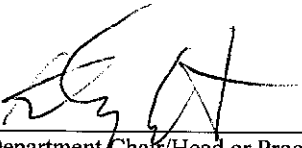


UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES
GRADUATE FACULTY APPLICATION

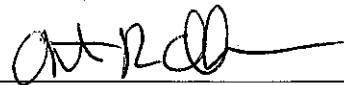
1. Name: Brendan Frett, Ph.D.
2. UAMS Graduate Program Sponsor: Pharmaceutical Sciences Graduate Prog Major field: Medicinal Chemistry
3. Present UAMS academic title or administrative position: Assistant Professor, Dept. Pharmaceutical Sci, COP
- Date appointed this rank/position: 8/1/2016 Employed by: College of Pharmacy, UAMS

4. **Comments of Department Chair/Head or Program Director including: evidence of scholarly development, effectiveness as a teacher, quality of publications and reallocation of duties if this application is approved.**

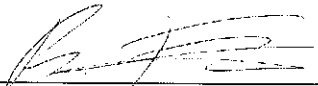
Dr. Frett is a new addition to the program and brings expertise in the area of medicinal chemistry, especially focused on small molecule kinase inhibitors. He will participate in graduate student education through current didactic core courses, as well as elective courses. In addition, he is a member of the current drug discovery and development group and will be asked to serve on dissertation committees and eventually recruit and direct graduate student dissertation research.


Department/Chair/Head or Program Director

8/20/17
Date


Graduate Council Representative

I have read the comments of my Department Chair/Head or Program Director and I do, do not (circle one) wish to supply additional information in support of my application.


Applicant's Signature

04/20/2017
Date

Approvals

Chair, Graduate Faculty Committee

Date

Chair, Graduate Council

Date

Dean of the Graduate School

Date

5. **List your planned involvement in graduate education (courses, theses, dissertations):**

My goal is to teach two graduate courses per semester. As a new faculty member, I am currently prioritizing laboratory work to establish a research program. As I progress in my research and position, I will be eager to take on additional teaching responsibilities.

6. **Briefly summarize your experience in graduate-level classroom teaching:**

This semester (Spring 2017), I was a lecturer in the team-taught course PSGP 6114 "Practice in Drug Discovery and Development". I gave two 2.5 hour lectures.

7. **Briefly summarize your experience in research and student research mentoring:**

My research experience is in drug discovery and development. I have mentored many graduate students and post-docs in the laboratory and also in career development.

Rajiv Lakkaniga, Graduate Student, UAMS, 2016-Present.
Dr. Naresh Gunaganti, Postdoc, University of Arizona and UAMS, 2016-Present.
Dr. Jaideep Bharate, Postdoc, University of Arizona and UAMS, 2016-Present.
Caitlin McHugh, Intern in Market Assessment, Synactix Pharmaceuticals, 2016.
Nicholas McConnell, Graduate Student, University of Arizona and UAMS, 2014-Present.
Lingtian Zhang, Graduate Student, University of Arizona and UAMS, 2015-Present.
Ben Rounseville, Undergraduate Student, University of Arizona, 2014-2016
Christina Warner, Undergraduate Student, University of Arizona, 2014-2015.
Natalie Debolske, Undergraduate Student, University of Arizona, 2014-2015.
Max Zocchi, Undergraduate Student, University of Arizona, 2014-2015.
Gabriela V. Fernandez-Curvro, Graduate Student, University of Arizona, 2014.
Briana Tully, Summer Internship, University of Arizona, 2012

8. **Attach Curriculum Vita** showing educational background (including institutions attended, degrees awarded and dates), honors or awards received, scholarly or professional organization affiliations, teaching experience (give school, dates and advanced and graduate subjects taught), including student theses and/or dissertations supervised. Cite publications and research in progress.

Brendan Frett, Ph.D.

University of Arkansas for Medical Sciences
College of Pharmacy
325 Jack Stephens Drive
Little Rock, Arkansas 72205
bfrett@uams.edu
501-526-0893



EDUCATION **Ph.D.**, Pharmaceutical Sciences, **June 2014**
Emphasis in Drug Discovery and Development
University of Arizona, Tucson, AZ
GPA: 4.0/4.0

B.A., Biochemistry & Molecular Biology, **May 2009**
The College of Wooster, Wooster, OH
Major: Biochemistry & Molecular Biology
Minor: History

