## **GW Pharmaceuticals plc**

**Investor Presentation**July 2015



### **Disclaimers**



#### FORWARD-LOOKING STATEMENTS

This presentation contains forward-looking statements that are based on our management's beliefs and assumptions and on information currently available to management. Forward-looking statements include information about our current expectations for future events, including potential results of operations, the timing of clinical trials, demand for our commercially available products and products in development and the clinical benefits, safety profile and commercial potential of Sativex® and Epidiolex®. These forward-looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors that could cause our actual results, performance or achievements to be materially different than any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements represent our management's beliefs and assumptions only as of the date of this presentation. You should read our most recent Annual Report, as filed on Form 20-F with the Securities and Exchange Commission, including the Risk Factors set forth therein and the exhibits thereto, completely and with the understanding that our actual future results may be materially different from what we expect. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

#### **EXPANDED ACCESS STUDIES**

Expanded access studies are uncontrolled, carried out by individual investigators independent from us, and not typically conducted in strict compliance with Good Clinical Practices, all of which can lead to a treatment effect which may differ from that in placebo-controlled trials. Data from these studies provide only anecdotal evidence of efficacy for regulatory review, contain no control or comparator group for reference and are not designed to be aggregated or reported as study results. Moreover, data from such small numbers of patients may be highly variable. Information obtained from these studies, including the statistical principles that the independent investigators have chosen to apply to the data, may not reliably predict data collected via systematic evaluation of efficacy in company-sponsored clinical trials or evaluated via other statistical principles that may be applied in those trials. Reliance on such information may lead to Phase 2 and 3 clinical trials that are not adequately designed to demonstrate efficacy and could delay or prevent our ability to seek approval of Epidiolex. Expanded access programs may provide supportive safety information for regulatory review. Physicians conducting these studies may use Epidiolex in a manner inconsistent with the protocol, including in children with conditions different from those being studied in our own sponsored trials. Any adverse events or reactions experienced by subjects in the expanded access program may be attributed to Epidiolex and may limit our ability to obtain regulatory approval with labeling that we consider desirable, or at all.

### **GW Pharma Overview**

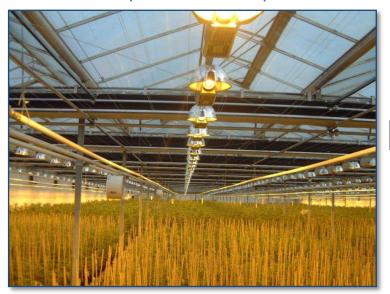


- World leading position in development of plant-derived cannabinoid therapeutics
  - Proprietary cannabinoid product platform targeting broad range of disease areas
  - Commercialized product, Sativex®, approved in 27 countries (ex-U.S.) for MS Spasticity
- Epidiolex® (CBD) orphan program in pediatric epilepsy
  - Promising data from Expanded Access INDs
  - 2 Phase 3 trials in Dravet syndrome underway
  - 2 Phase 3 trials in Lennox-Gastaut syndrome underway
  - Phase 3 trial in Tuberous Sclerosis Complex expected to commence H2 15
  - NDA filing expected mid-2016 for Dravet and LGS
  - GW retains global commercial rights
- Promising clinical stage cannabinoid product pipeline
  - Sativex U.S. Phase 3 opportunities in Cancer Pain and MS Spasticity
  - Orphan programs in glioma and NHIE
  - Phase 2 trials in Schizophrenia and Type 2 diabetes

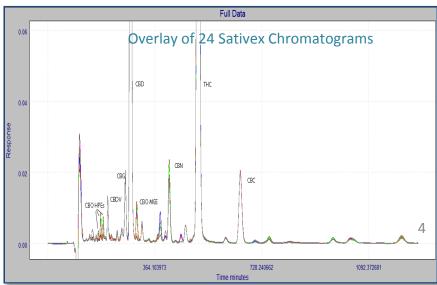
## Our Proprietary Cannabinoid Product Platform: Overview



- Cannabis plant is unique source of >70 cannabinoid molecules
  - Only THC is known to cause psychoactive effects
  - Cannabinoids capable of targeting diseases across therapeutic areas
    - Endocannabinoid system, TRP channels, adenosine uptake, serotonin receptors
- GW's novel proprietary plant "chemotypes" target selected cannabinoids
  - CBD, THC, CBC, CBG, CBN, THCV, CBGV, CBDV, THCA, CBDA etc
- In-house formulation, processing, manufacturing and regulatory expertise
- Exclusivity via 55 patent families, know-how, complex formulations
  - Specialized field provides substantial barriers to entry

