EDISON

GW Pharmaceuticals

Company outlook

Leaving clinical risk behind

Pharma & biotech

Positive data from the two Phase III trials in Lennox-Gastaut syndrome (LGS) patients, coupled with the previously announced positive Dravet syndrome Phase III, seem to indicate that Epidiolex (cannabidiol or CBD) works across different seizure disorders. This increases our confidence in the Phase III programs for tuberous sclerosis complex (TSC) and infantile spasms (IS). A single NDA filing for both LGS and Dravet is expected mid-2017 with a launch in mid-2018.

Year end	Revenue ($m)	PTP* ($m)	EPADS* ($)	DPADS ($)	P/E (x)	Gross yield (%)
09/15	35.7	(69.7)	(2.64)	0.0	N/A	N/A
09/16	12.9	(106.1)	(3.32)	0.0	N/A	N/A
09/17e	12.6	(128.7)	(4.26)	0.0	N/A	N/A
09/18e	51.2	(100.4)	(3.30)	0.0	N/A	N/A

Note: *PTP and EPS are normalized, excluding amortization of acquired intangibles, exceptional items and share-based payments.

Consistent, highly statistically significant results

Across the three Phase III trials in Dravet and LGS, Epidiolex hit the primary endpoints by reducing seizures by 39%, 44% and 42% at the 20mg/kg dose (the second Phase III in LGS also tested a 10mg/kg dose, which reduced seizures by 37%) in a statistically significant fashion.

Limited regulatory risk

Given the consistent profile across Dravet and LGS, as well as the fact that the patients in these trials were mostly children who still had uncontrolled epilepsy, despite being on an average of three other anti-epileptic drugs, regulatory risk appears low. Based on FDA guidance, GW Pharmaceuticals (GW) plans to submit one NDA for both Dravet and LGS in mid-2017. We model a launch in mid-2018.

Treating unmet medical needs

Dravet and LGS are extremely malignant forms of pediatric epilepsy where the long-term prognosis for patients is very poor due to the deterioration of mental acuity. While these markets are relatively niche, a total of 20-30% of those treated for epilepsy are considered to be uncontrolled and hence will be candidates for Epidiolex therapy as the goal is to control seizures as much as possible.

Valuation: $136.08 per ADS

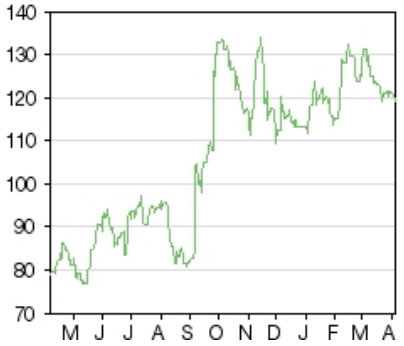
Our valuation is $3.43bn or $136.08 per ADS, up from $2.16bn or $98.84 per ADS previously, mainly after increasing the probability of success for LGS from 70% to 90% and for TSC from 60% to 80%, and including the infantile spasms (IS) indication, which we believe has a 60% chance of success. This was mitigated somewhat by our more conservative view of 2018 revenues due to the expected mid-year launch (its fiscal year-end is 30 September) and the capital raise in July, although we project that is the last one prior to profitability, which we expect in 2019. Also, we have removed GWP42004 for type 2 diabetes, Sativex for cerebral palsy and GWP42003 for schizophrenia from our model.

5 April 2017

Price	**US$119.00**
Market cap	**US$2999m**

Net cash ($m) at 31 December 2016	444.6
ADSs in issue	25.2m
ADS code	GWPH
ADS exchange	NASDAQ
Depository	Citibank

Share price performance



%	1m	3m	12m
Abs	(9.4)	1.8	61.6
Rel (local)	(8.5)	(2.0)	41.5

52-week high/low	US$134.0	US$74.4

Business description

GW Pharmaceuticals is a UK-based specialty pharma company focused on cannabinoids. Sativex is marketed in various European countries for multiple sclerosis spasticity. The lead pipeline candidate is Epidiolex for refractory childhood epilepsy, now undergoing Phase III studies with an FDA submission expected mid-2017.

Next events

AAN data presentation	April 2017
NDA filing	Mid-2017

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Edison profile page

Investment summary

Company description: Cannabinoid medicines specialist

Founded in 1998, GW Pharmaceuticals is a UK-based biopharmaceutical company that discovers, develops and commercializes proprietary cannabinoid (cannabis-derived) medicines for a broad range of diseases. GW's cannabinoid platform generated the world's first plant-derived cannabinoid therapeutic, Sativex, for the treatment of spasticity due to multiple sclerosis (MS), sold by multiple global partners. GW is also developing a broad pipeline of cannabinoid medicines targeting primarily central nervous system (CNS) disorders including epilepsy, autism and neonatal hypoxic-ischemic encephalopathy (NHIE). The company is expected to file for FDA approval in Dravet and LGS, particularly severe forms of epilepsy. GW listed on AIM in 2001 (though it de-listed in 2016) and on the Nasdaq exchange in 2013.

