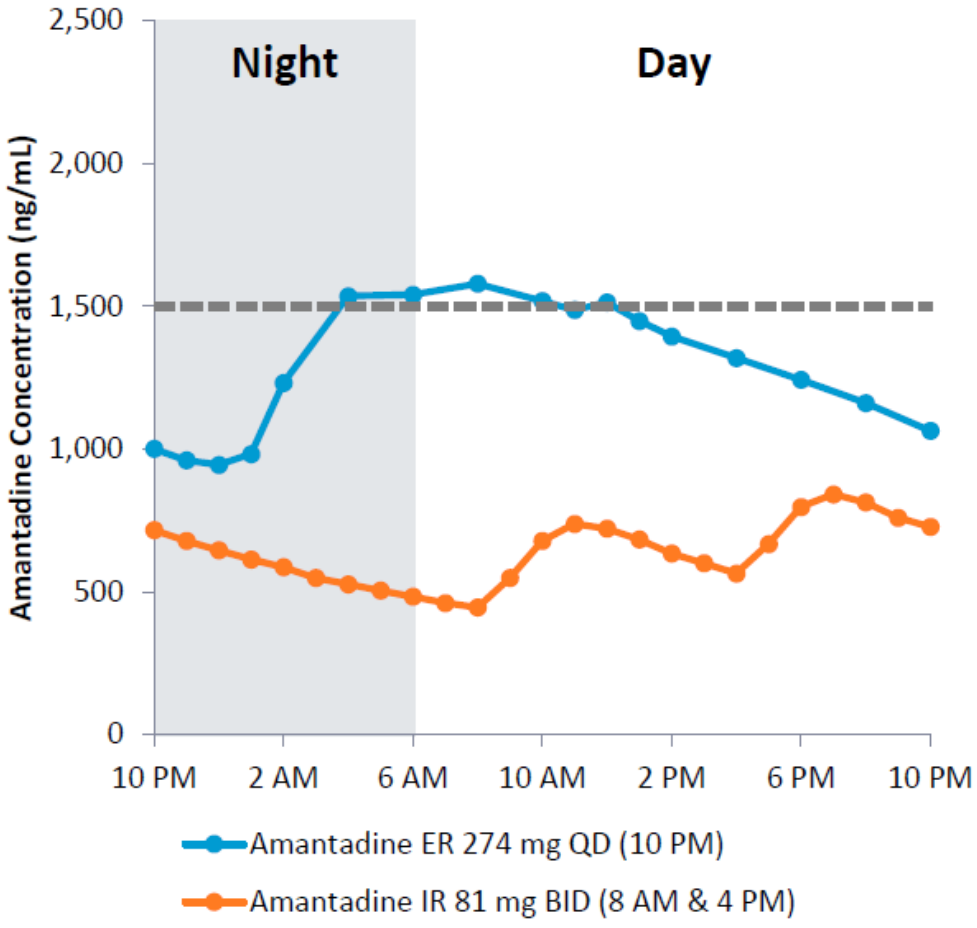
[1] Adamas 2017 10-K, p. 6.
[2] See e.g. Forest Laboratories FY2012 Q2 earnings call, October 18, 2011, discussing Forest's newly granted Namenda XR patent and the product's planned launch in "late 2012 or early 2013" (source: Capital IQ).

backed by superior evidence. As patients and doctors learn more, doubts will fade, and Adamas's revenue will surge.

III. Gocovri Is a Good Drug

Since Gocovri's active ingredient is amantadine – a drug long available in generic form and long used by some doctors to treat levodopa-induced dyskinesia (LID) – it's tempting to treat Gocovri's dramatic Phase 3 success as simply a new argument in favor of its generic, immediate-release (IR) counterpart. However, this unscientific leap of faith runs counter to multiple lines of evidence, all of which point to the weakness of generic amantadine and the superiority of Gocovri. Of course, this is no accident: Adamas carefully designed Gocovri's pharmacokinetic profile to deliver much higher and more stable levels of its active ingredient throughout patients' waking hours, when dyskinetic symptoms tend to cause more problems.

Gocovri vs. Generic Amantadine: Major Pharmacokinetic Differences



Source: Adamas Investor and Analyst Day presentation, September 18, 2017, slide 18

As shown in the graph above, which displays the expected pattern of amantadine levels in the blood for patients taking Gocovri once daily at night (blue line) as opposed to a typical dose of generic amantadine twice a day (orange line), Gocovri simply performs differently, achieving concentrations of ~1,000-1,500 nanograms per milliliter of plasma – roughly 2x higher than what its immediate-release counterpart delivers, with a smoother time course. In light of these stark differences, it's no wonder that Gocovri works materially better than generic amantadine – a drug with a long history of disappointment.

Generic IR Amantadine Doesn't Work Well

In 2003, the Cochrane Collaboration, a leading voice in the movement for evidence-based medicine, published a review of the use of generic amantadine for dyskinesia in Parkinson's disease (1). The conclusion was discouraging:

> In view of the lack of evidence it is impossible to determine whether amantadine is a safe and effective treatment for levodopa-induced dyskinesias in patients with Parkinson's disease.

While the authors identified several published studies purporting to show the benefits of amantadine, they judged most of them flawed, with major shortcomings including a lack of controls and an absence of randomization. Among the handful of acceptable studies, all were small, covering only 53 patients in total. While this small sample size precluded a rigorous analysis of safety, the authors noted that "[a]mantadine has a reputation for inducing severe psychiatric side effects." While they acknowledged the "urgent need for an orally active agent which can reduce severe dyskinesia," the poor evidence for generic amantadine made it impossible to recommend.

The following year, an influential study by a group of Italian researchers went further by calling into question the *durability* of generic amantadine's benefits (2) (emphasis added):

> Our results show that 300 mg/day Ama[ntadine] reduce Parkinson's disease dyskinesia by 45% in the first month of treatment (15 and 30 days), highly significant in comparison with baseline or with placebo.
>
> **Three to eight months later the improvements disappeared…**

In other words, while amantadine (given at a relatively high dose) did ameliorate dyskinesia, the benefit was *very short-lived.* Moreover, the study uncovered a "rebound effect": when patients went off amantadine, their dyskinesia suddenly worsened, becoming, on average, even more severe than at baseline. Many also experienced high fevers. With all of these negatives in mind, the authors rightly concluded that generic amantadine "cannot be viewed as a long lasting solution to the occurrence of dyskinesia," despite the tantalizing evidence of its short-term benefits. (While a later study claimed to contradict the finding of merely short-term efficacy for

amantadine (3), it used a much different trial design in which patients *already on* amantadine were randomized to either continue or discontinue the treatment. The discontinuers did deteriorate, but, as the authors admitted, this result may simply reflect harmful symptoms of withdrawal rather than proving that the drug itself was still helping.)

A cloud has thus hung over generic amantadine for years. In 2013, two researchers summarizing the scientific consensus on drugs of its class (NMDA-receptor antagonists) for the treatment of LID wrote that "the results from clinical trials…have been so far not that exciting. This is mainly due to the limited therapeutic effect and the potentially serious adverse effects associated with nonselective blockade [of the NMDA receptor]. Therefore, no agent of this group, including amantadine, has been approved for the treatment of dyskinesia" (4). Consistent with those "not that exciting results," the American Academy of Neurology, in its guideline summary for Parkinson's patients and their families, characterizes the evidence for "consider[ing generic amantadine] for reducing dyskinesia" to be "weak."

It's a testament to the "urgent need" for a dyskinesia treatment that, despite the weakness of the evidence supporting generic amantadine and its lack of FDA approval for dyskinesia, many doctors still prescribe it (off label) to some of their Parkinson's patients. However, in real-world use as in the clinical literature, generic amantadine appears to fall short. In an Adamas-sponsored study, researchers analyzed "a large database of anonymized commercial and Medicare patient insurance claims from Symphony Health Solutions" to assess how long Parkinson's patients with prescriptions for generic, immediate-release amantadine actually stay on the drug. Based on a sample of 7,100 patients, only a small minority – 34% – continue taking amantadine for a full year. The other two-thirds drop it.

