Michaël D. B. Fenster

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API Project Leader ■ Chemical & Synthetic Development

Highly effective and collaborative API Project leader in Chemical Development with experience over the full development timeline from IND Toxicology to launch. 12 years in big pharma (Bristol-Myers Squibb) with consistent high performance. Proven track record for quickly delivering robust, safe, efficient and cost effective processes from mgs to multi-kgs with focus on results and pragmatism. Effective leader of teams and coordination of cross-functional activities. Author of 18 publications and 2 patents.

Core competencies include:

- Personnel management
- Project management
- Excellent presentation skills
- Strong soft skills
- API team leadership
- Process research and development
- Technology transfer to pilot and commercial plant
- Regulatory strategy
- Quality by design (QbD)
- Fate and tolerance (Impurity control strategy)
- Genotoxic control strategy
- Validation campaign for commercial supplies
- FMEA - quality risk assessments cGMP awareness
- Commercial awareness
- Strategic thinking
- Bilingual: French-English

PROFESSIONAL EXPERIENCE

2016-present: Principal Scientist, Bristol-Myers Squibb, New Brunswick, USA

- Career manager for 4 direct reports
- Project Leader of late stage asset with team of 8 internal scientists (analytical, chemistry, and engineering) and 3 vendor sites responsible for technological improvements resulting in increased robustness and 3-fold overall yield improvement
- Project Leader / Chemistry Leader of early asset
- Co-Chair of Department Talent Governance
- Part-Time Rotation for Interdisciplinary Project Leader

2013-2016: Senior Research Investigator II, Bristol-Myers Squibb, New Brunswick, USA

- Project Leader of 5 early stage assets, one of which has progressed to Ph2; responsible for leading project teams of up to 10 scientists and coordinated with leaders from other functions within the Pharmaceutical Development organization.
- Proposed and implemented improved synthetic routes to API under aggressive timelines.
- Proposed and supervised the development of a new synthetic route that afforded API in 6 steps (17% overall yield), representing a dramatic improvement from the original 10 step (0.03% overall yield).
- Led project team of five PhD level scientists; direct Manager for 2 PhD level chemists.
- Adherence to and knowledge of cGMP and regulatory requirements
- Managed several outsourced campaigns with external suppliers to ensure successful process execution and timely delivery of intermediates.
- Contributed to IND filing activities.
- Organic Process Research & Development reviewer

2009-2013: Senior Research Investigator I, Bristol-Myers Squibb, New Brunswick, USA

- Project Leader for two early stage assets; responsible for leading teams of up to 8 scientists to deliver API in support of IND Toxicology and First-in-Human Studies.
- Engaged cross-functional teams within the Pharmaceutical Development organization.

- Served as lead chemist for a program that progressed from PhI to validation; partnered with the lead engineer to drive process development required to ensure successful scale up execution and tech transfer for commercial manufacture.
- Coordinated a team of three scientists to streamline the synthesis of an advanced intermediate to supply a clinical candidate: yield improvement of 20%, removal of 4 unit operations (60% reduction), and a 2-fold increase in throughput resulting in significant time and monetary savings
- Initiated Design of Experiments (DoE) and mechanistic model with DynoChem to determine design space and ensure Quality by Design (QbD) for a challenging chemical transformation.
- Direct Manager of a PhD level employee.

2006-2009: Research Investigator II, Bristol-Myers Squibb, New Brunswick, USA
- Proposed, coordinated, and implemented a complete change in synthetic route to the API. Work completed in only three months prior to 120 kg campaign. Changes produced a 30% savings in raw material cost, accelerated cycle time and eliminated two process steps, thus reducing waste stream quantities and increasing overall yield from basic starting material by 40%. *Overall cost savings were in excess of US$1 million.*
- Participated in the development and execution of three campaigns to deliver API for toxicology, first-in-human (FIH), and subsequent clinical studies.
- Oversaw outsourcing activities to ensure timely delivery of intermediates of expected quality.
- Developed skills required for successful process execution, such as reaction condition optimization, reaction kinetics, work-up, distillations, crystallization, and filtration performance.
- Participated in developing process metrics to evaluate three synthetic routes to API.

Summer 1997: Research Assistant, Dow Chemical Inc., Sarnia, Canada
Supervisor: Deb Walker
Research: Development and Validation of Tearing Methods for Polyethylene Films
- Devised numerous robotic tear methods of plastic films to determined failure mode resulting in four internal publications.

Summer 1996: Research Assistant, Pulp and Paper Institute of Canada, Montréal, Canada
Supervisor: Professor Dimitri S. Argyropoulos
Research: Effect of Metal Ions on the Reaction of Hydrogen Peroxide with Kraft Lignin Model Compounds
- Carried pressurized experiments to determined possibility of improving paper production by use of metal ions.

