FCTDI

FOX CHASE THERAPEUTICS DISCOVERY, INC.

Fox Chase Therapeutics Discovery, Inc.

a remarkable difference in scientific discovery

Pennsylvania Biotechnology Center
3805 Old Easton Road
Doylestown, PA 18902

www.fctdi.com

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FOX CHASE THERAPEUTICS DISCOVERY, INC.

Non-Confidential Summary of Collaboration and Service Offering

Fox Chase Therapeutics Discovery, Inc., (FCTDI) founded in 2008, is an emerging biotechnology company located in **Doylestown. PA** whose mission is to advance basic scientific discoveries by providing value-added early drug discovery and medicinal chemistry research support to advance preclinical small-molecule drug and diagnostic candidates prior to entry into human clinical trials. Originally named Fox Chase Chemical Diversity Center, Inc. (FCCDC), our name has changed to FCTDI to reflect a broader mission of innovation in drug discovery research. FCTDI has independent research programs targeting to treating specific diseases. In addition, FCTDI partners with suitable biomedical research collaborators on selectedprojects or can function as their company's proprietary medicinal chemistry research function. We bring a unique and highly experienced team of internal scientists and collaborative external partners to leverage cutting edge scientific advances. FCTDI staff have over 350 years of collective drug discovery experience, drawing from a diverse background of pharmaceutical and biotech companies including Johnson & Johnson, BMS, GSK, Wyeth/Pfizer and Merck. FCTDI has fully functional, onsite BL2 biology and medicinal chemistry laboratories with a 400-MHz NMR, LC/MS (4), microwave reactors (2), IKA ElectraSyn 2.0 reactor (1) and Gilson semi-prep HPLC (4) instruments for compound and library purification and analysis. As a distinguishing factor relative to other possible collaborators, FCTDI has a >34,000 member chemical inventory of reagents and starting materials onsite.

Our research has resulted in a compound currently in Phase II/III human clinical trials (troriluzole) by Biohaven Pharmaceuticals, an Epstein Barr Nuclear Antigen EBNA-1 inhibitor currently in clinical trials for the treatment of nasopharyngeal carcinoma at Stanford University with The Wistar Institute, and a tau aggregation inhibitor in the clinic for the treatment of Alzheimer's disease. We have also licensed a topical agent to treat Molluscum contagiosum together with the University of Pennsylvania and the biotech company, VeraDermics.

Our research capabilities empower programs at multiple stages of product development including probe molecule identification and synthesis, *in silico* computational prescreening, hit triage, hit to lead medicinal chemistry, and lead optimization. We prepare or assist in the creation of new intellectual property and the preparation of patent applications.

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Leadership Team

Allen B. Reitz, Ph.D., Chief Executive Officer and Founder

- Ph.D. in Chemistry, UC San Diego
- Executive Master's, Wharton School, Univ. of Pennsylvania
- Worked at Johnson & Johnson for 26 yrs
- 9 Compounds in human clinical trials including mazapertine and troriluzole
- Co-authored 180 scientific publications, inventor on 79 issued US patents

Kathleen Czupich, M.B.A., Chief Financial Officer

- >25 Yrs of demonstrated accomplishment in the medical research industry in M&A, valuations and due diligence.
- M.B.A. from Lehigh University, B.S. from Penn State University
- Managed financial and administrative aspects of >$50+ Million in federal grants mainly from the NIH

Jay E. Wrobel, Ph.D.
Vice President, Academic Relations

- At Wyeth, directly involved in bringing forward nine development track candidates (phase 0 and beyond) in a variety of therapeutic areas
- PI or Key Personnel on 17 SBIR/STTR funded grants
- 79 publications, inventor on 84 patents

Richard W. Scott, Ph.D., Vice President, Research

- Ph.D., Microbiology, University of Pennsylvania
- 38 years in the pharmaceutical industry
- Leadership in multiple disciplines including anti-infectives and neurobiology
- >69 Peer reviewed publications, 17 US patents

Jeffrey C. Pelletier, Ph.D.
Director of Chemistry

- >35 years of experience in Medicinal Chemistry
- Experience in Big Pharma (Wyeth), Biotech and Academia
- Been with FCTDI for >10 years
- Coinventor of troriluzole
- >100 patents and publications

Katie B. Freeman, Ph.D., Director of Biology

- PhD in Microbiology, University of Virginia
- >25 years experience in Pharma and Biotech
- Developed multiple in vitro assays on varied platforms to support SAR and compound mechanism of action studies
- >25 papers, inventor on 7 US patents.