Though it's impossible to know from this data set *why* patients are giving up, the researchers posited "a poor efficacy : tolerability ratio." In other words, the drug isn't helping enough to justify its side effects. By creating, in Gocovri, a form of amantadine with a significantly different pharmacokinetic profile than its immediate-release counterpart, Adamas hoped to remedy many of its failings – and, based on the evidence outlined below, we believe it succeeded.

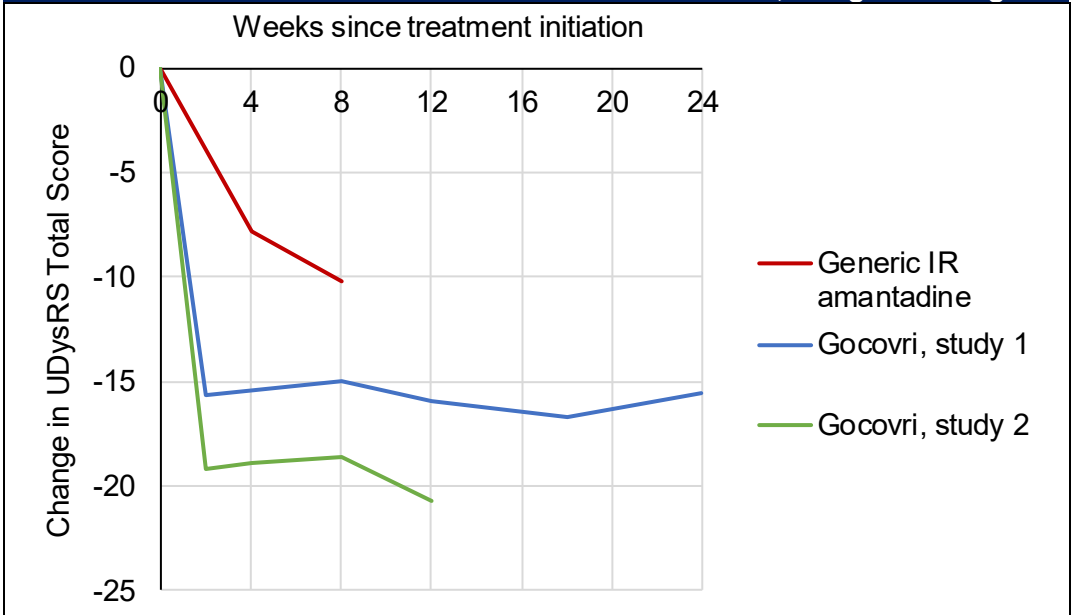
Gocovri Outperforms Generic IR Amantadine

In Gocovri's two pivotal trials, patients assigned to the drug experienced large and statistically significant improvements by week 12 in a measure called the Unified Dyskinesia Rating Scale (UDysRS) total score, which "combines patient-based assessments of dyskinesia with objective evaluations of disability and impairment"; a previous independent study found that UDysRS was the scale that best detected treatment responses (5). One downside of UDysRS, however, is that it's relatively new, making it difficult to benchmark Gocovri's results against those of older studies. Moreover, Gocovri's trials pitted the drug against placebo, not generic IR amantadine – a normal, if frustrating, industry practice for extended-release variants. Thus we have no scientifically exact way to compare Gocovri with generic IR amantadine. However, triangulating

across multiple data sets, there is still much to learn, all of it pointing toward Gocovri's superiority.

First, consider efficacy with respect to Gocovri's primary endpoint: the UDysRS total score. In Gocovri's first and second Phase 3 trials, Gocovri patients' scores improved on average by 16 and 21 points, respectively. By contrast, in the same small study that pinpointed UDysRS as the best available measure of dyskinesia, subjects taking generic IR amantadine enjoyed only a 10-point average improvement (5). In addition, this improvement was only measured out to eight weeks, leaving open the possibility that, over time, the benefit might fade; meanwhile, Gocovri's effects clearly persist much longer, as the graph below demonstrates. (Indeed, an open-label extension of these Phase 3 trials has shown sustained efficacy out to at least two years (6).)

Gocovri vs. Generic IR Amantadine: More Effective, Longer Lasting



Source: Pahwa et al. 2017 (7), Oertel et al. 2017 (8), Goetz et al. 2013 (5), Kerrisdale analysis

Though this is not a true head-to-head comparison (since we are juxtaposing results from three different studies), the differences are certainly suggestive: by week 8, Gocovri leads to improvements *47% to 84% larger* than those associated with generic IR amantadine, and it's clear that these improvements stick. (Note that this comparison likely *understates* the real-world difference since the underlying generic-amantadine study used a high dose of 300 mg per day, 60% greater than what average patients take based on insurance data, thus potentially leading to a stronger treatment effect.[3])

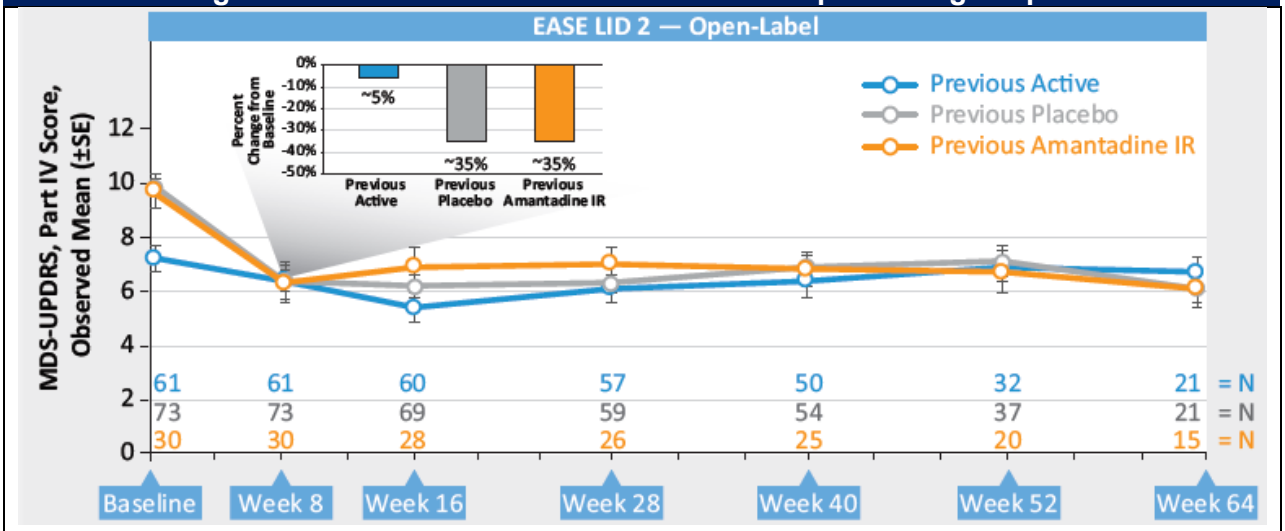
[3] Navarro et al.'s 2017 poster presentation notes that, among patients persisting on IR amantadine after six months, "the mean fulfilled dose was 187 mg amantadine HCl/day (151 mg amantadine)." Note that 300 mg of amantadine HCl is equivalent to 242 mg of pure amantadine, while a daily dose of Gocovri

Second, consider a more tangible metric than UDysRS total score: “on” time *with* troublesome dyskinesia. This refers to the amount of time in a day that a patient is “on” – that is, free from primary Parkinson’s symptoms, with the help of levodopa – yet still suffering from what he or she perceives as “troublesome” involuntary movements as a side effect of levodopa. If Gocovri works better than generic IR amantadine, then it should lead to less time spent with troublesome dyskinesia, and this indeed appears to be the case. In two recent withdrawal trials, for instance, patients who had already been taking generic amantadine for years and continued on it during the trials experienced an average of 2.1-2.8 hours per day of “on” time with troublesome dyskinesia at baseline and 2.3-2.5 hours after treatment, for an overall average of 2.4 hours (3) (9). By contrast, after 12 weeks of Gocovri treatment, patients reported an average of only 1.1 and 1.5 hours in the two Phase 3 studies, for an overall average of 1.3 hours. This 46% delta (1.3 vs. 2.4 hours) is roughly consistent with the UDysRS comparison above and again suggests that Gocovri can outperform generic IR amantadine.