EDUCATION

Post-Doctoral Research Fellow (2004-2006), Max-Planck-Institute, Mülheim, Germany
Supervisor: Professor Alois Fürstner
Research: Synthesis of Latrunculin Analogues and Total Synthesis of Spirastrellolide A
- Proposed and coordinated efforts towards the synthesis of Spirastrellolide A, resulting in four publications. Two publications were highlighted as journal covers and third was designated as VIP.
- Supervised one Post-Doctoral Fellow, a PhD student, and two technicians.
- Completed structure activity relationship studies of Latrunculin analogues in a short period (three months) by synthesizing numerous analogues; culminated in three publications.

Ph. D. in Chemistry (2004), University of British Columbia, Vancouver, Canada
Supervisor: Professor Gregory R. Dake
Thesis Title: Formation of 1-Azaspirocycles via Semipinacol Rearrangements and its Application to the Synthesis of Fasicularin
- First student to join the group; helped initiate research programs.

- Supervised three honors students as well as incoming PhD students.
- Responsible for laboratory equipment maintenance and purchase.
- Presented work at conferences to audiences of up to *ca. 400 people.*
- Research culminated in five publications.

B. Sc. in Chemistry (1998), McGill University, Montréal, Canada with honours and a bio-organic option

PERSONAL

Birthplace: Montréal, Canada

US Green Card Holder

Citizenship: Canadian and Swedish

Languages: Fluent in French and English; knowledge of German, Spanish, and Swedish

Member of the American Chemical Society since 2001

Reviewer for Organic Process Research and Development

AWARDS

Numerous Internal Bristol-Myers Squibb Chemical Development Recognition Awards **2006-2018**

- Excellent Project Leadership on Commercial Route Development
- Excellent Project Leadership for an Accelerated Ph2 API Delivery
- Outstanding Leadership of 2014 R&D Symposium
- Excellent Leadership for a Rapid Development and Execution of an IND Tox Delivery
- Outstanding Leadership of 2013 R&D Symposium
- Successful Validation Campaign
- Organizing Committee of 2012 R&D Symposium
- Successful LTSS Campaign and Demonstration of Robust Process with High Variability
- Successful pre-LTSS Campaign
- Organizing Committee of 2011 R&D Symposium
- Green Chemistry Awards for Significant Improvements to API Synthetic Route
- Early adoption of e-Notebook

Natural Sciences and Engineering Research Council of Canada Post-Doctoral Research Fellowship **2005**

Deutscher Akademischer Austausch Dienst Post-Doctoral Research Fellowship **2004**

Alexander von Humboldt Post-Doctoral Research Fellowship **2004**

Boehringer Ingelheim Graduate Research Scholarship **2003**

R. U. Lemieux Poster Award (85th Canadian Society for Chemistry Conference) **2003**

Gladys Estella Laird Research Fellowship **2001-2002**

C. A. McDowell Graduate School Entrance Scholarship **1998**

Dow Chemical Undergraduate Achievement Award **1997**

EXTERNAL PRESENTATIONS

12. ***Fenster, M. D. B.*** "Process Invention, Improvements, and Delivery of Kilogram Quantities of API to Enable Clinical Studies in Advanced Cancer" to be presented at the Harvard BMS Lecture in Synthetic Organic Chemistry, Cambridge, MA, November 26th 2018 (Oral presentation by M. Fenster)

11. ***Fenster, M. D. B.;*** Hallow, D.; Domagalski, N.; Hobson, L.; Lou, S.; Ferreira, G. "Discovery and Development of a Robust Process for the Final Intermediate of Asunaprevir" Presented at the 2015 Gordon Research Conference (GRC) on Organic Reactions and Processes, Lewiston, ME, July 2015 (Poster presentation by M. Fenster)

10. Young, I.; Katipally, K.; Zhu, J.; Kolotuchin, S.; Simmons, E; ***Fenster, M. D. B.*** "Necessity for Extreme Purity Upgrade During the Synthesis of a Type 2 Diabetes Drug Candidate " Presented at the 2015 Gordon Research Conference (GRC) on Organic Reactions and Processes, Lewiston, ME, July 2015 (Poster presentation by I. Young)

9. ***Fenster, M. D. B.***; Hanson L. R.; Katipally, K.; Paul, T.; Rao, R.; Simmons, E. M.; Young, I. S.; Zhu, J. J.; "Scalable Synthesis of a GPR40 Agonist" Presented at 248th National Meeting of the American Chemical Society, San Francisco, CA, August 2014; ORGN 119. (Oral presentation by M. Fenster).