Valuation: $3.43bn or $136.08 per ADS

Our valuation is now $3.43bn or $136.08 per ADS, up from $2.16bn or $98.84 per ADS previously. The difference is mainly due to increasing the probability of success for LGS from 70% to 90% and for TSC from 60% to 80%, including the infantile spasms (IS) indication, which we believe has a 60% chance of success, and increasing the probability of success in glioma from 30% to 40%. This was mitigated somewhat by our more conservative view of 2018 due to the expectation for a mid-year launch (any delays in reimbursement or even in doctors seeing patients can have a magnified impact on revenues for the year as its fiscal year end is 30 September). It was also mitigated by the $289.8m capital raise in July, though we project that is the last one prior to profitability, which we expect in 2019. In addition, we have removed GWP42004 for type 2 diabetes, GWP42003 in schizophrenia and Sativex for cerebral palsy from our model due to negative data in diabetes, the company's announcement that it has no plans to further develop in schizophrenia at this time and negative data in cerebral palsy. It is important to note that Epidiolex also holds wider potential in other refractory forms of childhood epilepsy, which we do not currently capture in our model.

Sensitivities: Clinical, regulatory and commercial

GW Pharma is subject to the sensitivities common to most biopharmaceutical companies, such as potential clinical or regulatory failure or delay, commercialization risks (launch, uptake, pricing, reimbursement, competition) and reliance on partners. With investor focus on Epidiolex in Dravet syndrome and LGS, any regulatory hiccups in relation to these indications could have a significant impact on the valuation of the company. Also, with an increasingly price-sensitive reimbursement environment, there could be downside to net realized price expectations.

Financials: Fully funded to execute clinical/commercial plans

GW finished Q117 with $444.6m in cash, thanks to raising an additional $289.8m in cash in an equity offering last year. It has also completed delisting from AIM. As most of the investor base traded the NASDAQ listing, this has not had any significant negative impact on the share price and liquidity. Based on our estimates (which include $250m in total cash burn in 2017 and 2018 prior to profitability in 2019), GW has enough cash to achieve its goals without additional capital.

Focusing on intransigent CNS diseases

GW has developed a broad pipeline, which is focused on areas of continued unmet medical need despite a number of approved therapies. Epilepsy patients have quite a number of choices for treatment, but 36% have pharmacoresistant epilepsy[1] that cannot be controlled by even three or more drugs taken concurrently. GW is focused on some of the most difficult-to-treat subpopulations in Dravet and LGS. It has recently expanded this to tuberous sclerosis complex (TSC), another subtype of epilepsy, and is expanding to other CNS areas such as schizophrenia, where it recently had proof-of-concept data, and NHIE, a severe issue for newborns that often leads to disease or lifelong brain damage.

Exhibit 1: GW Pharmaceuticals' pipeline and expected newsflow

Product	Indication	Cannabinoids (ratio)	Stage	Status and next steps
Epilepsy				
Epidiolex (GWP42003-P)	Dravet syndrome	CBD	Phase III	First Phase III trial (n=120) positive with a 39% seizure reduction and p=0.0123. Second Phase III trial (n=186) ongoing. NDA mid-2017. EU pre-submission meeting H117, application H217.
Epidiolex (GWP42003-P)	Lennox-Gastaut syndrome	CBD	Phase III	2x Phase III studies (n=171 + n=225) with 44% and 42% seizure reductions. P-value 0.0135 and 0.0047, respectively. NDA mid-2017. EU pre-submission meeting H117, application H217.
Epidiolex (GWP42003-P)	Tuberous sclerosis complex	CBD	Phase III	Phase III study (n=210) ongoing.
Epidiolex (GWP42003-P)	Infantile spasms	CBD	Phase III	Commenced first part of two-part Phase III trial. Expected to recruit 10 patients in first part by mid-2017. Pending review by independent safety review panel, second part would commence.
Epidiolex	Childhood epilepsy syndromes (DS + LGS + others)			Expanded access, physician-led, IND treatment program. >1,100 patients total in program to date. As of 1 January 2017, around 650 patients were receiving treatment under expanded access INDs in the US.
GWP42006	Adult epilepsy	CBDV	Phase II	Part A (n=32) focusing on dose-ranging pharmacokinetic and safety data completed, in adults with inadequately controlled focal seizures; recruiting Part B (n=130), the efficacy segment, with data in H217.
Other orphan diseases				
GWP42002/ GWP42003	Refractory glioma	THC/CBD (1:1)	Phase II	Phase II trial (n=21) data reported in combination with dose-intense temozolomide. 83% one-year survival compared to 53% in control (p=0.042). Exploring next steps.
GWP42003 (IV)	Neonatal hypoxic ischemic encephalopathy (NHIE)	CBD	Preclinical	Phase I commenced with data expected in 2017.
Non-orphan diseases				
GWP42006	Autism spectrum disorders	CBDV	Phase II	Physician led open-label studies expected to commence H117. Phase II placebo-controlled trials to commence H217.
GWP42003	Schizophrenia	CBD	Phase IIa	Proof-of-concept data interesting but company is not advancing at this point due to other priorities.

