Epilab

Epilab is dedicated to contract research in early stage anti-epileptic drug and neuropathic pain medication discovery. We provide a high-throughput screening against a therapeutically relevant ion channel protein.

Team members

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1. Executive Summary

With 65 million people affected worldwide, epilepsy is one of the most common neurological disease.[1] Despite the introduction of several 3rd generation anti-epileptic drugs (AEDs) and neuropathic pain drugs. Current therapeutics fail to control seizures in ~35% of epileptic patients and exhibit mild to severe side-effects.[2, 3] Approximately 20% of the adult European population have chronic pain and in addition to the physical and emotional burden, the financial cost to society is currently estimated at more than €200 billion/year in Europe and $150 billion/year in the USA.[4] Epilab aims to develop a protein-based assay for screening of novel AEDs and neuropathic drugs which specifically bind voltage-gated calcium (Ca) channel. This protein is a proven target site for epileptic and neuropathic pain medication.[5, 6] We aim to provide a new drug-screening assay for the identification of novel therapeutics with higher efficacy and affinity.

2. Market Analysis

2.1. Problem

Current therapeutic drugs against epilepsy or neuropathic pain exhibit a wide range of adverse side effects such as dizziness, depression, heart problems, weight gain, anxiety, and off-target proteins.[2, 6, 7] The absence of off-target biomolecules is crucial for an AED and neuropathic pain drugs as most patients are treated for several years, majority of which need to take these drugs for their entire life. A common target for many of the AEDs is voltage gated Ca channel and its various isoforms. Due to inherent complexity of the Ca channel, no report is available for the recombinant production this protein for binding assays, which limits the opportunity to develop new drugs.

Two widely-used AEDs marketed by Pfizer – gabapentin (Lyrica™) and pregablin (Neurontin™), are thought to specifically target the identical site on voltage gated Ca channel (present in all Ca channels), due to their chemical and structural similarities. Both are primarily used in patients suffering from neuropathic pain but also used in certain types of epilepsy.[6] In 2009, the FDA recommended manufacturers of AEDs (including gabapentin and pregablin) to update product labeling to include a warning about an increased risk of suicidal thoughts or actions and help patients understand this risk. Additionally, both drugs have a relatively short half-life of ~7hrs, and therefore require three tablets a day. From a clinical perspective, the ideal AED does should be 1 or 2 tablet per day, so novel AED with higher half-life are very much in demand.

2.2. Market Need

- Our customers are major pharmaceutical companies (e.g. Baxter Healthcare Corporation, Bristol Myers Squibb, Cephalon, Genentech, GlaxoSmithKline, Johnson & Johnson, Pfizer, Novartis AG, Roche, Sanofi S.A, Sunovion) which develop drugs for pain and/or epilepsy.
- These companies need new drugs with improved efficacy and fewer side-effects.
- The mechanism of action for almost all of the current available therapeutics against epilepsy or neuropathic pain are unknown.
- Need a robust, cheap, and fast first-step drug screening method to identify novel drug scaffolds.
- Few companies are utilizing a multiplexed recombinant protein-based assay for drug discovery against ion channels involved in neuropathy and epilepsy, due to the complexity associated with their expression and purification.[7]
- Most AEDs and neuropathy medication face of patent expirations (as with Lyrica and Neurontin).

2.3. Market Size

The global neuropathic pain market is said to reach $8.3 billion (US), while the epileptic market is said to reach $5.47 billion (US) by 2024.[8] Companies typically spend 2-5 million for initial stages of drug discovery and validation,[9] and if 1% of neuropathic pain and epileptic market is spent on drug screening, the total accessible market is projected to be around $138 million. Our goal is to capture about 0.5-2% of neuropathic pain and epilepsy drug screening market within five years. The combined sales of Lyrica and Neurontin alone were $2-3 billion in 2008,[10] though the revenues are steadily declining as these drugs are nearing patent expiration.