Further confirmation of Gocovri’s superiority comes from an open-label extension to Gocovri’s pivotal trials. This study enrolled not just patients from the Gocovri and placebo arms of the previous trials but also patients excluded from those trials *who were already taking generic IR amantadine.* If Gocovri were no better than generic, then patients who switched from generic to Gocovri would experience no change in their dyskinesia. But that’s not what happened. Patients switching from generic IR amantadine to Gocovri quickly saw a 35% improvement in their dyskinesia symptoms (as measured by another common rating scale known as the MDS-UPDRS Part IV), and this improvement persisted week after week. Strikingly, these patients performed almost exactly the same as patients who had previously been taking placebo: they started with virtually identically MDS-UPDRS Part IV scores (~9.5), enjoyed almost the exact same magnitude of improvement on Gocovri (~35%), and stayed at their improved level for weeks. It appears that, for these amantadine veterans, generic IR amantadine was no longer accomplishing anything; by contrast, switching to Gocovri rapidly and durably ameliorated their symptoms.

contains 274 mg of amantadine. The difference in pure amantadine exposure in the studies compared above is thus small and does not plausibly explain the large difference in treatment benefit.

Switching from Generic IR Amantadine to Gocovri Sparks Large Improvements



Source: Isaacson et al. 2017

Consistent with its superior efficacy, Gocovri also appears to inspire better patient compliance than its generic IR counterpart. Though a perfect comparison is impossible, data from the open-label extension study indicate that, after at least a year on Gocovri, only ~20% of patients have dropped the drug due to adverse reactions[4] – a figure that compares very favorably with the *more than three-fold higher* rate of discontinuation (66%) at one year that we see from the generic IR amantadine data discussed above. While additional patients did drop Gocovri for reasons unrelated to adverse drug reactions (like a need to take a medication that the trial rules prohibited), we estimate that, in the open-label extension study overall, 64% of Gocovri patients were still on the drug after one year[5] – virtually *double* the proportion that remains on generic IR amantadine. Evidently the poor "efficacy : tolerability ratio" seen as the driver of generic IR amantadine's low real-world adherence is greatly improved by the differentiated pharmacokinetics of Gocovri.

Finally, it's important to note that Gocovri has one proven benefit that generic IR amantadine doesn't: it reduces "off" time, i.e. the amount of time when patients' primary Parkinson's symptoms are not well-controlled by their levodopa treatment. In Gocovri's first Phase 3 study, "off" time improved for Gocovri patients 0.9 hours more than it did for placebo patients, a treatment difference that was statistically significant (7); in its second Phase 3 study, the

[4] See Hauser et al. 2017 poster presentation, "Expanded Results of an Ongoing Long Term Open-label Phase 3 Study of ADS-5102 (amantadine) Extended-Release Capsules for Treatment of Levodopa Induced Dyskinesia (LID) (EASE LID 2 Study)," Figure 3. We are averaging the 52-week percentage of patients not discontinuing due to an adverse drug reaction for the previous-placebo and previous-active groups for an estimate of ~80% non-discontinuation/~20% discontinuation.

[5] Based on the Hauser et al. 2017 presentation, Figure 1, there were 99 patients still enrolled after a year or more, 13 patients who completed the full study, and 63 who discontinued; conservatively, we assume that all who discontinued did so in the first year. Thus the one-year discontinuation rate is 63/(99+13+63)= 36%.

treatment difference was 1.1 hours and again was statistically significant (8). As the authors of the first study put it (7) (emphasis added):

> To our knowledge, this is the first demonstration of an oral treatment reducing **both LID and OFF time** in patients with PD with dyskinesia.

By contrast, generic IR amantadine, though shown to reduce LID over the short term in a handful of studies, was never thought to reduce "off" time. Perhaps its more volatile pharmacokinetics and lower maximum effective dose made any such reduction too small to be detectable through the noise. Whatever the source of Gocovri's superiority to its generic counterpart is, it's a strong positive that it manages to address the major side effect of levodopa treatment – dyskinesia – while actually *enhancing* levodopa's primary benefit (reducing "off" time). By contrast, one common early approach to treating levodopa-induced dyskinesia – simply reducing the patient's levodopa dose – usually leads to higher "off" time and thus presents an ugly trade-off.

Of course, Gocovri ultimately is "just" a different formulation of amantadine. But different formulations give rise to different pharmacokinetics, and there's no good reason to doubt that different pharmacokinetics can give rise to different outcomes for patients. Generic IR amantadine probably does improve levodopa-induced dyskinesia over the short run, but the proof is thin, while the evidence of long-term impotence and poor tolerability leading to rapid abandonment by patients is genuinely disturbing. It's not merely a regulatory quirk that generic IR amantadine is not FDA-approved for levodopa-induced dyskinesia; there simply is no high-quality data proving that its benefits outweigh its costs in this indication.

By contrast, Gocovri's benefits are extremely well documented, have passed FDA muster, and appear to exceed those of its generic counterpart. It (uniquely) reduces "off" time, reduces dyskinesia to a much greater degree, strongly improves the condition of patients who switch from generic amantadine, and inspires two to three times as many patients as its generic counterpart to stay on the drug. While there may not be an ideal head-to-head comparison, the data we do have all point in the same direction. To be sure, cynicism is the proper attitude to adopt when it comes to many of the pharmaceutical industry's minor "innovations," but Gocovri is different: it marks a real advance for patients with LID, and it deserves to become standard of care.

IV. Gocovri Will Be a Commercial Success

Reformulated and Repurposed Drugs Often Generate Great Value

Despite the clinical advantages outlined above, drugs like Gocovri – altered versions of existing, sometimes old medications that are already available in different forms via generics manufacturers – tend to provoke skepticism: *will physicians and payors really enable such trickery to succeed?* In some cases, this attitude represents an irrational prejudice in favor of

brand-new molecules, which intuitively seem more exciting and "scientific" than just finding better ways of deploying old ones. Patients, however, don't care how long ago the active ingredients of the drugs they're taking were discovered; they care about how well they work and what side effects they cause. Gocovri's differentiated pharmacokinetics, the result of its high-dose extended-release formulation, make it the best available treatment for levodopa-induced dyskinesia, as well as the only one with FDA approval for the indication; ultimately these factors, not the age of amantadine, will drive commercial success for Gocovri.

However, even drugs *without* similar attractions – drugs that sometimes *do* merit disdain – have flourished financially, defying their critics at every turn. Below, we review several major examples and go on to provide additional detail. If *these* drugs could, in spite of their shortcomings, generate billions of dollars of value – largely through a combination of somewhat greater convenience, limited competition, and pure salesmanship – then a far more defensible drug like Gocovri can surely thrive.