8. Hallow, D.; ***Fenster, M. D. B***.; Ramirez, A.; Wethman, R.; Domagalski, N. "Implementation of Reaction Modeling and Process Analytical Technology in Design Space Development." Presented at the AIChE Annual Meeting, Pittsburgh, PA, November 2012. (Oral presentation by N. Domagalski).

7. ***Fenster, M. D. B.*** "Process Chemistry in the Pharmaceutical Industry: Key Concepts and Selected Examples" Invited lecture for the McGill Chemical Society Seminar Series, Montreal, PQ, February 2011 (Oral presentation by M. Fenster).

6. Mack, B. C.; Domagalski, N.; Hallow, D.; ***Fenster, M. D. B***.; Hobson, L.; Tabora J. E. "Implementation of Genetic Algorithms In the Generation of High-Order Statistical Models." Presented at the AIChE AnnualMeeting, Minneapolis, MN, October 2011 (Oral Presentation by B. Mack)

5. Domagalski, N.; ***Fenster, M. D. B.***; Doubleday, W.; Tom, J. "Crystallization for An API Intermediate" Presented at the 2009 AIChE Annual Meeting, Nashville, TN, November 2009 (Oral Presentation by N. Domagalski)

4. Kiau, S.; Gonzalez-Bobes, F.; ***Fenster, M. D. B.***; Kolotuchin, S.; Kolla, L.; Soumeillant, M. "Cyclopropanation of Alkenes with Diazomalonates Using Rh_2esp_2 as Catalyst" Presented at the 37th Northeast Regional Meeting of the American Chemical Society, Burlington, VT, June 2008, paper NERM 359. (Poster presentation by S. Kiau)

3. ***Fenster, M. D. B.***; Dake, G. R. "Asymmetric Total Synthesis of Fasicularin." Presented at the 39th International Union of Pure and Applied Chemistry Congress and the 86th Conference of the Canadian Society for Chemistry, Ottawa, ON, August 2003, paper OR.9.015. (Oral presentation by M. Fenster).

2. Dake, G. R.; ***Fenster, M. D. B.*** "Progress Towards the Asymmetric Synthesis of Fasicularin." Presented at the 85th CSC Conference and Exhibition, Vancouver, BC, June 2002; paper 1099. (Poster presentation by M. Fenster).

1. Dake, G. R.; ***Fenster, M. D. B.*** "Construction of Azaspirocyclic Ketones through α-Hydroxy-Iminium Ion Semipinacol Rearrangements." Presented at 222nd National Meeting of the American Chemical Society, Chicago, IL, August 2001; paper ORGN 337. (Poster presentation by M. Fenster).

SCIENTIFIC PUBLICATIONS

20. Burcu, S. A.; Deerberg, J.; Domagalski, N. R.; Eastgate, M. D.; Fan, Y.; Fenster, M. D. B.; González-Bobes, F; Green, r. A.; Kopp, N. D.; La Cruz, T. E.; Lauser, K.; Lee, H. G.; Luo, H. Y.; Savage, S.A.; Sfouggatakis, C.; Zaretsky, S.; Zheng, B.; Zhu, Y. "Process for the Preparation of N-((1R,2S,5R)-5-(*tert*-butylamino)-2-((S)-3-(7-*tert*-butylpyrazolo[1,5-A][1,3,5]triazin-4-ylamino)-2-oxopyrrolidin-1-yl)cyclohexyl)acetamide", Patent Appl. 12897-WO-PCT, Provisional application filed July 20th 2017

19. Young, I. S.; Simmons, E. M.; Fenster, M. D. B.; Zhu, J. J.; Katipally, K. R. *Org. Process Res. Dev.* **2018**, *22*, 585-594

18. Hanson, R. L.; Zhiwei, G.; Gonzalez-Bobes, F.; ***Fenster, M. D. B.***; Goswami, A. *J. Mol. Catal. B: Enzym.* **2016**, *133*, 20-26.

17. Ramirez, A.; Hallow, D. M.; ***Fenster, M. D. B.***; Sha, L.; Domagalski, N. R.; Tummala, S.; Srivastava, S.; Hobson, L. A. *Org. Process Res. Dev.* **2016**, *20*, 1781-1791.

16. Ayers, S.; Zhongping, S.; Marshall, J.; ***Fenster, M.***; Yande, H.; Pathirana, C. "An unexpected product from the attempted acetal formation of 2,4,6-trihydroxybenzaldehyde" *Tetrahedron Letters* **2015**, 56, 5132-5134.