3.1. How are Customer Needs Addressed Today

Electrophysiology is the ‘gold standard’ methodology for ion channels drug screening, allowing detailed kinetic and pharmacological analysis of potential drug molecules in real time. However, this classical approach is labor intensive, expensive and generally low-throughput. Additionally, high-voltage-activated channels (particularly Ca channel) are difficult to express and require co-expression of ancillary subunits.[11] To address these limitations, a number of high-throughput assays have been developed for ion channel drug screening. These include radioactive flux assays, atomic absorption spectroscopy, fluorescence assays and colorimetric

assays.[12-13] However, such methodologies possess some limitations associated with physiological correlation, temporal resolution, or require radiolabeled compound.[12-13]

3.2. Environmental Scan

COMPANY	TECHNOLOGY	THREAT	ADVANTAGE	DISADVANTAGE
Genentech	Cell-based and structure-based drug screening	Medium (focus on few Ca channels)	Well-established, lots of resources	Costly, slow, out-source their screening
Xenon pharmaceuticals	electrophysiology (under contract with Genentech)	Medium (focus Na channels, not Ca channels)	High-throughout physiologically relevant	Slow, costly do not offer a screen for Ca channels
Exquiron	Radiolabeled, fluorescence assays, and label free-mass spec (MS)	Low (not popular)	High-throughout, Label free-MS	May or may not be physiologically relevant, costly
SB Drug Discovery	Cell-based assays and electrophysiology screening	Medium (focus on different protein receptors)	High-throughout Physiologically relevant	costly, slow (no drugs in market yet)
Aviva Biosciences	electrophysiology screening	Medium (work on several channels, including CaV1.2)	High-throughout, physiologically relevant	Costly, slow, do not offer a screen for Ca channels
Lectus Therapeutics	Proteomics- based approach to identifying ion channel modulators	High (Direct competitor)	Medium to low cost, Fast	Low specificity Physiological relevance

3.3. Competitive Advantage

We use a cell-free based assay using novel recombinant protein construct which contain therapeutically relevant drug target sites offer greater specificity of drug targeting. The similar mechanism of action (binding to identical site on Ca channels) between gabapentin and pregablin, allows for probing of new drugs that may interact with this important drug binding site. Thus a platform for screening of novel therapeutics which exhibit better affinity to specific Ca ion channels has tremendous clinical potential. Currently, most companies focus on sodium channels for epilepsy and neuropathic pain drug screening, while our screening allows for screening against calcium channels, using a cheaper and faster approach for the initial binding identification compared to that of electrophysiology screening.

Importantly, the same domain of the voltage-gated Ca channel is involved in other neuronal disorders such as ataxia, anxiety, retinal dystrophy, and night blindness.[6]

3. Commercialization Plan

4.1. Science / Technology Overview

Given our strong expertise in the characterization of ion channels, we are able to recombinantly express a protein region of Ca ion channel in large quantity, which can then be used as a template for screening drug libraries for epilepsy and pain therapeutics. This domain is highly stable and binds with both gabapentin and pregablin, which provides a proof of concept to screen for novel anti-pain and AEDs. Currently we are working on the development a rapid and real-time multiplex surface plasmon resonance (SPR) assay for the screening of binding compounds against this protein domain in a high-throughput manner. SPR assay will allow us to quantify the binding kinetics of drug compounds with our target in terms of association/dissociation rates in parallel. This assay can easily be adapted to other protein targets.

4.2. Growth Strategy

We will file provincial patent for our screen once the terms are negotiated with the UBC liaison office. Subsequently we will incorporate Epilab; and work on promoting our work by attending targeted conferences/meetings and build network with opinion leaders in the field. These efforts will help us in obtaining contracts with leading pharmaceutical companies. We will charge $1M/screen to our potential customers including 2% royalty on successful drugs. For providing high-throughput screening services to our clients, Epilab will sub-contract the national research council for access to SPR services at low cost.