Source: GW Pharmaceuticals, Edison Investment Research. Note: THC = tetrahydrocannabinol; CBD = cannabidiol; THCV = tetrahydrocannabivarin; CBDV = cannabidivarin.

Epidiolex demonstrates efficacy across epilepsy

Epidiolex has now demonstrated efficacy in statistically significant Phase III trial results in a heavily pretreated refractory population suffering from Dravet and LGS (see Exhibit 2) with data recently presented at the American Epilepsy Society Annual Meeting (2-6 December in Houston, TX). In addition, an expanded access program has allowed for the treatment of hundreds of patients across the epileptic spectrum (including TSC and IS, areas where GW is in or about to get into Phase III).

[1] Kwan P, Brodie MJ. N Engl J Med. 2000; 342:314-319.

Exhibit 2: Epidiolex trial data in Dravet and LGS

Indication	Doses tested	Number of patients	Average age	Average number of AEDs currently prescribed	Number of previously tried AEDs	Median baseline seizure frequency	Epidiolex seizure reduction	Placebo seizure reduction	p-value	Dropouts due to AEs
Dravet	20mg/kg	120	10	3	4	13 convulsive seizures	-39% (20mg/kg)	-13%	0.0123	13%
LGS Trial 1	20mg/kg	171	15	3	6	74 drop seizures	-44% (20mg/kg)	-22%	0.0135	14%
LGS Trial 2	20mg/kg and 10mg/kg	225	16	3	7	85 drop seizures	-42% (20mg/kg), -37% (10mg/kg)	-17%	0.0047 (20mg/kg), 0.0016 (10mg/kg)	8% (20mg/kg), 1% (10mg/kg)

Source: GW Pharmaceuticals

The nightmares of Dravet and LGS

Dravet syndrome is an extremely malignant form of childhood epilepsy that typically presents itself within the first year of life with prolonged febrile and afebrile, generalized clonic or hemiclonic epileptic seizures in otherwise normally developing children. The incidence of Dravet ranges from 1:20,000 to 1:40,000 births, which suggests an overall disease prevalence of 5,500 patients in the US and 6,700 European patients.[2] The primary genetic cause is a mutation of the SCN1A gene, which, while helping to increase the rate of diagnosis, has not done much for the outcomes of these patients. 10-14% of Dravet patients end up dying, typically around the age of six or seven.[3]

Besides the risk of death, by the time the children are teenagers they exhibit either severe or profound learning disabilities. In one study of 31 typical and borderline Dravet patients (14 were typical Dravet, 17 were borderline) who were followed until adulthood, 22.6% could speak no words at all, 29% could speak several words, 29% could make primitive conversation and 16.1% could make simple conversation and read to some extent. Only one (3.2%) with borderline Dravet could lead an independent life, although he developed psychosis.[4]

LGS, like Dravet, is another rare form of epilepsy, although it typically starts later in life, at between two and eight years of age vs six months for Dravet. As with Dravet, outcomes are extremely poor for these patients, with 90% becoming mentally handicapped with a progressive reduction in IQ. The mortality rate is high, although the exact percentage varies based on the study and ranges between 3% and 25%.[5] Incidence estimates for LGS vary, but it accounts for approximately 2-5% of all childhood epilepsies. This suggests 16,000 pediatric patients with LGS in the US and 24,000 in Europe with prevalence potentially doubling if including adult LGS patients according to the LGS foundation.

As patients and physicians are comfortable using a combination of drugs to treat these disorders, we would expect the addition of Epidiolex, with its novel mechanism of action, to be widely adopted especially as 78-89% of patients who experience adverse events view them to be mild to moderate. In our model we assume 50% penetration in the US and 25% penetration in the EU in both Dravet and LGS, with peak sales of $200m and $600m, respectively.

Risks to approval

Three issues, however, seem to be concerning to investors: drug-drug interactions, potential liver toxicity and the EMA approval of Dravet.

2 Brunklaus A et al. Brain 2012: 135; 2329–2336.

3 Sakauchi et al. 2011 Epilepsia, 52(6): 1144–1149.

4 Akiyama M et al. 2010, Epilepsia, 51(6): 1043–1052.

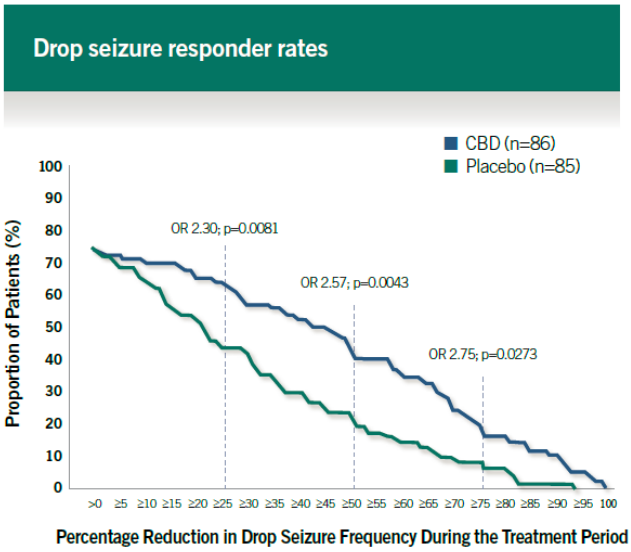
5 Rijckevorsel, K. Neuropsychiatric Disease and Treatment 2008:4(6) 1001–1019.