15. Savage, S. A.; Domagalski, N. R.; Mack, B.; Vemishetti, P. Qiu, Y.; Fenster, M.; Hallow, D. M.; Ferreira, G.; Rogers, A. Sha L.; Hobson, L. "Preparation of Asunaprevir as Hepatitis C Virus Inhibitors", **2015**, WO 2015200305

14. Benson, S.; Collin, M.-P.; O'Neil, G. W.; Ceccon, J.; Fasching, B.; ***Fenster, M. D. B.***; Godbout, C.; Radkowski, K.; Goddard, R.; Fürstner, A. "Total Synthesis of Spirastrellolide F Methyl Ester–Part 2: Macrocyclization and Completion of the Synthesis" *Angew. Chem. Int. Ed.* **2009**, *48*, 9946-9950.

13. González-Bobes, F.; ***Fenster, M. D. B.***; Kiau, S.; Kolla, L.; Kolotuchin, S.; Soumeillant M. "Rhodium-Catalyzed Cyclopropanation of Alkenes with Diazomalonates" *Adv. Synth. Catal.* **2008**, *6*, 813-816.

12. Fürstner, A.; Fasching, B.; O'Neil, G. W.; ***Fenster, M. D. B.***; Godbout, C.; Ceccon, J. "Toward the Total Synthesis of Spirastrellolide A. Part 3: Intelligence Gathering and Preparation of a Ring Expanded Analogue" *Chem. Comm.* **2007**, *29*, 3045-3047.

11. Fürstner, A.; Kirk, D.; ***Fenster, M. D. B.***; Aïssa, C.; De Souza, D.; Nevado, C.; Tuttle, T.; Thiel, W.; Müller O. "Latrunculin Analogues with Improved Biological Profiles by "Diverted Total Synthesis: Preparation, Evaluation, and Computational Analysis" *Chem. —Eur. J.* **2007**, *13*, 135-149.

10. Fürstner, A.; De Souza, D.; Turet, L.; ***Fenster, M. D. B.***; Parra-Rapado, L.; Wirtz, C.; Mynott, R.; Lehmann C. W. "Total Syntheses of the Actin-Binding Macrolides Latrunculin A, B, C, M, S and 16-*epi*-Lactrunculin B" *Chem. —Eur. J.* **2007**, *12*, 115-134.

9. Fürstner, A.; ***Fenster, M. D. B.***; Fasching, B.; Godbout, C.; Radkowski, K. "Toward the Total Synthesis of Spirastrellolide A. Part 2: Conquest of the Northern Hemisphere" *Angew. Chem. Int. Ed.* **2006**, *45*, 5510-5515.

8. Fürstner, A.; ***Fenster, M. D. B.***; Fasching, B.; Godbout, C.; Radkowski, K. "Toward the Total Synthesis of Spirastrellolide A. Part 1: Strategic Considerations and Preparation of the Southern Domain" *Angew Chem. Int. Ed.* **2006**, *45*, 5506-5510.

7. Fürstner, A.; Kirk, D.; ***Fenster, M. D. B.***; Aïssa, C.; De Souza, D.; Müller, O. "Diverted Total Synthesis: Preparation of a Focused Library of Lantrunculin Analogues and Evaluation of their Actin-Binding Properties" *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 8103-8108.

6. ***Fenster, M. D. B.***; Dake, G. R. "An Asymmetric Formal Synthesis of Fasicularin" *Chem. —Eur. J.* **2005**, *11*, 639-649.

5. Dake, G. R.; ***Fenster, M. D. B.***; Fleury, M.; Patrick, B. O. "Investigations of α-Siloxy-Epoxide Ring Expansions Forming 1-Azaspirocyclic Ketones" *J. Org. Chem.* **2004**, *69*, 5676-5683.

4. Dake, G. R.; ***Fenster, M. D. B.***; Hurley, P. B.; Patrick B. O. "Synthesis of Functionalized 1-Azaspirocyclic Cyclopentanones Using Bronsted Acid or *N*-Bromosuccinimide Promoted Ring Expansions" *J. Org. Chem.* **2004**, *69*, 5668-5675.

3. ***Fenster, M. D. B.***; Dake, G. R. "A Formal Construction of Fasicularin" *Org. Lett.* **2003**, *5*, 4313-4316.

2. ***Fenster, M. D. B.***; Patrick, B. O.; Dake, G. R. "Construction of Azaspirocyclic Ketones through α-Hydroxyiminium Ion or α-Siloxy Epoxide Semipinacol Rearrangements" *Org. Lett*. **2001**, *3*, 2109-2112.

1. Sun, Y.; ***Fenster, M.***; Yu, A.; Berry, R.; Argyropoulos, D. S. "The Effect of Metal Ions on the Reaction of Hydrogen Peroxide with Kraft Lignin Model Compounds" *Can. J. Chem.* **1999**, *77*, 667-675.