WORK EXPERIENCE

08/2016-Present **Assistant Professor**, UAMS, Little Rock, AR

05/2014-Present **Co-Founder**, Synactix Pharmaceuticals, Inc., Tucson, AZ

09/2014-Present **Co-Founder**, Promutech Pharmaceuticals, Inc., Tucson, AZ

RESEARCH EXPERIENCE

07/2014-07/2016 **Postdoctoral Research Associate and Laboratory Manager**, University of Arizona, Tucson AZ
College of Pharmacy, Medicinal Chemistry

05/2011-06/2014 **Graduate Research Assistant**, University of Arizona, Tucson, AZ
College of Pharmacy, under Dr. Hong-Yu Li

Dissertation title "Discovery and Development of Novel RET Inhibitors for the Treatment of Pervasive Malignancies"

05/2008-05/2009 **Research Assistant**, Ohio State University, Wooster, OH
Ohio Agricultural Research and Development Center (OARDC)
Department of Animal Sciences, under Dr. Thaddeus Ezeji

TEACHING EXPERIENCE

08/2009-06/2010 **Teacher**, Evanston Township High School, Evanston, IL
Teacher for Advancement via Individual Determination (AVID) program
Assisted underperforming students in the development of math and science skills.
Teacher for Youth Technology Corps (YTC) program.
Helped students learn to build and program computers.

08/2007-05/2009 **Teaching Assistant**, The College of Wooster, Wooster, OH

Taught undergraduates the principles of chemistry in both the classroom and laboratory and evaluated their progress.

PUBLICATIONS

18. Wang, J.; Cheng, P.; Pavliukov, M.S.; Zhang, Zhuo; Kim, S.-H.; Minata, M.; Mohyeldin, A.; Xie, W.; Chen, D.; Goidts, V.; **Frett, B.**; Hu, W.; Li, H.; Shin, Y.J.; Lee, Y.; Nam, D.H.; Wang, M.D.; Nakano, I. Targeting NEK2 attenuates glioblastoma growth and radio-resistance via stabilizing EZH2, *J. Clin. Invest.* (2017) In Press.
17. Xi J.; Fang, Y.; **Frett, B.***; Zhu, M.-L.; Zhu, T.; Kong, Y.-N.; Guan, F.-J.; Zhao, Y.; Zhang, X.-W.; Li, H.; Ma, M.; Hu, W., Structure-based design and synthesis of imidazo[1,2-a]pyridine derivatives as novel and potent Nek2 inhibitors with in vitro and in vivo antitumor activities, *Eur. J. Med. Chem.* (2017) 126, 1083-1106.
16. Fang, Y.; Kong, Y.; Xi, J.; Zhu, M.; Zhu, T.; Jiang, T.; **Frett, B.**; Hu, W.; Li, H.; Ma, M.; Zhang, X. Preclinical activity of MBM-5 in gastrointestinal cancer by inhibiting NEK2 kinase activity, *Oncotarget*, (2016) 6, 79327-79341.
15. **Frett, B.**; Carlomagno, F.; Moccia, L.; Brescia, A.; Federico, G.; De Falco, V.; Admire, B.; Chen, Z.; Qi, W.; Massimo, S.; Li, H. Inside Back Cover: Fragment-Based Discovery of a Dual pan-RET/VEGFR2 Kinase Inhibitor Optimized for Single-Agent Polypharmacology (Angew. Chem. Int. Ed. 30/2015). *Angew. Chem. Int. Ed.* (2015), 30, 8847.
14. **Frett, B.**; Carlomagno, F.; Moccia, L.; Brescia, A.; Federico, G.; De Falco, V.; Admire, B.; Chen, Z.; Qi, W.; Massimo, S.; Li, H. Fragment-based discovery of a dual pan-RET/VEGFR2 kinase inhibitor optimized for single-agent polypharmacology. *Angew. Chem. Int. Ed.* (2015), 30, 8717-8721.
13. **Frett, B.**; McConnell, N.; Smith, C.; Shah, N.P.; Li, H. Computer Aided Drug Discovery of Highly Ligand Efficient, Low Molecular Weight Imidazopyridine Analogues as FLT3 Inhibitors. *Eur J Med Chem* (2015), 94, 123-131.
12. Wang, Y.; **Frett, B.**; McConnell, N.; Li, H. Metal-Free, Efficient Hydrazination of Imidazo[1,2-a]pyridine with Diethyl Azodicarboxylate in Neutral Media. *Organic & Biomolecular Chemistry* (2015), 13, 2958-2964.
11. **Frett, B.**; Moccia, M.; Carlomango, F.; Santoro, M.; Li, H. Identification of two novel RET kinase inhibitors through MCR-based drug discovery: design, synthesis and evaluation. *Eur J Med Chem* (2014), 86, 714-723.
10. **Frett, B.**; McConnell, N.; Wang, Y.; Xu, Z.; Ambrose, A.; Li, H. Identification of pyrazine-based TrkA inhibitors: design, synthesis, evaluation, and computational modelling studies. *MedChemComm* (2014), 5, 1507-1514.
9. Fang, Li; **Frett, B.**; Li, H. Selective Reduction of Halogenated Nitroarenes with Hydrazine Hydrate in the Presence of Pd/C. *SynLett* (2014), 25, 1403-1408.
8. Wang, Y.; **Frett, B.**; Li, H. Efficient Access to 2,3-Diarylimidazo[1,2-a]pyridines via a One-Pot, Ligand-Free, Palladium-Catalyzed Three-Component Reaction under Microwave Irradiation. *Organic Letters* (2014), 16, 3016-3019.
7. **Frett, B.**; Brown, RV; Ma, M; Hu, W.; Han, H.; Li, H. The Therapeutic Melting Pot of Never in Mitosis Gene A-Related Kinase 2 (Nek2): A Perspective on Nek2 as an Oncology Target and Recent Advancements in Nek2 Small Molecule Inhibition. *J Med Chem* (2014), 57, 5835-5844.
6. Wang, Y.; Saha, B.; Li, F.; **Frett, B.**; Li, H. An expeditious approach to access 2-arylimidazo[1,2-a]pyridin-3-ol from 2-amino pyridine through a novel Petasis based cascade reaction. *Tetrahedron Letters* (2014) 55, 1281-1284.
5. **Frett, B.**; Wang, Y.; Li, H. Targeting the K-Ras/PDE δ Protein-Protein Interaction: The Solution for Ras-Driven Cancers or Just Another Therapeutic Mirage? *Chem Med Chem* (2013), 8, 1620-1622.
4. Wang, Y., Kaiser C., **Frett, B.**, Li, H., Targeting mutant KRAS for anticancer therapeutics: a review of novel small molecule modulators. *J Med Chem* (2013), 56, 5219-5230.
3. Saha, B., **Frett, B.**, Wang, Y., Li, H., A p-toluenesulfinic acid-catalyzed three-component Ugi-type reaction and its application for the synthesis of α -amino amides and amidines. *Tetrahedron Letters* (2013), 54, 2340-2343.
2. Roberts S., Saha B., **Frett, B.**, Li H., Title (Z)-N-(tert-butyl)-N'-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-2-phenyl acetimidamide, *Acta Cryst E* (2013), E69, o902.
1. Gunawan S., Ayaz M., De Moliner F., **Frett, B.**, Kaiser C., Patrick N., Xu Z., Hulme C. Synthesis of tetrazolo-fused benzodiazepines and benzodiazepinones by a two-step protocol using an Ugi-Azide reaction for initial diversity generation. *Tetrahedron* (2012), 68, 5606-5611.