Evidence of a drug-drug interaction with clobazam has repeatedly occurred but, based on our discussion with Elaine Wirrell, MD, a pediatric neurologist at the Mayo Clinic in Rochester, MN, worries are overblown. If Epidiolex use does increase the blood levels of clobazam, it is easy to reduce the level of clobazam without negatively affecting efficacy. Also, according to data from the expanded access program presented at the 2015 American Epilepsy Society Annual Meeting, Epidiolex responder rates were approximately the same as those on clobazam (53%) as for those not on clobazam (54%) hence concerns that Epidiolex efficacy is only being seen due to a more efficacious clobazam seem unfounded.

Another worry is the potential for liver toxicity. Poster presentations at the 2016 American Epilepsy Society Annual Meeting showed that 20% of patients in the Epidiolex arm in the Dravet trial had elevated liver enzymes (ALT or AST at >3x the upper limit of normal) compared to 2% in the placebo arm. Also, in the first LGS trial, 23% of patients in the Epidiolex arm had elevated liver enzymes compared to 1% in the placebo arm. However, it is important to note that 87.5% of these patients were also on valproic acid, which is commonly hepatotoxic and has been associated with at least 100 fatal cases due to acute or chronic liver injury, according to the US Library of Medicine LiverTox database. Also, a number of other anti-epileptic drugs (AEDs) have known hepatotoxicities, namely felbamate, lamotrigine, topiramate, carbamazepine and phenytoin, so even where valproic acid is not involved the signal could be coming from one of the other AEDs the patients are on. Finally, all the liver enzyme elevations resolved whether or not the patient withdrew from the trial and none of those with elevated enzymes had concurrent elevated bilirubin at >2x the upper limit of normal, which would have indicated drug-induced liver injury. This is an important fact given the FDA guidance documents regarding drug-induced liver injury (DILI):
“In general, the type of liver injury that leads to severe DILI is a predominantly hepatocellular injury. Hepatocellular injury is indicated by rises in AT activities in serum reflecting release of alanine or aspartate aminotransferase (ALT or AST) from injured liver cells. The ability to cause some hepatocellular injury, however, is not a reliable predictor of a drug’s potential for severe DILI. Many drugs that cause transient rises in serum AT activity do not cause progressive or severe DILI, even if drug administration is continued. It is only those drugs that can cause hepatocellular injury extensive enough to reduce the liver’s functional ability to clear bilirubin from the plasma or to synthesize prothrombin and other coagulation factors that cause severe DILI. It is important to identify those drugs as early as possible.”

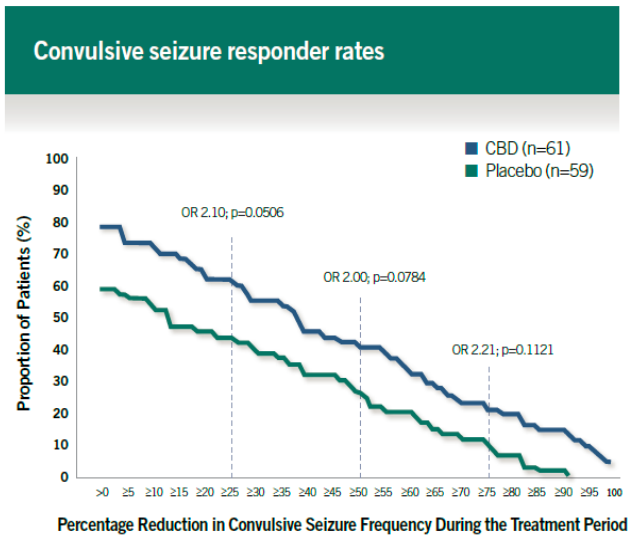
The third concern relates to approval in the EU as the EMA has historically preferred the metric of the proportion of patients who have experienced a greater than or equal to 50% reduction in seizures. While this metric in the first LGS trial hit statistical significance with a p-value of 0.0043 (see Exhibit 3), it was missed in the Dravet trial with a p-value of 0.0784 (see Exhibit 4).

Exhibit 3: Responder rates in the first LGS trial



Source: GW Pharma

Exhibit 4: Responder rates in the Dravet trial



Source: GW Pharma

It is unclear whether the EMA will demand a statistically significant benefit in responder rates in Dravet patients for approval given the data showing a statistically significant reduction in seizures and secondary endpoints such as improvement in caregiver global impression of change (p=0.0155 in the Dravet trial). However, given this is a pediatric population that is heavily pretreated and refractory to current medication, regulatory authorities should be more likely to be flexible than in another patient population. Also, a second Dravet study that could provide supportive data is enrolling, with a data readout likely in 2017. In a worst-case scenario, eliminating the EU Dravet opportunity entirely would only reduce our peak sales estimate for Dravet by $46m (24%), with our total valuation declining by around 3%. In contrast, the market opportunity for LGS in the EU is much larger, with $163m in peak sales and, as mentioned, is where Epidiolex hit statistical significance in the responder analysis.