- Raptor Pharmaceutical Corp.: acquired last year for $800mm (~5x consensus peak revenue)
    - Main asset: delayed-release version of an old drug; already achieved 66% market share in the US after only three years, despite price of ~$250,000/year (~30x premium relative to the incumbent branded treatment)
- Acorda Therapeutics: $1B+ market cap
    - >$500mm run-rate revenue generated by a repackaged, extended-release formulation of a drug already available much less expensively from compounding pharmacies
    - ~20x price premium relative to alternative therapy
    - Potentially dangerous drug (originally used to induce seizures in animals) whose efficacy is openly questioned
- Celator Pharmaceuticals: acquired last year for $1.5B after reformulating two widely used generic drugs initially approved in the 1960s and '70s
    - Only change made: new formulation allows for altered dosing (three 90-minute infusions rather than a seven-day continuous infusion)
- AMAG Pharmaceuticals: ~$550mm market cap
    - Main drug has achieved 67% market share[6] despite competing with an identical product available from compounding pharmacies for ~1/20 the price
    - Key selling point: only product FDA-approved for its indication (just like Gocovri for levodopa-induced dyskinesia)

[6] See AMAG presentation, August 3, 2017, slide 19. Makena share of total hydroxyprogesterone caproate market is 47%/(47% + 23%) = 67%.

Repackaging Old Drugs: Case Studies of Rapid Growth and High Market Share

Company	Drug	List price per year	Metric	2010	2011	2012	2013	2014	2015	2016
Raptor	Procysbi	$ 251,340	Revenue[2]				$ 17	$ 69	$ 94	$ 130
			Market share[3]				9%	35%	48%	66%
Acorda	Ampyra	$ 26,940	Revenue	$ 133	$ 211	$ 266	$ 303	$ 366	$ 437	$ 493
			Market share[1]	3.4%	5.5%	6.9%	7.8%	9.5%	11.3%	12.8%
			% of pts who have ever tried drug	*16%*	*25%*	*37%*	*45%*	*50%*	*55%*	*60%*
AMAG	Makena	$11,466	Revenue[4]		$ 12	$ 54	$ 108	$ 166	$ 252	$ 334
			Market share		3%	13%	25%	39%	59%	78%

Source: company disclosures, Kerrisdale analysis

Notes:

1. Ampyra peak market share estimated based on total patient population.
2. Management's Procysbi revenue guidance in 2016 Q2 was $125-135mm.
3. Market share for earlier years approximated based on that year's revenue divided by peak revenue times peak market share. This understates market share in earlier years because it does not factor in 1) price increases or 2) impact of part-year patients in early years.
4. FY 2011-2013 ending March 31 2012-2014.

Raptor/Procysbi: A Dubious Delayed-Release Reformulation Succeeds

Raptor Pharmaceuticals was a small company that developed Procysbi, a delayed-release version of the old, off-patent drug cysteamine for the treatment of cystinosis, a rare genetic disease. While the older form of the drug was priced at approximately $8,000 per patient per year, Raptor priced Procysbi at approximately *$250,000* per patient per year.[7]

Going into its clinical trials, the anticipated benefit of Procysbi was that it would "require less frequent dosing and reduce gastro-intestinal side effects compared to the current standard of care."[8] While the less frequent dosing was true (twice daily as opposed to four times daily), the side effects in the Phase 3 trial turned out to be *worse* than the much cheaper standard of care; for instance, as Procysbi's FDA label shows, vomiting, nausea, abdominal pain, and headache are all more frequent with Procysbi than with immediate-release cysteamine. Moreover, Raptor's drug appeared to be less effective than IR cysteamine at improving a key clinical measure, white-blood-cell cystine concentration, though the difference didn't cross the threshold of statistical significance.

Despite these clinical limitations and the fact that Raptor priced Procysbi at such an enormous premium to its immediate-release counterpart, the drug's convenience – and its marketing – won out. In its final earnings call as a public company, Raptor announced that it had achieved a

[7] See e.g. New York *Times*, "Parental Quest Bears Fruit in a Kidney Disease Treatment," April 30, 2013.
[8] Raptor FY 2011 10-K, p. 2.

66% share just three years after receiving FDA approval. It was then acquired by Horizon Pharmaceuticals for $800mm – a strikingly high 4-5x multiple of the consensus range for peak Procysbi revenue of $150-200mm. Even though Procysbi, like Gocovri, is "just" a modified-release version of an old drug – and, unlike Gocovri, costs a quarter of a million dollars – that didn't stop it from quickly dominating the market and becoming a desirable acquisition target.

Acorda/Ampyra: FDA Seal of Approval Breathes New Life into a Troubled Old Drug

Acorda Therapeutics's drug Ampyra, an oral potassium-channel blocker indicated to improve walking ability in people with multiple sclerosis, has achieved rapid, high penetration into its target market despite a high list price, the availability of a significantly cheaper alternative with the same active ingredient, and questionable efficacy. Ampyra is an FDA-approved extended-release version of the drug 4-aminopyridine (4-AP), which had long been available from compounding pharmacies for roughly $50 a month.[9] First identified in 1902 as a bird toxin and seizure-inducing agent, 4-AP had been studied in the 1970s and '80s as a treatment for neurological conditions including multiple sclerosis.[10] In 1990, the pharmaceutical firm Elan Corporation developed an extended-release version, but after a series of failed clinical trials, the reformulated drug wound up in the hands of Acorda. Acorda then suffered another trial failure but ultimately discovered a successful niche for extended-release 4-AP: increasing the percentage of MS patients who experience a >20% improvement in walking speed. (Note, however, that Ampyra has a placebo-adjusted response rate of only ~30%, implying that it fails for ~70% of patients.)

Ampyra was approved by the FDA on January 22, 2010, and launched with a list price of $1,056 per month, with annual price increases of approximately 10% since then. Today the price is $2,245 per month, or $26,940 per year – comparable to the $28,500 annual list price of Gocovri. Yet while Gocovri clearly does its job, even the sell side has admitted that Ampyra has, at best, marginal value, with at least one analyst initially skeptical that the FDA would even approve the drug, given its "low efficacy signal…seen in only a subset…of treated patients."[11] Furthermore, a post-marketing study of Ampyra failed to show that the drug was effective to a statistically significant degree. Despite all this, roughly 60% of the addressable multiple-sclerosis market has tried Ampyra to date:[12]

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[9] Deutsche Bank, November 24, 2008 (survey of 30 compounding pharmacies).

[10] 4-AP arguably parallels amantadine in that old, small, relatively low-quality studies hinted at efficacy, but not until extended-release drugs were developed did stronger evidence emerge.

[11] Morgan Joseph, June 6, 2007.

[12] Note that MS is a difficult market to assess because roughly 80% of patients have relapsing/remitting MS, which includes periods of remission in which chronic treatment with a drug like Ampyra wouldn't make sense. Thus the fraction of patient that has ever used Ampyra gives a better sense of its marketing success than market share at a single point in time. In addition, many patients who try it will inevitably drop it given its low response rate.

Ampyra: An Extended-Release Version of an Off-Patent Drug Achieves Widespread Adoption	
Total pts with MS	400,000
% with walking difficulty	70%
Of which: % wheelchair-bound	30%
Pts with walking difficulty	280,000
Less: wheelchair-bound	84,000
Ampyra addressable market	196,000
Pts on Ampyra	25,000
Current market share	13%
Cumulative pts who have *tried* Ampyra	120,000
as % of addressable market	61%

Source: company filings, Kerrisdale analysis

Moreover, despite its shortcomings, Ampyra penetrated the addressable market rapidly, going from approval to, by our estimates, 50% penetration in just four years. Nor has Ampyra's reach been circumscribed by the size of the pre-existing market for off-patent, immediate-release 4-AP: while only 3,000-10,000 patients were on immediate-release 4-AP pre-Ampyra,[13] Acorda reached 31,000 patients within a single year – 3-10x more – all with an extended-release version of the same molecule.

