CURRICULUM VITAE

DAVID M. MOTTOLA, PHD

OVERVIEW: Pharmaceutical/Biotech Industry Experience

- 21+ years R&D experience – in start-up, mid-size and large pharma settings
- Cofounded new pharmaceutical company and led start-up activities
- Led key global drug development strategies and activities: nonclinical program, IND submission, Phase 1 Clinical Pharmacology program, Phase 2 studies, FDA/EMA regulatory strategy and discussions, CMC support, Phase 3 multi-national pivotal studies, NDA submission, post approval commitments, Orphan Drug Designation filings, business development and due diligence activities, etc.
- Direct management and oversight of many R&D functional areas: Clinical Operations, Clinical Sciences, Project Management, Statistics and Data Management, Regulatory Affairs and Compliance, Pharmaceutical Development, etc.
- Therapeutic area experience: cardiovascular, cardiopulmonary, hepatology, ophthalmology
- 5 NDA approvals, 2 Orphan Drug Designation approvals

EDUCATION:

- *Ph.D., Pharmacology*, University of North Carolina, Chapel Hill, NC
- *B.S., Biology*, State University of New York, Binghamton, NY

EMPLOYMENT HISTORY:

2013 – Present **ACRIS Pharmaceuticals, LLC**
Chapel Hill, North Carolina

- *Cofounder, President & Chief Operating Officer*

1999 – 2012 **United Therapeutics Corp**.& **Lung (Rx), LLC** (subsidiary of United Therapeutics)
Research Triangle Park, North Carolina, and Silver Spring, Maryland

Held progressive leadership roles at United Therapeutics starting in 1999 and in 2010 was asked to lead Research and Development activities for Lung (Rx), LLC, a wholly owned subsidiary of the parent company, United Therapeutics.

- *Executive Vice President, Research and Clinical Development* (Lung Rx, LLC)

CURRICULUM VITAE

Positions held at United Therapeutics:
- *Senior Vice President, Clinical Operations, Clinical Quality and Standards and Preclinical Sciences*
- *Senior Vice President, Clinical Operations and Preclinical Sciences*
- *Senior Vice President, Product Development*
- *Vice President, Product Development*
- *Director, Clinical Affairs*

1996 – 1999 **Bausch & Lomb Pharmaceuticals Inc**.
Tampa, Florida
- *Senior Manager, Clinical and Scientific Affairs*
- *Manager, Clinical Affairs*

1992 - 1996 **Burroughs Wellcome Co./ Glaxo Wellcome Inc**.
Research Triangle Park, North Carolina
- *Principal Clinical Research Scientist*
- *Senior Clinical Research Scientist*
- *Clinical Research Scientist*
- *Clinical Research Associate*

PROFESSIONAL EXPERIENCE*:*

- Led company start-up activities including business strategy, IP evaluations, deal structure oversight, fund raising, company infrastructure set-up and management
- Direct responsibility for R&D department activities (strategic vision, leadership, goal setting, budget projections and management, resource allocation, project priorities, personnel development, department growth, and SOPs/policies, etc.)
- Managed and directed activities across various R&D functional departments (clinical, nonclinical [pharmacology and toxicology], pharmaceutical development, analytical sciences, statistics and data management, project management, regulatory and compliance, etc.)
- Led and supported multiple global/multi-national proprietary drug development programs (Phases 1 - 3) covering various therapeutic areas
- Foster key opinion leader (KOL) relationships and KOL management
- Directed and supported Phase 3 study Oversight Committees (Steering Committee, DSMC, Adjudication Committee)
- Actively contributed to regulatory submissions for multiple New Drug Applications (NDA), European Marketing Authorization Application (MAA), Investigational New Drug (IND) applications and equivalent applications in Europe and Asia, Orphan Drug Designation applications, and generic ANDA submissions and various responses to queries from regulatory authorities
- Oversight of all functional aspects of development programs (e.g., clinical, non-clinical, chemistry, manufacturing, controls (CMC), overall budgets, international project team, etc.)
- Directed/authored project specific documents (e.g., clinical development plans, protocols, study reports, etc.) and project-related publications (manuscripts and abstracts)