PATENTS

- H. Li; **B. Frett***, M. Santoro, Carlomagno F., Preparation of Imidazole Analogues of RET Kinase Inhibitors as antitumor agents. PCT Int. Appl. (2015), WO 2015187818 A1 20151210.
- H. Li; **B. Frett***. Small Molecule Inhibitors of Nek2 and Uses Thereof. Provisional Patent Filed, October 31, 2016.
- H. Li, **B. Frett***, Neil Shah. Small Molecule Inhibitors of FLT3 and Uses Thereof. Provisional Patent Filed, June 20, 2016.
- H. Li, **B. Frett***, Neil Shah. Small Molecule Inhibitors of FLT3/ITD and Uses Thereof. Provisional Patent Filed in June 22, 2016.

ABSTRACTS

- B. Admire; R. Patel; **B. Frett**; S.H. Yalkowsky. *Preformulation study of a novel anti-cancer agent*, 2014 AAPS Annual Meeting and Exposition, November **2014**.
- **B. Frett**; H.Y. Li. *RET Inhibitors as Novel Therapeutics for Melanomas*, 11th International Skin Carcinogenesis Conference, June **2014**.
- **B. Frett**; H.Y. Li. *From Bench to Bedside: The Beautiful Reality of Academic-Based Pharmaceutical Development*, 2012 Frontiers in Biomedical Research Poster Forum, November **2012**.
- **B. Frett**; A. Sharma; H. Y. Li. *One-Step Access to 3-Aminoimidazoazines for the Development of Kinase Inhibitors Utilizing the Groebke-Blackburn-Bienayme Reaction*. National Medicinal Chemistry Symposium, May **2012**.