Thus Acorda managed to take an old, off-patent drug with a history of failed clinical trials and convert it into an extended-release commercial powerhouse that, despite weak efficacy and despite competition from compounding pharmacies, quickly swept through the addressable market and generated hundreds of millions of dollars of revenue. (It's worth noting that Acorda also monetized non-US rights to Ampyra for an upfront payment of $110mm, tiered double-digit royalties, and up to an additional $400mm in regulatory and sales milestones. Such a transaction is not factored into our valuation of Gocovri and would yield additional upside.) The reality is that MS patients want therapies with a chance of improving the walking difficulties that are among their most bothersome symptoms, just as Parkinson's patients want to address their dyskinesia. With few good alternatives, all of them off-label, the lone FDA-approved therapy in each area has enormous value, even if it is "just" a reformulation of an old drug.

Other Precedents

Celator Pharmaceuticals provides further evidence that modifying the delivery of old drugs can yield lucrative opportunities. Celator's sole drug, Vyxeos, is a reformulation of the existing standard-of-care treatment for acute myeloid leukemia (AML), a type of cancer. Historically, AML patients have been treated with "7+3," which is seven days of continuous cytarabine (a

[13] Source: Acorda 2010 Q3 earnings call, November 10, 2010.

chemotherapy medication) accompanied by three bolus doses of daunorubicin (another chemotherapy medication) given over the first three days. Cytarabine and daunorubicin are widely used generic drugs initially approved in the 1960s and 1970s. Vyxeos does nothing more than combine the two drugs and place them within a liposomal encapsulation that allows them to be given as three 90-minute infusions rather than a seven-day continuous infusion. In March 2016, Celator announced that Vyxeos achieved statistically significant results in its pivotal trial. Just three months later, Jazz Pharmaceuticals acquired Celator for a staggering $1.5 billion – a clear third-party endorsement of the great commercial potential of improving and repackaging old drugs. (Notably, Vyxeos is the only FDA-approved treatment for certain types of high-risk AML, again highlighting the value of being the only drug with that distinction for a given indication, as Gocovri is for levodopa-induced dyskinesia.)

Finally, an older but better-known precedent is Genentech's Lucentis, a monoclonal antibody used to treat the eye disease called wet age-related macular degeneration (AMD). Lucentis is derived from (and is a fragment of) bevacizumab, another monoclonal antibody sold under the brand name Avastin and FDA-approved for the treatment of systemic cancer. Since 2005, Avastin has also been used off-label for the treatment of wet AMD, and studies have shown that Avastin is just as effective as Lucentis for this indication – yet Lucentis reached over $4B in peak revenue despite a ~40x price premium over Avastin. Again, convenience (Lucentis was designed and packaged to be injected in the eye, while Avastin was not) and the FDA seal of approval for a specific indication (Lucentis was approved for wet AMD, while Avastin was not) proved to be the dominant factors driving commercial success, while a chorus of critics pointing out that Lucentis was little more than overpriced Avastin had no discernible impact.

Purists might condemn all of these products as rip-offs, while pragmatists might argue that "innovation" matters less than improving patients' lives, regardless of whether that involves creating new drugs or tweaking old ones. But whatever one's moral assessment, the facts clearly show that repackaged versions of old drugs – including modified-release formulations of off-patent molecules like Raptor's Procysbi, Acorda's Ampyra, and Adamas's Gocovri – can achieve high market share despite high prices and thereby generate high revenues, especially when they obtain FDA approvals that their competition lacks. Adamas's "extremely practical" approach to drug development is not off the beaten path; this is well trodden ground.

Gocovri Will Achieve Payor Support

One worry that always crops up with expensive drugs is that insurers and other payors like Medicare will refuse to buy in. Of course, all of the treatments just discussed are expensive, yet all of them ultimately earned enough coverage to generate substantial revenues, so this concern is clearly not fatal. Based on discussions with industry participants, including employees of insurance companies and pharmacy benefit managers, we believe that only a fraction of payors will attempt to impede access to Gocovri, and those that will will deploy mild, commonplace approaches like requiring prior authorization from doctors or more expensive third-tier co-pays from patients – tactics that Adamas is already preparing to counter with its

patient access support program, Gocovri Onboard, set to launch next month. At the end of day, generic immediate-release amantadine lacks strong evidence of efficacy, while Gocovri is the only proven, FDA-approved drug for LID, making it very difficult for payors to say no to.

Further aiding Gocovri is the fact that, based on our discussions with neurologists, as well as the clinical literature,[14] roughly half of patients with LID are old enough to be enrolled in Medicare Part D (prescription drug) plans. In 2009, the Centers for Medicare & Medicaid Services made it clear that such plans can't force patients to try off-label treatments when an on-label treatment is available:

> Part D sponsors will not be permitted to require an enrollee to try and fail drugs supported only by an off-label indication…before providing access to a drug supported by an FDA approved indication (on-label indication) unless the off-label indication is supported by widely used treatment guidelines or clinical literature that CMS considers to represent best practices.

Thus, given the poor quality of the evidence in favor of immediate-release amantadine described above, Medicare Part D sponsors can't compel patients to try it before they try Gocovri, smoothing the way for Adamas to gain market share. (However, even with such a requirement in place, Gocovri would still be an easy sell for the large pool of patients who have already tried but may have abandoned generic IR amantadine.) While one downside of the Medicare population is a prohibition on direct co-pay assistance (which makes it cheaper for *patients* to obtain expensive drugs without cutting the price to payors), Adamas has already alluded to its plans to use a standard industry technique and refer Medicare patients to charities that can provide financial assistance – charities funded in part by the likes of Adamas.[15] Payor hurdles may keep Gocovri adoption from peaking quickly, but the market already expects a slow ramp-up. The more important driver is how many patients Gocovri eventually reaches, which, given its utility and uniqueness, should be high.

Gocovri Will Reach Blockbuster Status

Before delving into specific assumptions about Gocovri, it's worth taking a step back to consider the total size of the addressable market. Today approximately 700,000 Parkinson's patients in the US are on levodopa, of whom ~175,000 experience moderate to severe dyskinesia as a side effect. At a net price of ~$20,000 per year, **Gocovri would thus generate $3.5 billion of annual revenue if it achieved 100% market share.** Of course, it won't (though the track records of drugs like Procysbi and Makena show that even dubious products can achieve very

[14] For example, in Pahwa et al. 2017 (7), the mean age is ~65 years; the same is true in Oertel et al. 2017 (8).

[15] See e.g. Investor and Analyst Day presentation, September 18, 2017, slide 64-66 ("transfer to foundations for government program support," "provision of information for government insured patients about available programs to assist with their out of pocket costs").

high uptake under the right conditions), but this figure establishes a clear benchmark. As the only FDA-approved drug for LID, with an unquestionable ability to improve patients' conditions, it stands to reason that Gocovri will eventually claim a sizable portion of this $3.5 billion opportunity. (Management has guided to peak penetration of 25-30%.) Given conventional valuation multiples for new drugs of ≥3x peak revenue, the back-of-the-envelope math easily supports a multi-billion-dollar present value for Gocovri (without even considering the potential for non-US revenue).