- Presented project/company information to regulatory authorities, project advisory boards, investigators, KOLs, and internal staff
- Worked closely with other company departments (e.g., compliance, legal, licensing, marketing, sales/commercial, etc.) to support development, launch and commercialization of new products
- Oversight of international department personnel selection (hiring/firing) and strategic growth
- Serve on Senior Management Council to discuss development programs, sales and marketing initiatives, budget issues and growth strategies
- Evaluation of strategic business opportunities, related due diligence, licensing agreements and/or strategic alliances
- Served on Joint Development Committees for partnered projects

PROFESSIONAL MEMBERSHIPS:

- American Thoracic Society

BIBLIOGRAPHY:

1. Gotzkowsky SK, Kumar P, Mottola D and Laliberte, K. Lack of a Pharmacokinetic Interaction Between Treprostinil Diolamine and Sildenafil in Healthy Adult Volunteers. J. Clin. Pharmacol. (submitted)

2. Whittle BJ, Silverstein AM, Mottola DM, and Clapp LH. Binding and activity of the prostacyclin receptor (IP) agonists, treprostinil and iloprost, at human prostanoid receptors: Treprostinil is a potent DP_1 and EP_2 agonist. Biochem. Pharmacol. 84:68-75, 2012

3. Gotzkowsky SK, Dingemanse J, Lai A, Mottola D and Laliberte, K Lack of pharmacokinetic interaction between oral treprostinil and Bosentan in healthy adult volunteers. J. Clin. Pharmacol. 50(7):829-34, 2010

4. Sandifer BL, Brigham KL, Lawrence EC, Mottola D, Cuppels C and Parker RE. Potent effects of aerosol compared with intravenous treprostinil on the pulmonary circulation. J. Appl. Phys. 99(6):2363-2368, 2005.

5. Mottola, DM, Lawler CP, Jones SR, Einhorn L, Booth RG, Wightman M, Nichols DE and Mailman RB. Functional selectivity of dopamine D2 receptors. I. Novel postsynaptic functional selectivity of dihydrexidine and its analogs in the rat central nervous system. J. Pharmacol. Exp. Ther. 301: 1166-1178, 2002.

6. Mottola, DM, S Laiter, VJ Watts, A. Tropsha, SD Wyrick, DE Nichols, and RB Mailman. Conformational Analysis of D_1 Dopamine Receptor Agonists: Pharmacophore Assessment and Receptor Mapping. J. Med. Chem. 39:285-296, 1996.

7. Brewster, WK, DE Nichols,VJ Watts, RM Riggs, DM Mottola, and RB Mailman. Evaluation of Cis and Trans-9- and 11-hydroxy-5,6,6a,7,8,12b-hexahydrobenzo[a]phenanthridines as Structurally Rigid, Selective D_1 Dopamine Receptor Ligands. J. Med. Chem. 38:318-327, 1995.

8. Knoerzer, TA, DE Nichols, WK Brewster, VJ Watts, DM Mottola, and RB Mailman. Dopaminergic Benzo[a]phenanthridines: Resolution and Pharmacological Evaluation of the

Enantiomers of Dihydrexidine, the Full Efficacy D_1 Dopamine Receptor Agonist. J. Med. Chem. 37:2453-2460, 1994.

9. Mottola, DM, WK Brewster, LL Cook, DE Nichols and RB Mailman. Dihydrexidine, a Novel Full Efficacy D_1 Dopamine Receptor Agonist. J. Pharmacol. Exp. Ther. 262: 383-393 1992.

10. Brewster, WK, DE Nichols, RM Riggs, DM Mottola, TW Lovenberg, MH Lewis and RB Mailman. Trans-10,11-Dihydroxy-5,6,6a,7,8,12b-Hexahydrobenzo[a]phenanthridine: A highly potent selective dopamine D_1 full agonist. J. Med. Chem. 33: 1756-1764 1990.

11. Lovenberg, TW, WK Brewster, DM Mottola, RC Lee, RM Riggs, DE Nichols, MH Lewis and RB Mailman. Dihydrexidine, a novel selective high potency full D_1 dopamine receptor agonist. Eur. J. Pharmacol. 166: 111-113 1989.