Based on FDA guidance, GW plans to submit one NDA for both Dravet and LGS around mid-2017 using data from a total of 1,500 patients, including 400 who have been on the drug for a year or more. The company expects an FDA pre-approval inspection of its manufacturing facility in H217 and to have a year's worth of active pharmaceutical ingredient (API) on hand by launch. We model US launch to occur in mid-2018 allowing for the FDA review as well as DEA rescheduling (which by law should take no more than 90 days). EMA submission is expected in H217, although it is unclear whether there will be separate submissions for LGS and Dravet and for which precise data will be required.

Given the consistent profile of Epidiolex across Dravet and LGS, as well as the fact that the patients in these trials were mostly children who still had uncontrolled epilepsy despite being on an average of three other AEDs, regulatory risk appears generally low.

The opportunity beyond the original label

Beyond Dravet and LGS, GW has a lot of opportunity for both label expansion and use off-label in the broad uncontrolled epilepsy market. It is estimated that 20-30%[6] of those treated for epilepsy are considered to be uncontrolled, with seizure free rates plummeting dramatically after failing the first drug. As the US pediatric epilepsy population alone is over 466,000 patients,[7] the uncontrolled

[6] French J et al., Neurology 2004;62;1261-1273.

[7] Russ et al., Pediatrics Volume 129, Number 2, February 2012.

pediatric population is between 93,000 to 140,000 in total, approximately four times greater than the Dravet and LGS opportunities combined.

There are two ways for Epidiolex to address this population: one is through label expansion into the different treatment-resistant epilepsies; and the other is through physician prescription of Epidiolex off-label, which we do not include in our model but could be significant. Note that all the different epilepsies are typically managed by pediatric neurologists, so GW's planned salesforce of 50-55 would not have to call upon a different type of physician to reach these other sub-types of epilepsy.

On the label expansion front, GW previously announced that it initiated a 210-patient Phase III in TSC with data expected in H217. TSC is a multisystem, autosomal dominant genetic disorder resulting from a mutation in one of two tumor suppressor genes, TSC1 (encoding hamartin) or TSC2 (tuberin). TSC is characterized by benign tumors, known as hamartomas, in various organs, most commonly the skin, brain, kidneys, heart and lungs. A hamartoma is composed of an overgrowth of mature cells and tissues, which normally occurs in the affected tissue. TSC affects both sexes and all ethnic groups, affecting as many as 25,000-40,000 individuals in the US and about one to two million individuals worldwide, with an estimated prevalence of one in 6,000 newborns (tuberous sclerosis fact sheet).

The signs and symptoms of TSC vary depending on the organs involved. The most common symptom is epilepsy, which occurs in around 80-90% of patients and is a significant cause of morbidity and mortality.[8] Seizures of all types may occur, the most common being infantile spasms, partial motor seizures and generalized tonic-clonic seizures. Seizure onset occurs in the first year of life in almost two-thirds of patients, and within the first three years in around 80% of patients.[9] The seizures are often severe, and up to two-thirds of TSC patients are refractory to available medical and surgical therapies.[2] Developmental delays occur in around 50-60% of TSC patients, ranging from mild learning difficulties to severe mental retardation, and about one-third of children with TSC meet the criteria for autism spectrum disorder, behavioral problems are common and can be difficult to manage. The prevalence of cognitive impairment and neuropsychiatric and developmental disorders has also been found to be higher in those with refractory epilepsy.

Under an expanded access IND from the FDA, Epidiolex has been made available in licensed clinics as an adjunct treatment in children and young adults with drug-resistant epilepsy. GW presented updated data on the trial at the American Epilepsy Society's annual meeting, showing encouraging outcomes in 10 TSC patients treated with Epidiolex under this program. Four of these TSC patients also had cognitive impairment. Six of the patients responded to adjunctive treatment with Epidiolex, with response defined as a 50% decrease in seizure frequency at 16 weeks of treatment compared to a four-week baseline period.

Importantly, patient 9 – who suffered from five separate seizure types, was on three concomitant anti-epilepsy drugs and had been on a total of seven in the past – became seizure free after two months of treatment and has remained seizure free for 10 months. Diarrhea was the only side effect attributed directly to CBD. Drowsiness and irritability were due to drug-drug interactions in five patients, which were alleviated with antiepileptic drug dose adjustments while maintaining seizure control.

Once data are available for a larger number of TSC patients, we will see whether the seizure response and cognitive and behavioral effects are repeated. If the results suggest wider cognitive/behavioral benefits, this could provide the basis for an expanded use of Epidiolex beyond epilepsy.

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[8] Krueger DA, et al. Everolimus Treatment of Refractory Epilepsy in Tuberous Sclerosis Complex. Ann Neurol. 74:679-687 (2013).

[9] Chu-Shore CJ, et al. The natural history of epilepsy in tuberous sclerosis complex. Epilepsia 51(7):1236-1241 (2010).