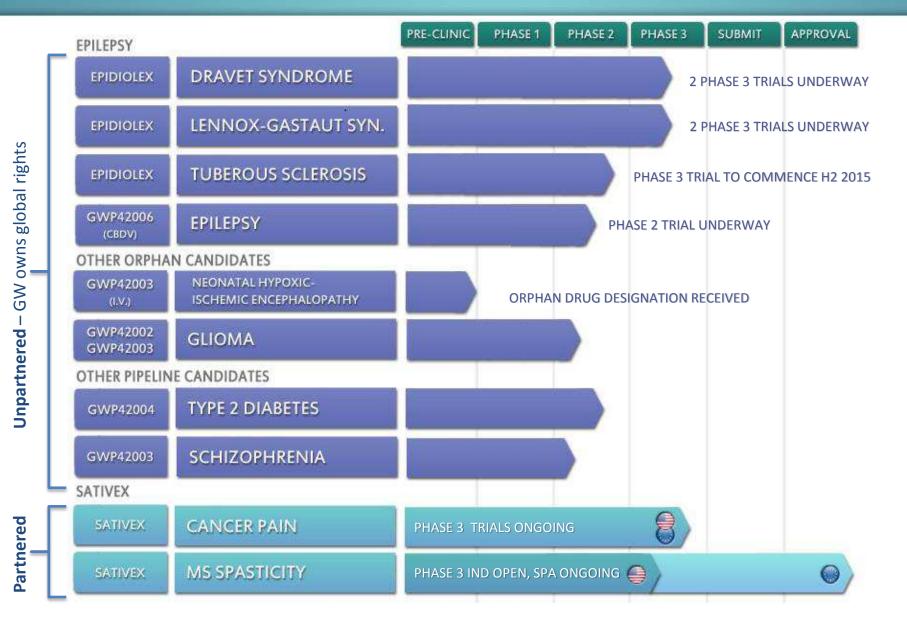






## **Our Pipeline**





## Treatment-Resistant Childhood Epilepsy: **Significant Unmet Need**



466,000 US CHILDREN WITH FPILEPSY

30%

PHARMACORESISTANT EPILEPTICS<sup>1,4</sup>

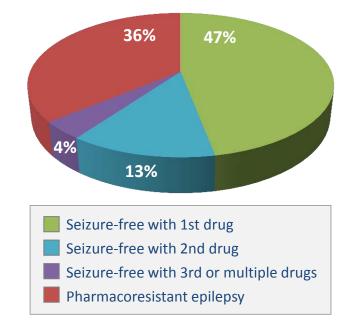
SEIZURES THAT PERSIST, DESPITE MULTIPLE AED TREATMENT<sup>2</sup>

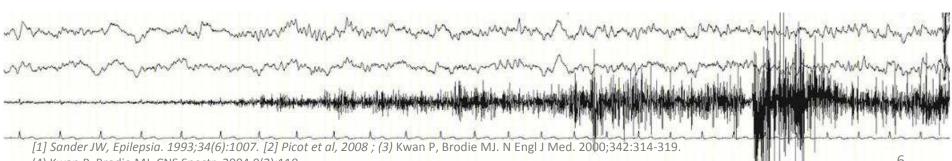
140,000 TARGET US POPULATION

REFRACTORY FPILEPSY COMPOSED OF MULTIPLE SYNDROMES

#### Response to AEDs in patients with newly diagnosed epilepsy<sup>3</sup>

little change to this statistic over last 15 years





(4) Kwan P, Brodie MJ, CNS Spectr. 2004;9(2):110

## Treatment-Resistant Childhood Epilepsy: Spectrum of Rare Disorders



Many different types of epilepsy syndromes, seizures and causes, including

LENNOX-GASTAUT SYNDROME

3 TO 4% OF CHILDHOOD EPILEPSY<sup>1</sup>

DRAVET SYNDROME

UP TO 5% OF ALL CHILDHOOD EPILEPSIES IN FIRST YEAR OF LIFE<sup>2</sup>

CDKL5

TUBEROUS SCLEROSIS COMPLEX

**FIRES** 

DOOSE SYNDROME

> DUP15q SYNDROME



ANGELMAN'S SYNDROME

STXBP1/OHTAHARA
SYNDROME

WEST SYNDROME (INFANTILE SPASM)