To refine our estimates, we spoke directly with physicians about Gocovri and reviewed management and sell-side physician surveys. All evidence points to a large market for Gocovri – so large, in fact, that we believe that some sell-side analysts have arbitrarily tamped down their estimates out of fear of looking irrationally optimistic relative to the current stock price. Below we summarize our key takeaways:

- Sell-side firm 1 physician survey, early 2017:
  - 26% of treated Parkinson's patients have "regular, debilitating LID"
  - Physicians would treat a weighted average of **30%** of LID patients with Gocovri
  - Anticipated penetration based on survey: 55,000 patients (→ ~$1.1B annual revenue)
- Sell-side firm 2 physician survey, late 2017:
  - Surveyed 25 movement-disorder specialists
  - When treating patients with LID:
    - 12% anticipated using Gocovri in a significant majority
    - 20% anticipated using Gocovri in a slight majority
    - 44% anticipated using Gocovri in a significant minority
    - 20% anticipated using Gocovri in a slight minority
    - Assigning numerical values of 75%, 50%, 30%, and 10%, respectively, to these categories, we estimate a weighted-average expected penetration of **34%** (→ ~$1.2B annual revenue)
- Adamas management research (reviewed at September 2017 investor day)
  - Surveyed 138 physicians treating Parkinson's disease in 2017 Q1
  - **54%** of patients will be prescribed Gocovri, of whom:
    - 44% will have previously received no dyskinesia treatment
    - 44% will have previously received a different, off-label treatment (generic IR amantadine, dopamine agonists, COMT inhibitors, or MAO-B inhibitors)
    - 11% will have previously been treated through a reduction or fractionation of their levodopa dose

Taking the lowest projected market share mentioned above – 30% – we further haircut Gocovri's prospects by assuming 20% non-compliance (patients failing to take their prescribed medication) and 30% discontinuation (patients completely abandoning the drug). Nonetheless, we still project that Gocovri will exceed $1B in annual revenue. Making a variety of other assumptions, including that market share will take eight years to peak (consistent with the upper

end of management's guided range), that revenue will drop to zero after 2030, when key patents expire, and that both the Parkinson's market and the price of the drug will grow at 3% per year, we value Gocovri alone at $1.6B, or $65 per share. (The low multiple of peak revenue is largely the result of the assumed slow revenue ramp.)

Gocovri: Summary of Kerrisdale Standalone DCF Model

	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Ending Gocovri patients	3,785	7,798	12,047	16,545	21,302	26,329	31,639	37,243	38,360	39,511	40,696	41,917	43,175
Revenue	$ 39	$ 124	$ 219	$ 325	$ 443	$ 575	$ 721	$ 882	$ 999	$ 1,059	$ 1,124	$ 1,192	$ 1,265
EBITDA	$ (100)	$ (22)	$ 63	$ 173	$ 290	$ 409	$ 541	$ 688	$ 791	$ 841	$ 895	$ 952	$ 1,012
Free cash flow	$ (113)	$ (40)	$ 33	$ 130	$ 162	$ 221	$ 315	$ 411	$ 473	$ 503	$ 535	$ 569	$ 606

NPV @ 10%	**$ 1,641**
Per share	**$ 65**

Source: Kerrisdale analysis

While this valuation presupposes that Adamas will remain an independent company, it's worth pointing out that we, like sell-side analysts, assume an accordingly high level of SG&A costs ($150mm per year, growing at 5% annually). As part of a larger drug company, though – especially one with an existing neurology business – Adamas could easily shed much of its redundant overhead and sales staff. Cutting SG&A by 30%, for instance, would, by our estimates, generate ~$230mm in present-value terms – a boost of ~$9/share or more than a third of the current stock price. Gocovri's unique market position, coupled with this straightforward financial upside, makes Adamas an attractive acquisition target.

In sum, investors are dramatically underestimating Gocovri's commercial prospects. A good drug with little effective competition is a valuable thing, and industry experience has shown time and again that even uninspiring and low-quality drugs can still produce high returns. As Gocovri grows its way toward blockbuster status, either the market will come to recognize its true value – or an outside buyer will.

V. Applying Gocovri to Multiple Sclerosis Is a Billion-Dollar Opportunity

Beyond LID, Adamas is also using the same Gocovri formulation of amantadine to pursue the multiple-sclerosis market, with Phase 3 trials expected to start in early 2018; we believe the drug could make it to market for MS in mid- to late 2019. Based on available Phase 2 data, we believe Gocovri[16] is highly likely to achieve clinical success in this area and will exceed the ~$500mm peak revenue of Ampyra, the Acorda MS drug already discussed above. In a small placebo-controlled trial, Gocovri has already achieved statistical significance, and an apples-to-

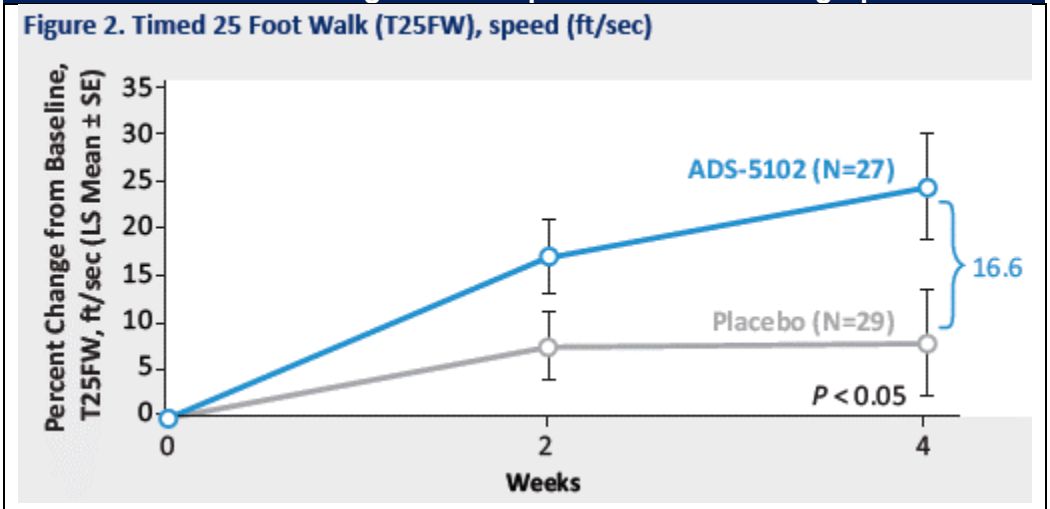
[16] The drug will likely be given a different name to distinguish the MS-gait indication from the LID indication, but here we simply call it Gocovri for the sake of simplicity.

apples comparison between trial results for Gocovri and Ampyra shows that Gocovri is a far superior treatment.

First, consider Ampyra's results. Goodman et al. 2013 analyzed the pooled data from Acorda's pivotal trials and calculated that Ampyra produced a 7.3% placebo-adjusted average improvement in walking speed relative to baseline. While the endpoint in this study was change in speed averaged over the duration of a trial, a subsequent four-week trial (Yapundich et al 2015) measured overall change in walking speed between baseline and four weeks of treatment. Investigators found that neither the 5 mg nor 10 mg groups achieved statistical significance, with patients in the 10 mg group seeing a 16.8% increase in speed, while patients in the placebo group saw a 13.1% increase in speed. The placebo-adjusted benefit is thus just 16.8% - 13.1% = 3.7%.

By contrast, in Adamas's Phase 2 study of Gocovri in MS, Gocovri conferred a placebo-adjusted benefit of 16.6% over the same four-week time frame – a far larger improvement, as the graph below shows:

Gocovri in MS: Significant Improvement in Walking Speed



Source: Adamas poster, "A Phase 2 Study of ADS-5102 (amantadine hydrochloride) Extended Release Capsules in Multiple Sclerosis Patients with Walking Impairment," presented February 23, 2017

Furthermore, patients in the ADS-5102 (Gocovri) group appear to be continuing to improve through the final data point, which was only four weeks, while the placebo group flatlined after just two weeks. It is possible that extending the duration of the trial, as Adamas will almost certainly do in Phase 3, will further distinguish Gocovri from 4-AP and Acorda's extended-release variation thereof, strengthening the drug's appeal.

If Adamas can deliver on the promise of Gocovri in MS, as suggested by the Phase 2 data, then the opportunity will be large. As of February 2017, approximately 120,000 patients have already

tried Ampyra, despite its modest efficacy[17] – a clear sign of the strong demand for a new, improved product to improve gait in MS patients. In addition, the fact that, by our estimate, there are only 25,000 patients *currently* taking Ampyra – a small fraction of the 120,000 who have tried it – points to widespread dissatisfaction with the drug, creating an opening for Gocovri to enter the market and capture significant share.