GW also commenced a Phase III in IS in December of 2016. IS, also known as West syndrome, is a potentially catastrophic form of epilepsy of early infancy that affects between 2,000 and 4,000 infants a year. IS presents between the ages of three and seven months, with 90% presenting within the first year of life. While the initial seizures/spasms typically resolve, 94% develop active epilepsy by age 10 with around 50% progressing to LGS. 80% of 10-year-olds with IS have some degree of mental retardation.[10]

Current treatments for IS are effective but can be associated with severe adverse events, especially in cases of long-term use. H.P. Acthar Gel (adrenocorticotropic hormone) had an 86.7% response rate (defined as complete suppression of spasms and hypsarrhythmia) in 15 patients in a two-week, randomized trial. However, it is associated with severe infections due to immunosuppression, hypertension, Cushing syndrome and metabolic abnormalities. Sabril (vigabatrin) was shown to have between a 7-16% spasm free rate in one study in 221 patients and an overall reduction in spasms of 68.9% in a post-hoc analysis of a 40-patient second study. Unfortunately, there is a black box warning of permanent vision loss associated with treatment, which can occur within weeks of initiation or sooner, or may even show up years after treatment has ended.

In the expanded access program, nine patients with refractory epileptic spasms were given Epidiolex. The age range was two to 16 years (hence, well after initial onset) and patients were already on multiple AEDs. Epidiolex reduced seizure frequency by 67% on average after two weeks with 33% achieving spasm freedom. The only side effect directly associated with Epidiolex in these patients was diarrhea though other adverse events such as somnolence, fatigue and decreased appetite are associated with therapy.

For TSC we estimate 50% penetration in the US and 25% penetration in the EU with peak sales of $250m. IS is a relatively small market. We are assuming 40% penetration in the US and 25% in the EU with peak sales of $50m in that indication.

Development in Glioma

GW recently reported positive proof-of-concept data of their proprietary THC/CBD combination in 21 patients with recurrent glioblastoma multiforme (GBM), a type of glioma (a tumor arising from glial cells). Glioblastoma is the most aggressive malignant primary brain tumor in adults, with an annual incidence of 3-5 per 100,000 (~10,000-15,000 new cases every year), with a median overall survival ranging between 10-15 months.[11]

Patients either received treatment or placebo in combination with dose-intense temozolomide, the standard first-line treatment for GBM. Patients in the treatment arm had an 83% one-year survival rate and a median survival of greater than 550 days compared to a 53% one-year survival rate in control and median survival of 369 days in the control arm. While small, the trial provides a signal for the use of cannabinoids in both glioma and oncology. The company is expected to provide an update on both efforts in the coming months.

NHIE: An unmet medical need among neonates

NHIE is a condition that results from an interruption of blood flow and oxygen delivery to the brain due to a variety of reasons including placental insufficiency, cord compression or fetal hemorrhage (see Exhibit 5). According to Medscape, incidence is currently estimated at 2.5 per 1,000 live births; so as there are four million live births per year in the US, according to the CDC, there are around 10,000 cases of NHIE per year. Without treatment, 23-27% with moderate to severe NHIE die before leaving the hospital, with the overall death rate at 30-38% at the 18- to 22-month time

[10] Pellock J, et al., Epilepsia, 51(10):2175-2189, 2010.

11 Seller M et al., Neuro-Oncology 15(1):4–27, 2013.

point.[12,13] Those who survive often have cerebral palsy (36%), epilepsy (16%), hearing (10%) and visual impairment (13%).[14]

Exhibit 5: Causes of NHIE

Maternal	Uteroplacental	Fetal
Cardiac arrest	Placental abruption	Fetomaternal hemorrhage
Asphyxiation	Cord prolapse	Twin to twin transfusion
Severe anaphylaxis	Uterine rupture	Severe isoimmune hemolytic disease
Status epilepticus	Hyperstimulation with oxytocic agents	Cardiac arrhythmia
Hypovolemic shock		

Source: University of Chicago Medical Center

GW Pharma is developing an iv formulation of GWP42003, where CBD is the primary cannabinoid but also contains other cannabinoid and non-cannabinoid components, for use in neonates. There are no clinical data yet, as the formulation is still in Phase I. The preclinical data seen so far have been quite remarkable, with brain activity and necrotic cell counts close to normal in newborn piglets.[15] CBD appears to be anti-inflammatory and modulates cerebral hemodynamic impairment and brain metabolic derangement, while also preventing the appearance of brain edema and seizures.

There are high costs associated with these infants, so if GW can demonstrate a large enough benefit it would be able to receive a premium price for its product. For the purposes of our valuation, we are currently assuming a price of $50,000 per treatment (which will last at least 72 hours and may last as long as a week) and a ~40% peak penetration, which results in ~$450m in worldwide peak sales.

Sativex: On the market for MS spasticity in 28 countries

Sativex is an oromucosal spray consisting of a formulated extract of the cannabis sativa plant, which contains the principal cannabinoids delta-9-tetrahydrocannabinol (THC) and CBD. Multiple sclerosis (MS) affects approximately 1.3 million people worldwide, of whom up to 80% suffer from spasticity, a symptom of MS characterized by muscle stiffness and uncontrollable spasms. There is no cure for spasticity and Sativex provides an alternative for patients who fail to respond to conventional oral therapies (Baclofen/Zanaflex).