Given our expertise in structural biology, Epilab will also offer structure based drug design service as these protein domains are good targets for X-ray crystallography. These approaches can yield novel chemical scaffold than current drugs and allow optimization of lead compounds, while generating additional revenue for our company. As part of our growth strategy, we will identify other therapeutically important protein targets and

use them as part of our screening platform. The long-term goal of the company is to become a drug discovery company. Epilab will not itself become involved in downstream pharmaceutical development, though it will retain royalty rights and form strategic alliances with research and chemistry labs to identify drug for licensing to pharmaceutical companies.

4.3. Milestones

No.	Deliverable	Resources	Timeline, costs
1.	Development of high-throughput SPR assay for the detection of lead compounds	Filip Van Petegem (FVP) lab tools and initial funding	6-12 months, 250-500k
2.	Incorporation of Epilab and patent filing	Second round of funding	6-12 months, 250-350k
3.	Screening service to pharmaceutical clients using chemical libraries and development of new targets	Client contracts and NRC partnership	6-12 months, 500-600k
4.	Screening service using structure based drug designing	Client contracts and FVP lab tools	12-24 months, 500-700K

4. Financial Plan

5.1. Financial Needs and Justification

Milestone #1: Epilab is seeking $250-500k in first round funding. The majority of the funds would go toward development of binding assay, optimization and setting up infrastructure to deliver our services.

Milestone #2: Epilab will require $250k for patent filing and other legal activities. We will be requiring additional $50-100k for marketing our work at conference and various other platforms.

Milestone #3: Develop first screen and optimization of SPR chips. We will be requiring $400-500k for performing the screening work. We will charge $1M from per pharmaceutical client for the screening. The profit obtained by our services will be utilized in the Identification important pharmaceutical targets, setup SPR chips with additional protein targets (different isoforms, ion channels) which could be utilized in our screening platforms.

Milestone #4: If requested, we will perform crystallization trials with identified drugs. We will provide three dimensional structures of identified drugs with their receptors. Epilab will charge $1.5M for providing this service.

5.2. Fundraising plan

For the first round of funding Epilab will apply for NSERC discovery/engage grants along with Michael Smiths I2C grant, which will cover our operating budget. Once a prototype for high-throughput assay is developed, we will be requiring money for legal and marketing activities. Epilab will raise funds from angel investors, friends and families and industrial matching funds. Our screening work will be supported by contracts with pharmaceutical companies. Epilab projects $2-3 million in revenue with $1 million in net income by year 2. The company should have a neutral cash flow from its additional contracts and expand its intellectual property portfolio. We expect to produce at least 2-3 novel therapeutic targets by year 3, and attract additional investments for carrying out drug screening in collaboration with research labs.

5.3. Exit

There is a considerable potential for revenues from royalty payments of successful drugs coming from our screening, as part of our exit strategy we will seek for royalty buy-out options. We seek to go public within 5-10 years of operations. The funds used will both help create liquidity for investors as well as allow for additional capital to develop our international strategy.

1. Team

Pankaj Panwar and Omid Haji-Ghassemi are a PDFs in the Filip Van Petegem lab at Dept. of Biochemistry. Dr. Panwar has a strong background in functional and structural characterization of various ion channels. He is recipient of Mitacs Elevate fellowship, based on his work on ion channels in collaboration with Xenon pharmaceuticals. Dr. Haji-Ghassemi has a fellowship from Michel Smith foundation with a strong background in structural characterization of antibodies and lectins using X-ray crystallography. He is also part of ongoing industry collaboration between his PhD supervisor, Dr. Stephen Evans (UVic) and Immunoprecise Ltd, and helped write the engage grant recently awarded to the lab of Dr. Evans. Epilab is further strengthened by the advice of Dr. Filip Van Petegem and Dr. Tim Vitalis. In future we plan to recruit researchers from various fields and seasoned business advisers for the Epilab. As the company expands, additional members (CEO, CFO etc.) are hired for professional development of the company.

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