Assuming a late 2019 launch, peak penetration of only 12% (consistent with Ampyra), and the same price as Gocovri for the LID indication, we predict near-blockbuster revenues for Gocovri in MS, albeit many years into the future, with nearer-term revenue surpassing $500mm by 2023:

Gocovri in MS: Significant Improvement in Walking Speed

	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Ending Gocovri patients (MS)	0	1,040	8,567	15,442	22,722	28,084	28,927	29,794	30,688	31,609	32,557	33,534	34,540
Revenue	$ -	$ 11	$ 105	$ 270	$ 441	$ 605	$ 699	$ 742	$ 787	$ 835	$ 886	$ 940	$ 997

Source: Kerrisdale analysis

Layering this revenue and related SG&A costs into our model, we find that the incremental value of Gocovri in MS, conditional on clinical success, is a massive $1.6B, or $62 a share – comparable to Gocovri in Parkinson's disease. Of course, with Gocovri in MS still awaiting Phase 3 data, this value is far from certain – but, given strong Phase 2 results, it's a good bet.

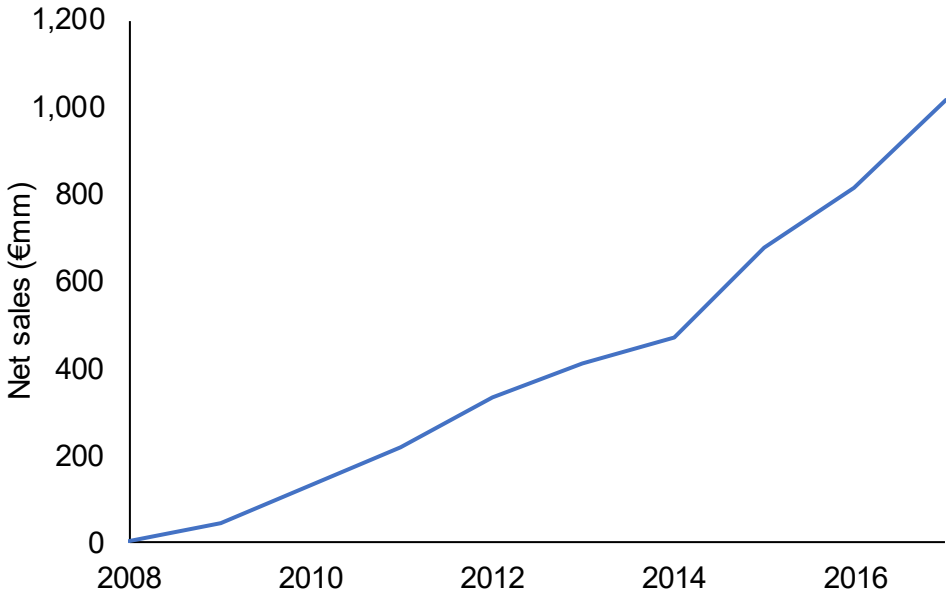
VI. "Vimpat XR" Alone Could Be Worth $300 Million

To the best of our knowledge, sell-side analysts – though uniformly bullish on Adamas – attribute no value to one of its two main pipeline assets: a high-dose, extended-release formulation of lacosamide, a popular (and patent-protected) epilepsy medication sold under the brand name Vimpat. With only Phase 1 trials completed to date, Adamas's extended-release Vimpat is still relatively early in its development, but Adamas believes that, thanks in part to the well-understand clinical profile of Vimpat itself, its variant is "Phase 3-ready"[18] today, with the potential to enter pivotal trials as early as next year. Though clearly riskier than the already proven Gocovri, "Vimpat XR" has massive commercial potential and could generate hundreds of millions of dollars for Adamas – a majority of its entire current enterprise value. As far as we know, this source of upside has never before been publicly quantified.

To understand the value of "Vimpat XR," we must first understand the value of its immediate-release forebear. Since its 2008 launch (first in Europe, then in the US the following year), Vimpat has been a major success for its manufacturer, the large Belgium-based pharmaceutical company UCB. Clinically, Vimpat has developed a reputation as a predictable, easy-to-prescribe drug, while, financially, it's currently on pace to generate more than a billion euros of annual net sales, flourishing even in a fiercely competitive epilepsy market:

[17] Acorda 2016 10-K, p. 2.
[18] Source: Adamas Analyst/Investor Day, September 18, 2017 (transcript via Capital IQ).

Vimpat Has Enjoyed Rapid, Steady Revenue Growth for Almost a Decade



Source: company filings, Kerrisdale analysis
Note: 2017 level estimated as 2017 H1 growth rate (25%) applied to 2016 FY level.

UCB projects that Vimpat will continue to grow, achieving peak sales of at least €1.2 billion ($1.4 billion) by 2020.[19] While there's no single inarguable answer to the question of how much Vimpat is currently worth (since UCB derives significant earnings from several other drugs), we estimate, on the basis of two sell-side analyses as well as a simple percentage of revenue, that it's roughly $3 billion:

Triangulating Vimpat's Value

Method	Value
Sell-side firm 1	$ 3,328
Sell-side firm 2	$ 2,009
% of revenue:	
Vimpat as % of revenue, 2017 H1	23%
UCB enterprise value	$ 14,577
Vimpat value, pro rata	$ 3,415
Average	$ 2,918

Source: sell-side reports,[20] company filings, Capital IQ, Kerrisdale analysis

[19] See UCB 2017 Half-Year Results presentation, slide 25.
[20] JPMorgan, March 23, 2017 (using "embedded value"), and Jefferies, August 7, 2017.

However, Vimpat has a problem: patent protection. Its key US and European patents expire in 2022, and UCB has no clear strategy to extend the life of this franchise, which is why the market assigns a relatively low multiple to its $1.4B of projected peak revenue.

Enter Adamas. Its patent applications covering its high-dose, extended-release version of Vimpat could protect the franchise till 2036[21] – and, given Adamas's track record of success with its Gocovri and Namenda-related IP, there is no reason to doubt the patentability of its invention, which, as with Gocovri, hinges on using tailored pharmacokinetics to improve patient outcomes. Not only is Adamas's "Vimpat XR" (designed to be taken just once a day at night) more convenient than immediate-release Vimpat (taken twice a day); it also has the potential to be more tolerable and more effective.

Phase 1a and 1b trials in healthy volunteers have already strongly suggested that "Vimpat XR" is no more likely and usually less likely to induce known Vimpat side effects like dizziness, oral numbness, abnormal dreams, and euphoria,[22] despite the fact that it contains 50% more of the active ingredient. Normally, of course, higher doses lead to more severe side effects, but it appears that the pharmacokinetics engineered by Adamas – delivering a ~1.7-fold higher concentration of lacosamide in the plasma smoothly, without abrupt spikes – overcome this problem. Intriguingly, previous Vimpat clinical studies indicated that higher doses could give rise to greater seizure reduction, but, unfortunately, not enough patients were able or willing to take such doses. Adamas's "Vimpat XR" opens the possibility of accessing this untapped potential via fewer side effects and greater convenience.