Sativex is approved as a treatment for MS spasticity in 28 countries (outside the US). The product is licensed to a number of partners across global territories, including Almirall (EU ex-UK/Mexico), Otsuka (US), Bayer (UK/Canada), Novartis (Australia/New Zealand/Asia/Middle East/Africa) and Ipsen (Latin America ex-Mexico). GW receives upfront fees, milestones and royalties from these collaborations. Sativex revenue totaled $1.8m in Q117, up 31% year-over-year. While it is a small product providing minimal value to GW currently, it did serve as proof of concept for cannabinoids as a medicinal product.

Valuation

Our valuation is now $3.43bn or $136.08 per ADS, up from $2.16bn or $98.84 per ADS previously. This is mainly due to increasing the probability of success for LGS from 70% to 90% and for TSC from 60% to 80%, including the infantile spasms (IS) indication, which we believe has a 60% chance of success, and increasing the probability of success in glioma from 30% to 40%. This was mitigated somewhat by our more conservative view of 2018 due to the expectation for a mid-year

12 Gluckman et al., Lancet 2005; 365, 663-670.
13 Shankaran et al., Pediatrics, 2008; 122(4):e791-8.
14 Azzopardi et al., NEJM 2014;371:140-149.
15 Lafuente et al., 2011, Pediatric Research 70:272-277.

launch (any delays in reimbursement or even in doctors seeing patients can have a magnified impact on revenues for the year as its fiscal year end is 30 September). It was also mitigated by the by GW's $289.8m capital raise in July, though we project that is the last one prior to profitability, which we project in 2019. In addition, we have removed GWP42004 for type 2 diabetes, GWP42003 in schizophrenia and Sativex for cerebral palsy from our model due to negative data in diabetes, the company's announcement that it has no plans to further develop in schizophrenia at this time and negative data in cerebral palsy.

Upside to our estimates exist as we currently do not model Epidiolex revenues outside of Dravet, LGS, TSC and IS, nor do we model revenues for adult epileptic patients. In addition, a potential acquirer would value GW more highly than we would as an independent company, as there would likely be synergies in any acquisition.

Outside of Epidiolex, the GWP42006 (Cannabidivarin, CBDV) Phase II trial in adults continues to enroll patients, with data expected in mid-2017. CBDV is also being investigated in autism spectrum disorders, with Phase II trials expected to start in H217. A Phase I of iv GWP42003 in neonatal hypoxic-ischemic encephalopathy (NHIE) started in October.

Exhibit 6: GW pipeline valuation assumptions

Product	Indication	Status	Probability of success (%)	Launch year (CY)	Peak sales ($m)	Peak market share (%)
Epidiolex	Dravet syndrome	Phase III	90%	2018	195	50%
Epidiolex	Lennox-Gastaut	Phase III	90%	2018	601	50%
Epidiolex	TSC	Phase III	80%	2018	255	50%
Epidiolex	IS	Phase III	60%	2019	45	40%
IV GWP42003	NHIE	Phase I	10%	2021	448	40%
GWP42002:GWP42003	Recurrent GBM	Phase Ib/IIa	40%	2020	246	30%
GWP42006 (CBDV)	Adult epilepsy	Phase IIa	25%	2023	677	10%

Source: Edison Investment Research

Financials

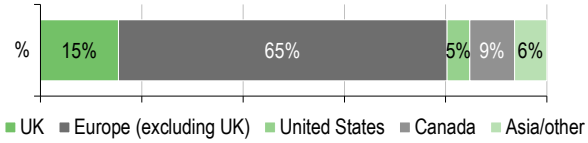
GW finished Q117 with $444.6m in cash, thanks to raising an additional $289.8m in cash in an equity offering last year. It has also completed delisting from AIM. As most of the investor base traded the NASDAQ listing, this has not had any significant negative impact on the share price and liquidity. Based on our estimates (which include $250m in total cash burn in 2017 and 2018 prior to profitability in 2019), GW has enough cash to achieve its goals without additional capital.