RASMUSSEN SYNDROME

GLUT 1
TRANSPORTER
DEFICIENCY

AICARDI SYNDROME

66% of patients being treated with Epidiolex in latest expanded access data have conditions other than Dravet and LGS

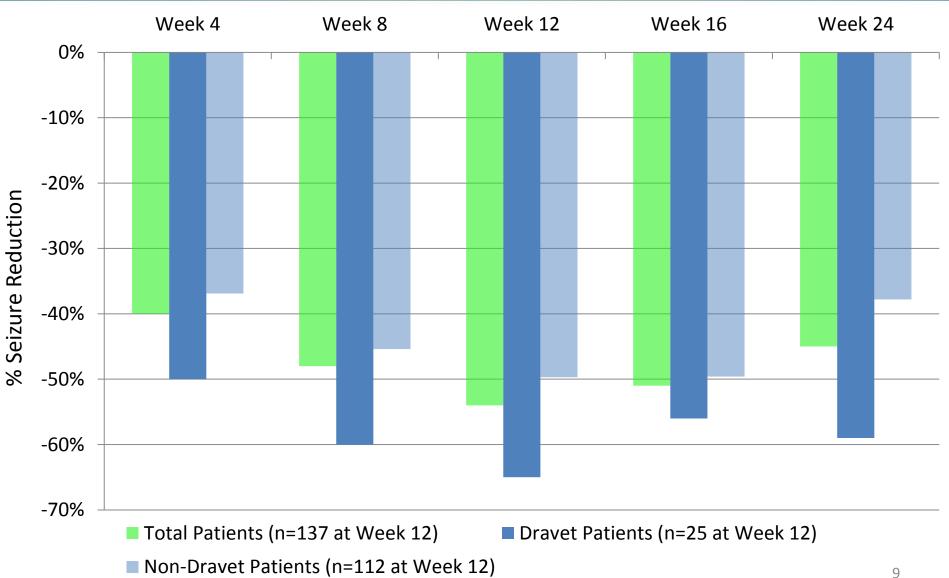
## American Academy of Neurology Data April 22, 2015



- New data issued in a poster presentation at the American Academy of Neurology on 137 patients from GW Expanded Access Program (EAP)<sup>1</sup>
- EAPs facilitate access to investigational drugs for treatment use for patients with a serious or immediately life-threatening diseases or conditions who lack therapeutic alternatives. Treatment is open label.
- Children and young adults treated with Epidiolex in this EAP suffer from
   12 severe types of epilepsy
- Epidiolex added to existing meds patients on average 3 other AEDs
- Mean age 11 years (range: 2-26)
- Median baseline convulsive seizure frequency 29.5 seizures per month (based on 4-week baseline period)

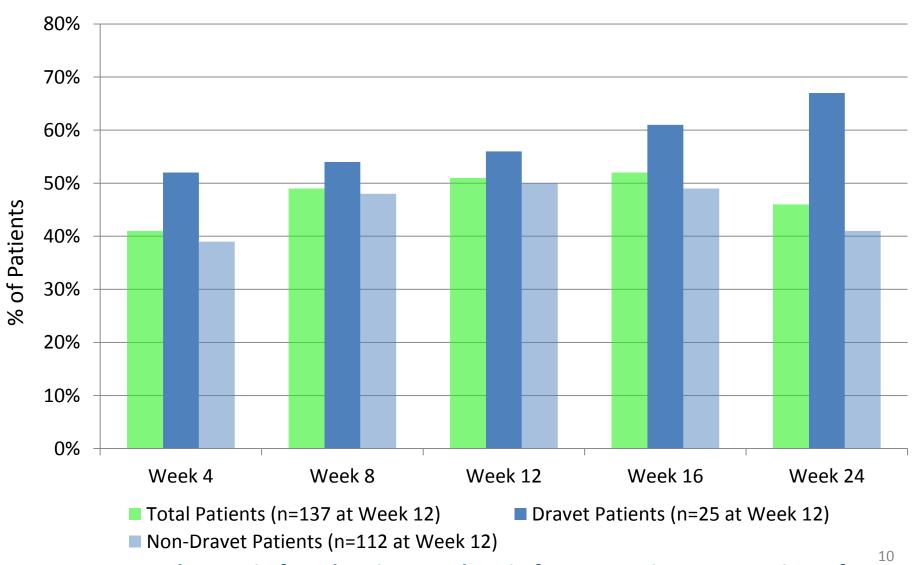
### **Median % Reduction in Total Seizures**