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For further information, visit our website (www.fctdi.com).

Contact: info@fctdi.com

Collaboration Options

- NIH/DOD small business grants (SBIRs, STTRs) or basic research grants (R01, U01)
- Multi-FTE research support (medicinal chemistry participation on multiple projects from client proprietary chemistry or biology platform)
- FTE based hit to lead, proof of concept studies
- FTE based lead optimization to preclinical drug candidates
- Foundation grants (e.g., Wellcome Trust, Muscular Dystrophy Association)
- VC or Angel investor based on specific disease indications

Project Goals and Deliverables

- Molecular probes to better understand and validate specific molecular targets
- Preclinical drug candidates from advanced screening hits
- Scale up of drug candidates, probes and chemical intermediates
- Evaluation and interpret ADME/PK properties
- The following drug-like libraries are available for screening: (1) a 4,799-member "FDA super library" including (a) Microsource Spectrum (2K), (b) the Johns Hopkins Compound Collection library of 1,529 known drugs of which 1,034 are unique to our collection, and (c) the LOPAC 1280 Library of Pharmacologically Active Compounds, (2) an ApexBio Discovery Probe library of 3,317 biologically diverse and bioactive compounds with known targets, and (3) a >100K small molecule library strategically designed to maximize chemical diversity.
- Guide preclinical drug candidates though the IND enabling process.
- Intellectual property management and protection of chemical matter.

Scientific and Support Staff

Current staffing: ~30 total, with 26 scientists, 13 Ph.D.-level, 9 M.S, 4 B.A.

- Synthesis Support and New Chemical Entity (NCEs) preparation.
  - ca. 16,000 News Chemical Entities (NCEs) prepared since 2008
  - Software licenses: SciFinder-n (structure/reaction searching), Instant J Chem (internal compound database, *in silico* calculations) and Schrodinger (computational chemistry)
  - Experience in bifunctional drug conjugate approaches
- Biology and Pharmacology
  - Biochemical assay development
  - Cytotoxicity screening using multiple cell lines
  - BL2 cell culture experiments
  - Molecular biology studies including RNAseq analysis

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FCTDI Equipment and Infrastructure

8,000 ft^2 laboratory space; 3,000 ft^2 office space.

Varian Mercury Plus 400-MHz Inova NMRs with multinuclear capability (^{1}H, ^{13}C, ^{31}P, ^{18}F).

HPLC/MS:

- Four Micromass ZQ Mass Spec. with Waters 2695 HPLC systems with 996 diode array detectors
- One Thermo-Finnegan Surveyor Plus HPLC with MSQ Plus Mass Spec
- Shimadzu Prominence and Agilent 1100 HPLCs

Chromatography:

- Three Gilson 215 semi-prep HPLC systems, multi-wavelength, automated fraction collection
- Three Teledyne IscoCombiFlashRf, automated chromatography system
- Three Isco Combiflash Sg 100c, personal chromatography systems

Evaporation:

- Genevac EZ2 Evaporation System; Two FTS Systems Flexi-dry Lyophilyzers.
- 18 Rotavapors with vacuum pumps (Buchi, Heidolph).
- 2 VWR Sheldon 1400E Vacuum Ovens with Edwards oil pumps

Hydrogenation: Three Parr 3911 Shaker hydrogenators

Reaction:

- Two Biotage Initiator microwave synthesizer with 60 position autosampler
- Innova platform shakers, model 2000
- Six J-Kem Gemini-2 dual temperature controllers with teflon-coated thermocouples.
- IDA ElectraSyn 2.0 apparatus for electrochemical reactions

BL2 Biology and tissue culture lab:

- Cytation 5 Cell imaging multi-mode reader with BioSpa automation
- BioRad Opus 384 Real-Time PCR Detection System
- Akta protein purification system
- Nikon Eclipse (TE 2000) microscope interfaced with image analysis software
- iBind and iBlot Automated Western System
- New Brunswick Environmental incubator shaker and incubator
- ABI Prism 7000 Sequence Detection System\
- Biotek Synergy 2 Multi-Detection Microplate Reader
- LabomediVU 1500 Microscope
- Fisher and VWR Carbon dioxide incubators
- Formulation screening suitable for preclinical in vivo studies

Onsite stockroom for chemical synthesis:
>34,000 Reagents and starting materials (ca. 2,400 boronic acids), bar coded, searchable database

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Therapeutic Area Experience

CNS (neurology, psychiatry cognitive disorders), Antiinfectives (antibacterial, antiviral, and antifungal), Cardiovascular (atherosclerosis, hyperlipidemia), Inflammation and Immunology, Metabolic Disorders (diabetes, diabetic complications, obesity), Oncology.

Targets: GPCRs, Ion Channels, Kinases, Nuclear Hormone Receptors, Proteases, Protein-Protein interaction, Phenotypic Screening.

Our Drug Discovery / Medicinal Chemistry Processes

- *Chemical hit evaluation*
  - Confirmation of activity, structure and purity
  - Remove promiscuous inhibitors or aggregators
- *Hit to chemical lead by improving drug-like characteristics via iterative SAR processes*
  - Prepare small focused libraries or individual compounds
  - Improve *in vitro* potency and selectivity over similar protein targets
    - Assays in-house for antimicrobial and antifungal targets
    - Capability to develop additional in vitro biological assays
  - Improve physiochemical properties such as aqueous solubility, log P and tPSA
  - Monitor and reduce early toxicity liabilities
    - Cytotoxicity in relevant cell lines and RBC hemolysis
  - Early assessment of PK profile
  - Early assessments of efficacy in disease models
  - Incorporate *in-silico* computational and structure-based design
    - Molecular modeling: pharmacophore design and docking
    - Physiochemical design for drug-likeness and toxicity derisking: Rule of 5, Ligand Efficiency (LE), Ligand-Lipophilicity Efficiency (LipE)
    - Iterative X-ray crystallography (through collaborators, where appropriate)
- *Choose chemical lead and optimize to preclinical drug candidate*
  - Lead status based on industry standard criteria and reviewed by consultants
  - Ensure patentability
  - Continue standard SAR optimization practices but focus on:
    - Minimize P450 cyp inhibition, cyp induction, efflux potential, plasma protein binding, and off target activities (e.g., hERG, Ames)
    - Optimize solubility in aqueous vehicles, microsomal stability in multiple species, permeability and PK profile in multiple species
  - Obtain efficacy and potency target goals in animal disease models
  - Evaluate toxicity in cell and animal models

Financial Accounting Conducted Onsite

Our CFO and financial accounting staff have extensive experience in fundraising and extramural grant administration. We can help identify appropriate grants, prepare and submit applications, ensure compliance and obtain funding from a variety of federal, state and private funding sources. FCTDI is audited by an external CPA firm on an annual basis.

Intellectual Property Management

Intellectual Property Management is a very important service that we provide our collaborators. Generally, new composition of matter and/or known chemicals resulting in novel methods of treatment will be produced during execution of research projects. Our staff has extensive pharmaceutical intellectual property patent experience with >240 issued U.S. patents and are well versed in the mechanics and opportunities afforded by patent filing and prosecution. We are directly involved in the preparation of draft documents which would be finalized and filed by our registered patent agent. We follow all good laboratory practices regarding confidentiality and the keeping of laboratory notebooks. Our spectral data is stored electronically on a server with a second back-up server also used to ensure records retention. We use ACD software to prepare spectral data write-ups, which saves a great deal of time in the preparation of patent applications. We use SciFinder-n to explore novelty both with regard to freedom to operate and the potential for the creation of new composition of matter intellectual property. We can work with any patent attorney or registered patent agents in the preparation of new patent applications.

Issued United States Patents

1. US 8,609,849. Hydroxylated Sulfamides Exhibiting Neuroprotective Action and Their Method of Use; with G. R. Smith, D. E. Brenneman, Y. Zhang, and Y. Du (Dec. 17, 2013).