Exhibit 7: Financial summary

$000s	2015	2016	2017e	2018e
Year end 30 September	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	35,675	12,894	12,620	51,216
Cost of sales	(3,273)	(3,399)	(5,038)	(5,002)
Gross profit	32,403	9,495	7,583	46,214
EBITDA	(68,212)	(104,901)	(128,158)	(99,442)
Operating profit (before goodwill and except.)	(69,959)	(106,649)	(129,905)	(101,190)
Intangible amortization	0	0	0	0
Exceptionals	0	0	0	0
Share-based payment	(1,578)	(1,610)	(1,642)	(1,675)
Operating profit	(71,538)	(108,259)	(131,547)	(102,865)
Net Interest	211	544	1,170	818
Profit before tax (norm)	(69,748)	(106,105)	(128,735)	(100,372)
Profit before tax (as reported)	(71,326)	(107,715)	(130,377)	(102,047)
Tax	15,623	28,144	19,436	12,246
Profit after tax (as reported)	(55,704)	(79,571)	(110,942)	(89,801)
Average number of ADS outstanding (m)	20.5	23.5	25.7	26.7
Earnings per ADS - normalized ($)	(2.64)	(3.32)	(4.26)	(3.30)
Earnings per ADS - basic ($)	(2.71)	(3.39)	(4.32)	(3.36)
Earnings per ADS - diluted ($)	(2.63)	(3.30)	(4.22)	(3.29)
Dividend per ADS ($)	0.0	0.0	0.0	0.0
BALANCE SHEET				
Fixed assets	43,258	60,824	90,326	110,454
Intangible assets	6,819	7,299	7,299	7,299
Tangible assets	35,916	48,684	78,186	98,314
Deferred tax asset	523	4,841	4,841	4,841
Current assets	318,928	505,648	367,437	259,875
Stocks	5,945	5,310	7,221	7,643
Debtors	3,591	5,695	6,549	7,532
Cash	293,590	467,990	327,014	218,048
Other	15,801	26,653	26,653	26,653
Current liabilities	(34,710)	(43,688)	(45,368)	(47,183)
Creditors	(30,624)	(40,330)	(42,347)	(44,464)
Short-term borrowings	0	0	0	0
Deferred revenue & advance payments	(4,086)	(3,358)	(3,022)	(2,720)
Long-term liabilities	(20,888)	(24,671)	(21,305)	(18,411)
Long-term borrowings	0	0	0	0
Deferred revenue	(8,406)	(6,694)	(6,024)	(5,422)
Other long-term liabilities	(12,481)	(17,978)	(15,281)	(12,989)
Net assets	306,588	498,113	391,090	304,735
CASH FLOW				
Operating cash flow	(64,858)	(93,738)	(130,331)	(100,155)
Net interest	203	544	1,170	818
Tax	6,431	(12,646)	19,436	12,246
Capex	(22,394)	(10,848)	(31,250)	(21,875)
Expenditure on intangibles	(143)	0	0	0
Acquisitions/disposals	3	0	0	0
Financing	168,734	291,088	0	0
Dividends	0	0	0	0
Net cash flow	87,976	174,400	(140,976)	(108,966)
Opening net debt/(cash)	(205,614)	(293,590)	(467,990)	(327,014)
HP finance leases initiated	0	0	0	0
Other	0	0	0	0
Closing net debt/(cash)	(293,590)	(467,990)	(327,014)	(218,048)

Source: GW Pharma accounts, Edison Investment Research

EDISON

Contact details	Revenue by geography
1 Cavendish Place London W1G 0QF United Kingdom +44 (0)20 7291 0555 www.gwpharma.com	

Management team

Chairman: Dr Geoffrey Guy

Dr Guy was a founder of GW and has served as chairman since 1998. He has over 30 years' experience in medical research and drug development. He founded Ethical Holdings (now Amarin) in 1985 and Phytopharm in 1989. He holds a BSc in pharmacology (University of London), a medical degree (MBBS) from St Bartholomew's Hospital and a diploma in pharmaceutical medicine (Royal College of Physicians).

CEO: Justin Gover

Mr Gover has been CEO since 1999. He has over 17 years' experience in the pharmaceutical industry. As CEO, he is responsible for directing operations and leads equity financings and business development activities. Before GW, he was head of corporate affairs at Ethical Holdings (1995-97), where he was responsible for strategic corporate activities. He holds an MBA from INSEAD and a BSc (hons) from Bristol University.

R&D director: Dr Stephen Wright

Dr Wright has been R&D director since 2004. He has over 20 years' experience in drug development. Before GW, he was SVP of clinical research and development at Ipsen. He has direct US drug development experience, first as medical director of Immunosciences, then as venture head of neuroscience at Abbott. He is a fellow of the Royal College of Physicians and Faculty of Pharmaceutical Medicine and visiting professor at the University of Reading. He holds an MD and MA (University of Cambridge) and a medical degree (MBBS) from the Royal London Hospital.

CFO: Scott Giacobello

Mr Giacobello was announced as CFO in March 2017. He has 25 years of finance and operational experience. Previously, he served as CFO for Chase Pharmaceuticals, a biopharmaceutical company focused on the development and commercialization of improved treatments for neurodegenerative disorders until its acquisition by Allergan. From 2008 through 2015, he held senior level finance positions at Allergan, most recently serving as Vice President of Finance for Global Research & Development. Mr Giacobello holds a bachelor's degree in business administration from the University of Notre Dame and is a Certified Public Accountant.

Principal shareholders	(%)
Capital Research and Management Company	11.99%
Scopia Capital Management	8.28%
Prudential PLC	8.14%
FMR, LLC	6.81%
Deerfield	3.69%
Viking Global Investors	3.62%
Bank of America	2.61%
Janus Capital	2.59%

Companies named in this report

Almirall (ALM.MC), Otsuka (3570.TO), Bayer (BAYN.DE), Novartis (NVS) and Ipsen (IPN.FP)

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