## **Total Seizures ≥50% Responders**

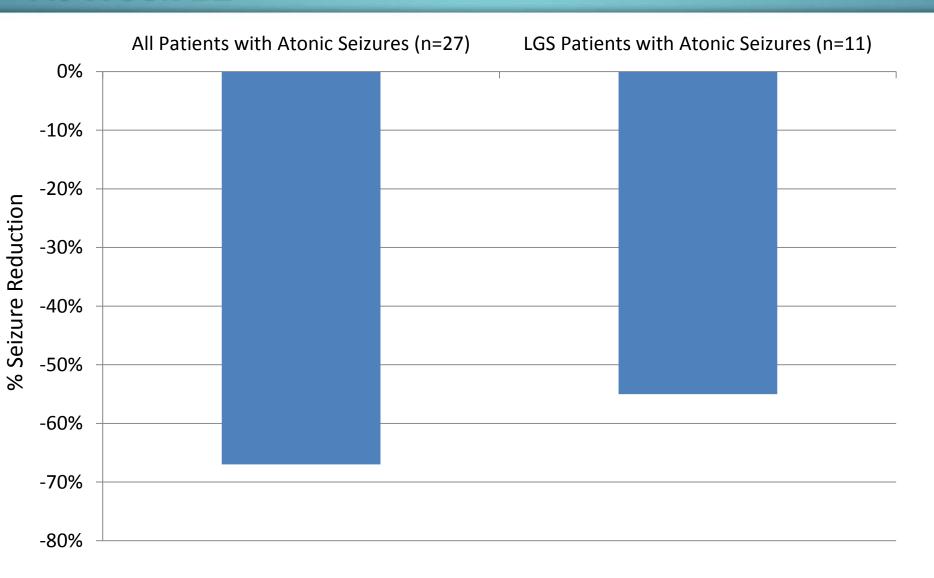




At Week 12, 9% of total patients and 16% of Dravet patients were seizure-free

## Median % Reduction in Atonic Seizures At Week 12





## Safety Data (213 patients, approx. 59 patient-years)



- Safety data on 213 patients (137 patients with 12 weeks treatment effect data plus additional patients who are still in first 12 weeks of treatment or withdrew from treatment)
- The most common AEs (occurring in 10% or more patients and resulting from all causes) were:

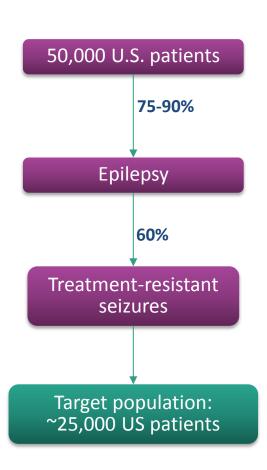
-	Somnolence	21%	(n=45)
-	Diarrhea	17%	(n=36)
-	Fatigue	17%	(n=37)
-	Decreased appetite	16%	(n=34)

- Most AEs were mild or moderate and transient
- 10 patients (5%) reported an AE leading to discontinuation, 3 of whom subsequently restarted treatment with Epidiolex
- There were 14 withdrawals from treatment due to lack of clinical effect
- Serious Adverse Events (SAEs) were reported in 52 patients, which were deemed possibly treatment related in 22 of these patients
- Included within these SAEs were 2 deaths both of which were deemed unrelated to Epidiolex by the independent investigators, one from SUDEP (sudden unexpected death in epilepsy) and one from respiratory failure due to aspiration

## New Epidiolex Target Indication: Tuberous Sclerosis Complex



- TSC is a genetic disorder that causes nonmalignant tumors to form in different organs, primarily the brain, eyes, heart, kidney, skin and lungs
- TSC results from a mutation in tumor suppression genes TSC1 or TSC2
- Of TSC patients with epilepsy, 70% experience seizure onset in their first year of life
- Co-morbidities include
  - Cognitive impairment (50%)
  - Autism spectrum disorders (up to 40%)
  - Neurobehavioral disorders (over 60%)