SCHOLARLY PRESENTATIONS

- **B. Frett**, *Single-agent, precision medicine engineered to simultaneously target RET, RET mutants, and tumor stroma*, 2016 International Thyroid Oncology Group (ITOG) Annual Meeting, University of Colorado, May 1, **2016**.
- **B. Frett**, *Discovery and Development of Dual-RET/VEGFR2 Inhibitors for the Treatment of RET-Driven Malignancies*, Department Seminar, College of Pharmacy, University of Arkansas Medical Sciences, February 26, **2016**.
- **B. Frett**, H.Y. Li, *Discovery and Development of Novel RET Inhibitors for the Treatment of Pervasive Malignancies*, Final Thesis Seminar, June 23, **2014**.
- **B. Frett**, H.Y. Li, *RET Kinase SAR Investigation and Updates on Advanced Medicinal Chemistry Projects*, Biological Chemistry Program Retreat, November 11, **2013**.
- **B. Frett**, H.Y. Li, *Academic Based Pharmaceutical Development: Overcoming Adversity in a Highly Competitive Market*. Biological Chemistry Program Seminar, February 12, **2013**.
- **B. Frett**, H.Y. Li, *From Bench to Bedside: The Beautiful Reality of Academic-Based Pharmaceutical Development*, 2012 Frontiers in Biomedical Research Poster Forum, November 7, **2012**.
- **B. Frett**, A. Sharma, H. Y. Li, *One-Step Access to 3-Aminoimidazoazines for the Development of Kinase Inhibitors Utilizing the Groebke-Blackburn-Bienayme Reaction*. National Medicinal Chemistry Symposium, May 21, **2012**.
- **B. Frett**, H.Y. Li, *Discovery and Development of RET and RET Mutant Inhibitors for The Treatment of Medullary Thyroid Cancer*, Drug Discovery and Development Seminar, College of Pharmacy, December 1, **2011**.
- **B. Frett**, S. Gunawan, C. Hulme, *Synthesis of Fused Benzodiazepine -Tetrazaoles*, Spring 2011 BCP Journal Club Poster Session, Department of Chemistry and Biochemistry, March **2011**.
- **B. Frett**, H.Y. Li, *Synthesis of Novel Benzimidazole Kinase Inhibitors for Future Therapeutics and Molecular Probes*, Fall 2010 BCP Journal Club Poster Session, Department of Chemistry and Biochemistry, December **2010**.
- **B. Frett**, G. Wondrak, *Mechanism of Heat Shock Induced by a 4-[bis(phenyl)methylene]-2,5-cyclohexadien-1-one (BPMC) Derivative*, Fall 2010 BCP Journal Club Poster Session, Department of Chemistry and Biochemistry, October **2010**.

GRANTS and FELLOWSHIPS

- P20 GM109005. PI. 'Mitigating The Side Effects of Cancer Therapy Through Syk Inhibition', **\$75,000**. April **2017-2018**.
- 3R41CA195826-01. PI, Grant Writer, SO. 'Synactix Pharmaceuticals I-Corps Application', **\$40,000**. Synactix Pharmaceuticals, Inc. March **2016-May 2016**.
- 1R41CA195826-01. PI, Grant Writer, SO. 'Pre-IND Study of Pz-1, a dual pan-RET/VEGFR2 inhibitor for the Treatment of RET-driven Disease', **\$299,976.00**. Synactix Pharmaceuticals, Inc. **Impact Score 27**. September **2015-December 2016**.
- 1R41CA199753-01. Key Personnel, Grant Writer, SO. 'Pre-IND study of PMT-254, a pan-FLT3 inhibitor for the treatment of FLT3 driven cancers', **\$285,520.36**. Promotech Pharmaceuticals, Inc. **Impact Score 22**. September **2015-August 2016**.
- 1R01CA176498-01A1. Key Personnel, Grant Writer. 'Selective RET Kinase and Its Mutant Inhibitors for the Treatment of Medullary Thyroid Cancer.' **12th Percentile**. January **2016-2019**.
- 1R01CA194094-01. Key Personnel, Grant Writer. 'Discovery and Development of a Selective pan-FLT3-ITD Kinase Inhibitor Clinical Candidate for the Treatment of FLT3-ITD-Driven AML.' **9th Percentile**. August **2015-2019**.
- 3T32GM008804-10S1. Fellow. NIH Training Grant Research Fellowship, **\$22,032**. July **2013-July 2014**.
- Caldwell Health Sciences Research Fellowship, **\$3,000**. January **2013**.
- 5T32GM008804-10. Fellow. NIH Training Grant Research Fellowship, **\$22,032**. July **2012-July 2013**.