2. US 9,725,427. Prodrugs of Riluzole and Their Method of Use; with G. R. Smith, M. McDonnell, S. Chen, M. D. Vera, B. E. Blass, J. C. Pelletier, V. N. Velvadapu, and J. E. Wrobel (Aug. 8, 2017).

3. US 9,856,214. EBNA1 Inhibitors and Their Method of Use; with T. E. Messick, G. R. Smith, P. M. Lieberman, M. E. McDonnell, Y. Zhang, and V. Velvadapu (Jan. 2, 2018)

4. US 10,112,895. Antivirals Against Molluscum Contagiosum Virus; with R. P. Ricciardi, M. H. Parker, S. D. P. Baugh, M. Nuth, and H. Guan (Oct. 30, 2018).

5. US 10,160,756. Antiviral Compounds and Methods Using Same; with R. N. Harty, B. D. Freedman, J. E. Wrobel, A. and H. M. Loughran (Dec. 25, 2018).

6. US 10,329,269. Indene Derivatives and Uses Thereof; with N. G. Dolloff, R. M. Robinson, and H. Baiyan (Jun. 25, 2019).

7. US 10,357,497. Pro-Drugs of Riluzole and Their Method of Use for the Treatment of Amyotrophic Lateral Sclerosis; with G. R. Smith (Jul. 23, 2019).

8. US 10,421,718. EBNA1 Inhibitors and Their Method of Use; with T. E. Messick, G. R. Smith, P. M. Lieberman, M. E. McDonnell, Y. Zhang and V. Velvadapu (Sept. 24, 2019).

9. US 10,442,763. EBNA1 Inhibitors and Their Method of Use; with T. E. Messick, G. R. Smith, P. M. Lieberman, M. E. McDonnell, Y. Zhang, M. Carlsen, and S. Chen (Oct. 15, 2019).

10. US 10,485,791. Riluzole Prodrugs and Their Use; with J. E. Wrobel, J. C. Pelletier, G. R. Smith and H. Bian (Nov. 26, 2019).

11. US 10,562,870. Prodrugs of Riluzole and Their Method of Use; with G. R. Smith, M. McDonnell, S. Chen, M. D. Vera, B. E. Blass, J. C. Pelletier, V. N. Velvadapu, and J. E. Wrobel (Feb. 18, 2020).

12. US 10,639,298. Prodrugs of Riluzole and their Method of Use; with G. R. Smith, H. Bian, J. E. Wrobel and J. C. Pelletier (May 5, 2020).

13. US 10,780,084. Antibody-Recruiting Molecules for the Treatment of Cancer; with D. Spiegel, H. M. Loughran, J. C. Pelletier, and M. E. Welsch (Sept. 22, 2020).

14. US 10,844,026. Prodrugs of Riluzole and their Method of Use; with G. R. Smith, M. McDonnell, S. Chen, M. D. Vera, B. E. Blass, J. C. Pelletier, V. N. Velvadapu, and J. E. Wrobel (Nov 24, 2020).

15. US 10,905,681. Riluzole Prodrugs and Their Use; with J. E. Wrobel, J. C. Pelletier, G. R. Smith, and H. Bian (Feb. 2, 2021).

16. US 10,981,867. EBNA1 Inhibitors and Methods Using Same; with T. E. Messick, G. R. Smith, P. M. Lieberman, M. E. McDonnell, Y. Zhang, M. Carlsen and S. Chen (Apr. 20, 2021).

17. US 11,052,070. Riluzole Prodrugs and Their Use; with J. E. Wrobel, J. C. Pelletier, G. R. Smith and H. Bian (July 6, 2021).

18. US 11,197,864. Pro-Drugs of Riluzole and Their Method of Use for the Treatment of Amyotrophic Lateral Sclerosis; with G. R. Smith (Dec. 14, 2021).

19. US 11,358,935. Prodrugs of Lanicemine and Their Method of Use; with J. C. Pelletier (June 14, 2022).

20. US 11,472,776. Quinazolines that Inhibit the Formation of Tau Oligomers and their Method of Use; with E. J. Davidowitz, J. G. Moe, H. Bian, C. Glucowski, J. Hendrix, A. S. Yehaskel, M. E. McDonnell, and H. Marie Loughran (Oct. 18, 2022).