## CBD for TSC

### 2014 American Epilepsy Society Poster





#### Cannabidiol (CBD) Treatment for Refractory Epilepsy in Tuberous Sclerosis Complex (TSC)



Geffrey AL, Pollack SF, Paolini JL, Bruno PL, Thiele EA
The Herscot Center for Tuberous Sciences's Complex and Pediatric Epilepsy Program
Massachusetts General Hospital

#### INTRODUCTION

Tuberous solerosis complex (TSC) is an autosomal dominant genetic disorder, characterized by benign hamartomas in various organs, including the brain, heart, lungs, skin, eyes, and kidneys. TSC results from a mutation in tumor suppressor genes TSC1 or TSC2.

The most common symptom of TSC is epilepsy, which occurs in 75-90% of patients, about 70% of whom experience seizure onset in their first year of life. Epilepsy occurs in over 50% of individuals with tuberous sclerosis complex (TSC), making it about 1.5 times more common than in the general epilepsy population. 9

This study explores cannabidiol (CBD) as a possible treatment of refractory epilepsy in TSC.

#### METHODS

Under an expanded access IND from the FDA, we are conducting a trial to determine the safety, tolerability, as well as efficacy of CBD (Epidiolex, GW Pharma) as an adjunct treatment in children and young adults with drug resistant epilepsy. Our 25 patients are a subset of a group presented in another abstract of all subjects by Devinsky, et al. (2014). Five of our 25 patients have TSC as the cause of their epilepsy. Data collected from the study were reviewed for demographics, epilepsy history, genetic analysis, and behavioral and cognitive issues. Cognitive impairment was defined by an IQ of <70. Cognitive and behavioral changes were based on parental report and/or clinician observation. Subjects were classified as responders if they showed greater than 50% decrease in seizure frequency after 16 weeks of treatment (including a 5 week titration of 5 mg/kg/day up to 25 mg/kg/day). Baseline seizure frequencies were measured for four weeks immediately preceding initiation of CBD treatment. during which they had two or more seizures per week, meeting study inclusion criteria.

#### RESULTS

#### Table 1. Overview of TSC cases treated with CBD

Case	Sex	Age	Mutation	Age at Sx onset	Hx of IS	Responder
1	M	13	TSC1	5 y/o	no	yes
2	M	5	7SC1	1 mo	no	yes
3	M	16	Unknown	6 y/o	yes	yes
7.4	M	14	TSC2	8 mo	yes	no
5	JF :	11	TSC2	3 mo	yes	no

Sx - seizure; Hx - history; IS - infantile spasms-

<u>Case 1</u>: 13 y/o male with a TSC1 mutation, behavioral problems and a history (hx) of 8 past anti-epileptic drugs (AEDs). At initiation of CBD treatment, the patient was concurrently on 2 AEDs. He had complex partial seizures that showed a 77% reduction of seizure after CBD treatment. Behavioral problems also improved. He experienced no adverse events thought to be related to CBD.

<u>Case 2</u>: 5 y/o male with a *TSC1* mutation, cognitive impairment, behavioral problems, and a hx of epilepsy surgery. He had also tried VNS (explanted due to infection) and 8 past AEDs. At initiation of CBD treatment, he was on 3 AEDs and had focal dyscognitive, tonic, and atypical absence seizures, which showed a 100, 69, and 100% reduction in seizure frequency, respectively. Overall, the patient exhibited a 97% reduction in seizure frequency, in addition to cognitive gains, including alertness and verbal capacity.

Case 3: 16 y/o male with TSC and no prior genetic testing, who had previously tried both the ketogenic diet and low glycemic index treatment (LGIT), in addition to 7 past AEDs. At initiation of CBD treatment, the patient was on 4 AEDs. He had three seizure types – focal dyscognitive, focal with secondarily generalization, and atonic – which showed a 98, 92, and 88% reduction in seizure frequency, respectively. The patient had an overall seizure reduction of 97%. He had drowsiness hypothesized to be due to CBD's interaction with phenytoin (PHT).