In our view, the most natural outcome is for UCB to license or acquire Adamas's drug. UCB has the well regarded Vimpat brand name and strong commercial infrastructure, including an experienced sales force with existing relationships in the epilepsy space; Adamas has an improved drug backed by clinical data and soon, we believe, long-lasting patent protection. Partnership makes sense, and, as Adamas showed with its 2012 Namenda deal with Forest Laboratories, it has the wherewithal to make such partnerships work. The timing is also good: though it will take Adamas years to complete pivotal trials and obtain FDA approval, the likely timeline would enable "Vimpat XR" to hit the market around the same time that immediate-release Vimpat loses patent protection and faces generic competition. We believe Adamas's CEO and founder was alluding to the potential for a deal when he made the following remarks at the company's recent analyst day:

> With regard to the IP situation around Vimpat, I think as everybody knows, Vimpat is a product with UCB. It is protected. It has been navigating its various intellectual property challenges here in the U.S. It's protected until 2022. And I think with the development program we're going to be laying out here, it kind of dovetails in nicely and allows us to have multiple opportunities here, both for Richard [King, Adamas's COO] and the Adamas team to bring the product to the market, as well as the potential of other

[21] See Adamas 2017 10-K, p. 7.
[22] See Adamas Analyst/Investor Day, September 18, 2017, slides 89 and 90.

> partnerships around the world with the innovators. So it's a situation we're very familiar with, with how we've developed the company. And it's an exciting one at that.[23]

While Adamas always has the option to commercialize the drug on its own, a partnership would almost certainly yield better results for all involved.

If immediate-release Vimpat, with only five years of patent protection left, is worth $3 billion, how much could "Vimpat XR," with potentially 14 years of protection from launch through expiration, be worth? To be sure, competition with future generic versions of lacosamide will limit the upside, though, as already discussed in the case of Gocovri, perhaps not as much as one might expect. For example, Adderall, Shire's popular ADHD drug, faced generic competition beginning in February 2002. Shire launched Adderall XR, an extended-release version, in October 2001[24] – just a few months earlier, giving it little time to convince patients and doctors to switch before they also had the option of an immediate-release generic. Nonetheless, Adderall XR very rapidly won almost 50% of the Adderall market (including generic IR, branded IR, and branded XR).[25] By 2002 – only its first full year on the market – Adderall XR already generated as much annual revenue as its immediate-release predecessor ever did; at its peak, prior to seeing its own patents expire, XR revenue was *3.5 times as high* as immediate-release Adderall's peak. Indeed, even now, with multiple generic immediate-release *and* extended-release products on the market, Adderall XR still produces more revenue in nominal dollars that "regular" branded Adderall ever did. Arguably, "Vimpat XR" would have an even better sales pitch, since, based on our discussions with industry participants, neurologists and their patients tend to particularly favor reliable branded drugs out of well-founded[26] concern that small differences between generic and branded formulations, as well differences between various generic formulations that might be freely substituted for each other by pharmacists without warning, could provoke seizures.

Conservatively, however, we don't assume "Vimpat XR" will reach the heights of Adderall XR. Instead, we use Namenda XR as a template. In the face of competition from generic Namenda, revenue for Namenda XR and Namzaric (which is simply Namenda XR paired with another drug, which is off-patent) have fallen to approximately 35% of peak Namenda revenue. We assume that "Vimpat XR" achieves a similar fraction of peak Vimpat revenue after a 2.5-year-long launch ramp, then remains fixed till the end of 2035, whereupon in drops to zero. In keeping with Adamas's past experience and pharma-industry precedent, we then assume that Adamas earns a $100 million upfront payment from UCB and 20% royalties. (Overall, we estimate that this structure would still give UCB the lion's share – almost two thirds – of the total

[23] Source: Adamas Analyst/Investor Day, September 18, 2017 (transcript via Capital IQ).
[24] See e.g. Shire 2001 10-K, p. 19.
[25] See e.g. Morgan Stanley, "Attention Overload on ADHD, but Attention Deficit on HIV," October 24, 2003, p. 30, Exhibit 56. By 2002, XR had 46% Adderall prescription share.
[26] See e.g. Berg et al., "Generic substitution in the treatment of epilepsy: case evidence of breakthrough seizures" (10).

economics of the drug.[27]) Using a 10% discount rate, we find that the after-tax value to Adamas of such a transaction would be $290 million, or $11 per share – amounting to almost half of the company's current market value before even considering Gocovri.

Valuing "Vimpat XR": Model Summary
($mm unless otherwise noted)

	2018	2019	2020	2021	2022	2023	2024	2025		2035
Net sales	$ -	$ -	$ -	$ 14	$ 205	$ 406	$ 484	$ 484		$ 484
Royalty rate	20%	20%	20%	20%	20%	20%	20%	20%	…	20%
Royalty	-	-	-	3	41	81	97	97		97
NPV @ 10%	$ 451									
Upfront payment	100									
Future R&D costs	(100)									
Net gain, pre-tax	$ 451									
Tax rate	35%									
Net gain, after-tax	**$ 293**									
Per share	**$ 11**									
Note: overall drug value	$ 841									

Source: Kerrisdale analysis

For a Phase 3-ready asset with a fairly well-understood clinical profile, this standalone valuation is undemanding and leaves open the possibility that, if necessary, Adamas could eschew dealing with UCB and go it alone. Importantly, "Vimpat XR" should be a relatively easy drug to sell. Indeed, one pharmaceutical salesman we spoke to – someone well versed in selling branded extended-release drugs against generic competitors – was so excited after hearing our explanation of "Vimpat XR" that he wondered aloud if he should look to jump ship to Adamas.

VII. Valuation Summary

Combining all of Adamas's sources of value, including Gocovri for levodopa-induced dyskinesia, royalties on Namenda XR and Namzaric,[28] Gocovri for multiple sclerosis, and "Vimpat XR" (monetized via a royalty sale), we arrive at eye-popping price targets:

[27] Assuming an incremental net margin of ~40% on "Vimpat XR" revenue, we find that the overall value of the drug to be split between UCB and Adamas is almost ~$900mm, roughly 30% of Vimpat IR's estimated current value of $3B.

[28] Though we model these separately from the rest of Adamas's value, they have little effect on the overall conclusion. In brief, we make the following assumptions:

- Namenda XR revenue of $350mm in 2018, $200mm in 2019, and $25mm in 2020
- Namzaric revenue of $200mm in 2018, $250mm in 2019, and $300mm in 2020-2025 with generics entering in January 2026
- Royalty rate of 3% on Namenda XR revenue and 13% on Namzaric revenue

Adamas Pharmaceuticals: Kerrisdale Valuation

	Value			
	Total ($mm)	Per share	Prob.	Exp. value per share
Gocovri (Parkinson's)	$ 1,641	$ 65		
Namenda-related royalties	95	$ 4		
Baseline total	$ 1,735	**$ 69**	100%	$ 69
% upside		198%		
Gocovri (MS)	$ 1,578	$ 62	50%	$ 31
"Vimpat XR"	$ 293	$ 12	50%	$ 6
Grand total	$ 3,606	$ 143		**$ 106**
% upside		520%		359%

Source: Kerrisdale analysis
Note: "Gocovri (Parkinson's)" value includes the impact of existing cash and debt, as well as assumed R&D necessary to carry the MS indication through Phase 3.

Even neglecting the less certain value of Adamas's Phase 3-ready pipeline assets, Adamas is worth $69 per share – a multiple of its current ~$25 trading price. And, even if we haircut our valuations of those pipeline assets by 50% to account for the probability of failure, we still arrive at an overall fair value of over $100 per share. Said differently, one could view the current price as reflecting an 23% probability that our overall valuation is correct and an 77% chance that Adamas – despite owning a potential blockbuster drug with the only FDA approval in its indication, along with two Phase 3-ready pipeline assets boasting unusually low clinical and market risk – is worthless. We believe market skepticism has reached absurd levels, deeply undervaluing Adamas and presenting a highly attractive balance of risk and reward.

VIII. Conclusion

Adamas deserves to be a multi-billion-dollar company. With a strong lead drug on the verge of full commercialization, the company's longstanding "extremely practical" approach to the pharmaceutical business will soon be validated, as patients and doctors come to enjoy the benefits of its high-dose, extended-release drugs. It may not be flashy, but it works, both clinically and commercially – a fact that purist skeptics overlook at their peril.

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