SCHOLARLY GROUPS and ORGANIZATIONS

- Member of the Biological Chemistry Program (BCP), University of Arizona, **2010-2014**.
- *Phi Alpha Theta*, National History Honors Society Member, **2009-Present**.

MENTORING and DEVELOPMENT

- Rajiv Lakkaniga, Graduate Student, UAMS, **2016-Present**.
- Dr. Naresh Gunaganti, Postdoc, University of Arizona and UAMS, **2016-Present**.
- Dr. Jaideep Bharate, Postdoc, University of Arizona and UAMS, **2016-Present**.
- Caitlin McHugh, Intern in Market Assessment, Synactix Pharmaceuticals, **2016**.
- Nicholas McConnell, Graduate Student, University of Arizona and UAMS, **2014-Present**.
- Lingtain Zhang, Graduate Student, University of Arizona and UAMS, **2015-Present**.
- Ben Miller, Undergraduate Student, University of Arizona, **2015**.
- Ben Rounseville, Undergraduate Student, University of Arizona, **2014-2016**
- Christina Warner, Undergraduate Student, University of Arizona, **2014-2015**.
- Natalie Debolske, Undergraduate Student, University of Arizona, **2014-2015**.
- Max Zocchi, Undergraduate Student, University of Arizona, **2014-2015**.
- Andrew Ambrose, Graduate Student, University of Arizona, **2014**.
- Gabriela V. Fernandez-Curvro, Graduate Student, University of Arizona, **2014**.
- Briana Tully, Summer Internship, University of Arizona, **2012**.

SKILLS

- Ability to produce biologically active compounds with desirable drug-like properties in high purity (>95% by LC-MS).
- Outstanding managerial skillset by providing outstanding leadership and direction.
- Highly skilled and gifted in the identification and development of novel small molecule inhibitors, designed numerous (>50) small molecule inhibitors with biochemical and cell based potency at < 1.0 nM.
- Proficient in mid throughput screening to generate compound activity data using enzyme screening and profiling assays (Screening of 100+ compounds simultaneously).
- Proficient in data analysis.
- Proficient in mid throughput assay development to screen biologically relevant compounds.
- Proficient in pharmacokinetic analysis (sample preparation, method development, and analysis of plasma samples).
- Highly proficient in synthetic development to generate various target compounds.
- Proficient in various formulation techniques and procedures.
- Proficient in multi-step organic synthesis (>12 steps).
- Proficient in large scale, multi-gram synthesis (>50 gram scale).
- Proficient in parallel synthesis/purification (20+ compounds in sequence).
- Proficient in lead optimization utilizing crystallography and activity data.
- Skilled in the characterization and structural identification of organic compounds
 - NMR (¹H, ¹³C, LC-MS).
- Experienced with synthetic techniques involving microwave chemistry.
- Proficient in chemistry software
 - ChemDraw
 - E-Notebook
- Proficient in chemical reaction databases
 - Reaxys
 - SciFinder
- Experienced in a variety of biological assays.
 - SDS-page, PCR, microarray, gel electrophoresis
- Proficient in computational-based drug discovery.
 - AutoDock Vina
 - Drug Discovery Studio
- Excellent communication and writing skills.
- Ability to collaborate effectively in a team.
- Outstanding talent in converting innovative research into high-impact publications.
- Extremely gifted in the art of grantsmanship and at producing exceedingly fundable research concepts.

HONORS and AWARDS

- Academic Achievement Award, College of Pharmacy, University of Arizona, August **2013**.
- Received honors for undergraduate senior thesis, *Synthesis, Purification, and Characterization of Products from the Siloxymethylation of Glucose for the Eventual Synthesis of the Retinoid C-Linked Retinoyl β -Glucuronide*. May **2009**.
- *Compton Scholarship Award* (\$60,000), College of Wooster, **2005-2009**.

REFERENCES

- Dr. Hong-yu Li, Ph.D., Professor of Medicinal Chemistry, University of Arkansas for Medical Sciences, Helen Adams & Arkansas Research Alliance Endowed Chair in Drug Discovery, College of Pharmacy, *Little Rock, Arkansas*.
 - 501-269-1154
 - HLi2@uams.com
- Dr. Neil Shah, M.D./Ph.D., Edward S. Ageno Distinguished Professor of Hematology/Oncology; Leader, Hematopoietic Malignancies Program, UCSF School of Medicine. *San Francisco, California*.
 - 415-476-3303
 - nshah@medicine.ucsf.edu
- Dr. Massimo Santoro, M.D./Ph.D., Professor of General Pathology, Università di Napoli "Federico II". *Naples, Italy*.