Case 4: 14 y/o male with a TSC2 mutation, cognitive impairment, and 9 past AEDs. At initiation of treatment, he had a vagus nerve stimulator (VNS) and was on the ketogenic diet and three AEDs. He had focal dyscognitive seizures that showed an increase in seizure frequency of 5% with CBD treatment. However, he has continued on CBD due to significant cognitive gains. He has experienced no adverse event s over the course of the trial

Case 5: 11 y/o female with a TSC2 mutation and cognitive impairment, in addition to a hx of IS, epilepsy sx, and 7 past AEDs. Upon initiation of CBD, she had a VNS and was on 3 AEDs. Her seizures were seizures were complex partial and complex partial with secondary generalization, which showed reductions of seizure frequency of 22 and 62%, respectively, with CBD. Overall, her seizure reduction was 40%. She also made cognitive gains, including vocalizations, ability to focus, and cognitive availability. She has experienced no adverse events over the course of the trial.

#### SUMMARY/CONCLUSIONS

- Three were responders with 77% (n=1) and 97% (n=2) decreases in seizure frequencies
- All three patients with cognitive impairment experienced cognitive gains, including improved alertness, comprehension, maintained eye contact, engagement, and responsiveness; this group included both nonresponders.
- One of the two subjects with behavioral problems showed improvements.
- No subjects experienced side effects or adverse events related to CBD; drug-drug interactions occurred in two patients

Refractory epilepsy occurs frequently in TSC. Although additional studies are needed, in this small population, it appears that CBD may be an effective treatment for refractory epilepsy in TSC.

#### REFERENCES

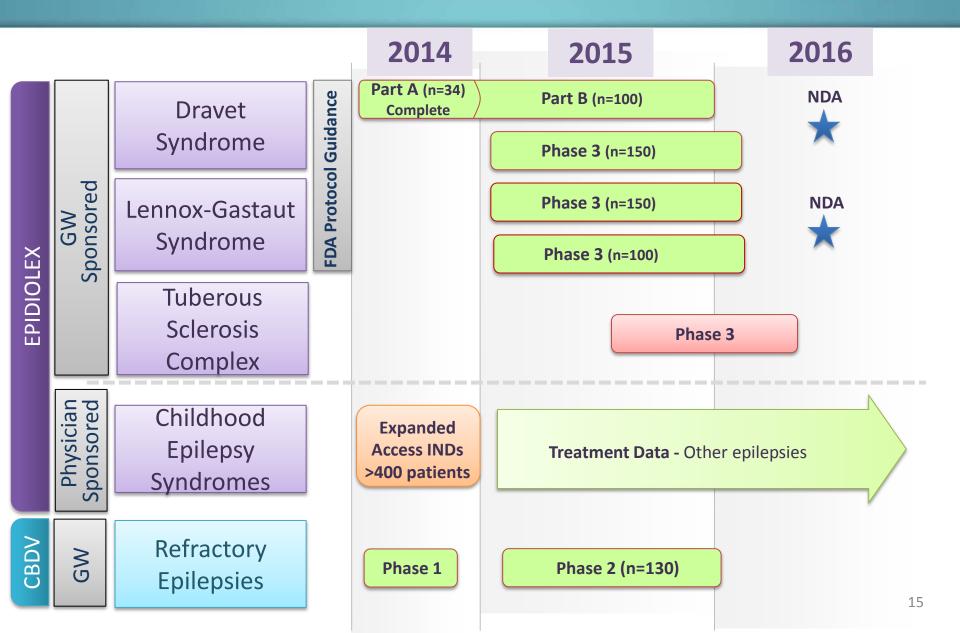
- 1. Leung AK, Robson WL. Tuberous scierosis complex: a review. Journal of pediatric health care: official publication of National Association of Pediatric Nurse Associates & Practitioners 2007:21:108-14.
- 2. Kwiatkowski DJ, Whittemore VH, Thiele EA. Tuberous sclerosis complex: genes, clinical features and therapeutics: John Wiley & Sons; 2010.
- 3. Chu-Shore CJ, Major P, Camposano S, Muzykewicz D, Thiele EA. The natural history of epilepsy in tuberous sclerosis complex. Epilepsia 2010;51:1236-41.