PATENTS:

Phares K and D Mottola, United Therapeutics Corp. US Patent No.: 7,384,978; 7,417,070; 7,544,713; 8,232,316; 8,252,839; 8,410,169 (Family ID 34079029) "Compounds and methods for delivering prostacyclin analogs" - Issued 2008-2013.

BOOK CHAPTERS:

Mottola, DM Nonanol. In *Browning's Toxicology and Metabolism of Industrial Solvents*, Vol. IV: Alcohols and Esters. RG Thurman and FC Kauffman eds. Elsevier Biomedical Press. 1992.

PUBLISHED ABSTRACTS:

1. Armstrong D, Wargin W, Mottola DM and Sullivan EJ. A Phase 1, single-center, single-dose, open-label, randomized crossover, comparative bioavailability and food effect study to compare BPS-314d-MR 15 µg and 60 µg tablet formulations to the existing BPS-MR 60 µg tablet formulation in healthy volunteers. American Thoracic Society Meeting, 2012.

2. Tapson V, Torres F, Kermeen F, Keogh A, Allen R, Franz R, Badesch D, Frost A, Shapiro S, Sigman, Grover R, Laliberte K, Mottola D, Galie N, and Simmoneau G. Results of FREEDOM-C: A pivotal study of oral treprostinil used adjunctively with an ERA and/or PDE5-inhibitor for the treatment of PAH. American Thoracic Society Meeting, 2009

3. White R, Allen R, Torres F, Jeres C, Pulido T, Carroll J, Yehle D, Laliberte K, Mottola D, Galie N, Simmoneau G, and Tapson V. Sustained Plasma Concentrations of Treprostinil following Chronic Dosing in Patients with Pulmonary Arterial Hypertension (PAH). American Thoracic Society Meeting, 2009

4. Rollins K, Laliberte K, Gotzkowsky, K, Wade M and Mottola D Overview of the drug-drug interactions potential with treprostinil. American Thoracic Society Meeting, 2009

5. White R, Allen R, Yehle D, Laliberte K, Mottola D, Galie N, Simmoneau G, Tapson V. Oral Treprostinil Diethanolamine Provides Sustained Therapeutic Plasma Concentrations Over a Wide Range of Doses in Patients with Pulmonary Arterial Hypertension. American Thoracic Society Meeting, 2008

6. Berman SS, RC Quick, C Johnson, D Strootman, K Rollins, D Mottola, McLafferty. Efficacy of an oral prostacyclin analog (treprostinil diethanolamine) in patients with advanced lower extremity peripheral arterial disease and ischemic rest pain. Society for Clinical Vascular Surgery Meeting, 2008

7. Laliberte K, Goetz B, Phares K, Mottola D. Sustained Treprostinil Plasma Concentrations Following Administration of UT-15C (Treprostinil Diethanolamine) Sustained Release Tablets in Healthy Volunteers. American Thoracic Society Meeting, 2007

8. Gotzkowsky K, Dingemanse J, Laliberte K, Goetz B, Mottola D. Lack of a Pharmacokinetic Drug Interaction Following Co-Administration of UT-15C (treprostinil diethanolamine) SR and Tracleer® (bosentan) in Healthy Volunteers. American Thoracic Society Meeting, 2007

9. Gotzkowsky K, Laliberte K, Goetz B, Mottola D. Lack of a Pharmacokinetic Drug Interaction Following Co-Administration of UT-15C (treprostinil diethanolamine) SR and Revatio™ (sildenafil citrate) in Healthy Volunteers. American Thoracic Society Meeting, 2007

10. Staszewski J, K Phares and D Mottola. Development of an oral prostacyclin analog (treprostinil diethanolamine) for the treatment of pulmonary arterial hypertension. American Chemical Society Meeting, 2006

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12. Gibbs JS, CP Arneson, D Mottola for treprostinil study group. Chronic infusion of treprostinil is safe, and appears to prolong survival over a three-year period in patients with pulmonary arterial hypertension. American Heart Association Meeting, Abstr. 2002.

13. Watson, D, J Donaldson, R Grover, D Mottola, K Guntupalli and J-L Vincent for the Wellcome International Septic Shock Study Group. The cardiopulmonary effects of 546C88 in human septic shock. Proceedings of the European Congress of Intensive Care Medicine, Abstr. 21:1.117 1995

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