#### **ACKNOWLEDGEMENTS**

Study drug provided by GW Pharmaceuticals. Funding from Massachusetts General Hospital Neurology Department and the Herscot Center

## **Epilepsy Expected Clinical Program**

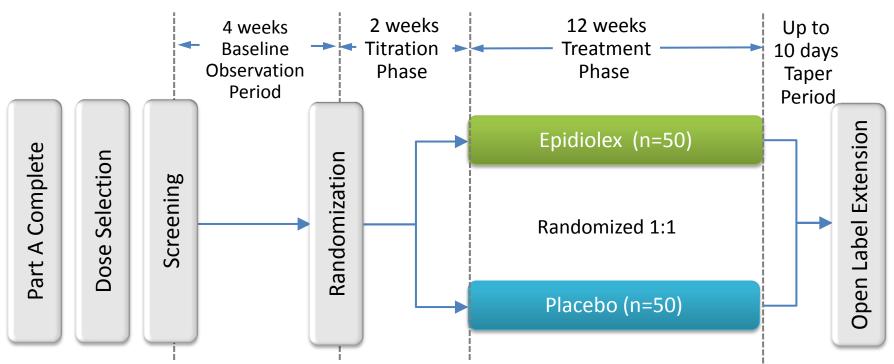




## Epidiolex Phase 3 Trial Design: Dravet Part B & LGS 1<sup>st</sup> Phase 3



Objective: Provide pivotal evidence of safety and efficacy



Primary Endpoint: % change from baseline in seizure frequency.

Dravet –convulsive seizures; LGS – Drop attacks

#### **Secondary Endpoints:**

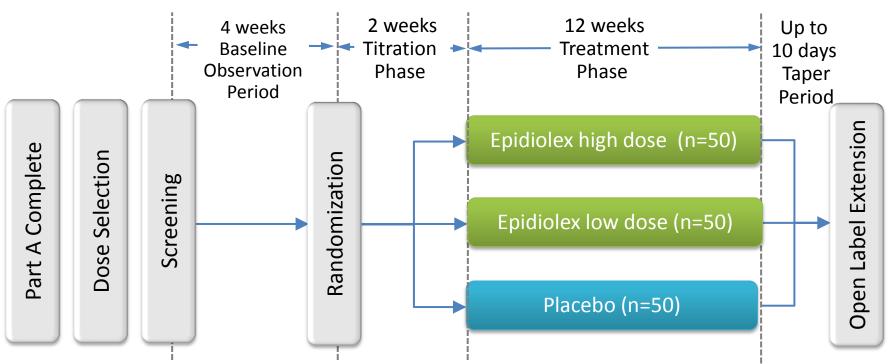
- Change in seizure subtypes
- % seizure freedom
- Responder rate
- Cognition

- Daytime sleepiness scale
- Night time sleep disruption
- Caregiver Global Impression of Change
- Palatability of the drug product
- Quality of Life

## Epidiolex Phase 3 Trial Design: 2<sup>nd</sup> Dravet and LGS



Objective: Provide pivotal evidence of safety and efficacy



Primary Endpoint: % change from baseline in seizure frequency.

Dravet –convulsive seizures; LGS – Drop attacks

- **Secondary Endpoints:**
- Change in seizure subtypes
- % seizure freedom
- Responder rate
- Cognition

- Daytime sleepiness scale
- Night time sleep disruption
- Caregiver Global Impression of Change
- Palatability of the drug product
- Quality of Life

## **GWP42006 (CBDV)**



CBDV is similar in chemical structure to CBD



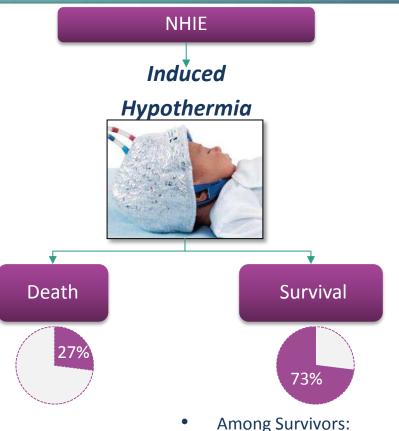


- CBDV has shown anti-epileptic properties across a range of in vitro and in vivo models of epilepsy
  - ▶ CBDV strongly suppressed seizures in six different experimental models commonly used in epilepsy treatment
  - ▶ CBDV exhibits few of the side effects caused by many existing AEDs
  - ▶ CBDV provides additional efficacy when combined with existing AEDs
  - Genetic biomarkers for response have been identified
- Phase 1 trial completed in 66 healthy subjects
  - CBDV well tolerated even at the highest tested dose
  - ▶ No serious or severe adverse events, nor any withdrawals due to AEs
- Phase 2 trial (n=130) in patients with epilepsy underway

## **New Orphan Development Program CBD IV Formulation for NHIE**



- GW has shown neuroprotective effects of CBD in 3 nonclinical models of NHIE across three species
- FDA Orphan designation granted for CBD in April 2015. IND to be submitted mid-2015
- NHIE: acute or sub-acute brain injury due to asphyxia resulting from deprivation of oxygen during birth
- No FDA approved medicines. Standard of care is induced hypothermia
- Underserved population of ~6,500-12,000 patients/year in the U.S.
- Significant morbidity and mortality remains despite use of hypothermia
  - 27% death rate with induced hypothermia



- - 28% Have major neurodevelopment issues
  - 26% Develop Cerebral Palsy

## GW has Studied Neuroprotective Effects of GW CBD in Animal Models of NHIE Since 2008

Three nonclinical models of NHIE across three species:

### Piglet

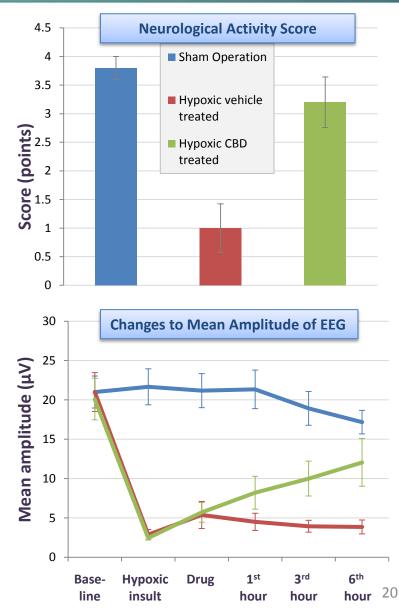
- CBD post-HI administration reduces necrotic and apoptotic cell death, recovers brain activity and restores neurobehavioral function in the short term.
- CBD post-HI administration enhances hypothermia protection.

### Rat

- CBD post-HI administration reduces the volume of brain damage and restores neurobehavioral function in the long term.
- CBD post-HI administration preserves myelinization.

### Mouse

 CBD is neuroprotective even when administered 18 h after HI.



## Other Pipeline Candidates: Significant Clinical Programmes



### **Orphan**

- NHIE
  - FDA Orphan designation
  - Expected next steps: Commence Phase 1 H2 15
- Glioma
  - Phase 1b THC:CBD trial underway (in recurrent glioblastoma)

### Non-Orphan

- Sativex
  - US Phase 3 Cancer Pain trials and MS Spasticity Phase 3 SPA discussions ongoing
- Schizophrenia
  - GWP42003 Phase 2a trial underway data due H2 15
- Type 2 Diabetes
  - Positive data from Phase 2a trial for GWP42004
  - GWP42004 Phase 2 dose ranging trial underway

### **Key Financial Data**



Cash at 31 Mar 2015 net proceeds from Apr 2015 offering net cash (at 6 May)

**Projected cash spend for FY 2015** 

Opex Capex (78)(34)

tal Current Options 21.6 0.8	
m 259.7 9.4	ary shares/m 259.7 9.4

## **Anticipated Newsflow**



<ul> <li>Epidiolex in Dravet</li> <li>Phase 2/3 Dravet data</li> <li>Phase 3 Dravet data</li> </ul>	Timing around end 2015 Q1 2016
<ul><li>Epidiolex in LGS</li><li>Phase 3 LGS data</li></ul>	Q1 2016
<ul><li>Epidiolex in TSC</li><li>Phase 3 TSC trial start</li></ul>	H2 2015
Epidiolex expanded access data	H2 2015
GWP42006 (CBDV)  Phase 2 trial data	H1 2016
<ul> <li>Pipeline</li> <li>Sativex 2<sup>nd</sup> and 3<sup>rd</sup> trial Phase 3 trial cancer pain data</li> <li>Phase 3 SPA for MS spasticity</li> <li>Phase 2a GWP42003 Schizophrenia trial data</li> </ul>	H2 2015 H2 2015 H2 2015

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