Delivery of Therapeutic siRNA in Cystic Fibrosis

A thesis to be submitted to The Maharaja Sayajirao University of Baroda, Vadodara for the Degree of

DOCTOR OF PHILOSOPHY IN PHARMACY

By Sushilkumar Patil M. Pharm

Supervised By
Dr. Ambikanandan Misra
Professer of Pharmaceutics



Faculty of Pharmacy,
The Maharaja Sayajirao University of Baroda,
Vadodara - 390001, Gujarat, India.

October, 2016

DEDICATED

TO

MY DEAR PARENTS

AND

MYENDEARING GUIDE

<u>CERTIFICATE</u>

This is to certify that the thesis entitled "Delivery of Therapeutic siRNA in Cystic Firbosis", submitted for Ph.D degree in Pharmacy by Sushilkumar Patil comprises the original research work carried out by him under my guidance and supervision.

Research Supervisor

Prof. Ambikanandan Misra

Pharmacy Department

Dean

Faculty of Pharmacy
The Maharaja Sayajirao University of
Baroda, Vadodara, Gujarat.

DECLARATION

I hereby declare that the thesis on the topic entitled "Delivery of Therapeutic siRNA in

Cystic Fibrosis" which is submitted herewith to 'The Maharaja Sayajirao University of

Baroda, Vadodara' for the award of Ph.D. in Pharmacy is the result of work done by me in the

Pharmacy Department, Faculty of Pharmacy, The Maharaja Sayajirao University of Baroda,

under the able guidance of Prof. Ambikanandan Misra, Pharmacy Department, Faculty of

Pharmacy, The Maharaja Sayajirao University of Baroda, Vadodara.

I further declare that the result of this work has not been previously submitted for

any degree.

(Sushilkumar Patil)

Place: Vadodara

Date:

Certified by and forwarded through the research guide,

Dr Ambikanandan Misra

Professor in Pharmacy,

Faculty of Pharmacy,

The Maharaja Sayajirao University of Baroda,

Vadodara-390001

ACKNOWLEDGEMENTS

Undertaking this PhD has been a true life-changing lesson for me which would not have been possible without the conducive environment created by people around me with their help and support. So I would like to take this opportunity to thank them for their indispensable role in this journey.

First of all, with due respect, I thank my supervisor, Dr. Ambikanandan Misra, Professor in Pharmaceutics, Faculty of Pharmacy, The Maharaja Sayajirao University of Baroda for his privileged guidance, suggestions and help in all possible aspects to make me achieve my goals. His immense experience and immeasurable knowledge showed me the way to make the work informative and exhaustive. His observations and comments helped me to establish the overall direction of the research and to move forward with investigation in depth. His constant encouragement, and appreciation kept me motivated throughout and helped me immensely in completing this report on time.

I am thankful to **Dr. M.R. Yadav**, former Dean and Head and Professor, Pharmacy Department, The Maharaja Sayajirao University of Baroda for providing me the necessary facilities for the research work. I am thanlful to

I am grateful to University grant commission (UGC), India for their initiatives in funding and fellowships for research students and for awarding me UGS-BSR Fellowship.

I would like to sincerely express my gratitude to Dr. S. P. Rathod, Professor in Pharmacology, Dr. (Mrs.) S.J. Rajput, Professor in Pharmaceutical Quality Assurance, Late Dr. (Mrs.) Rajani Giridhar, Professor in Pharmaceutical Chemistry, Dr. (Mrs.) K.K. Sawant, Professor in Pharmaceutics, and Dr. RC Mashru, Reader of Pharmaceutical Quality Assurance, Pharmacy Department, The Maharaja Sayajirao University of Baroda for their invaluable support and advice during the research work.

I am thankful to the coordinators at Shri G H Patel Pharmacy Building and TIFAC-CORE in NDDS, Pharmacy Department, The M.S.University of Baroda, and all person associated with this sophisticated research facility having a confluence of information and infrastructure to smoothly carry out the research studies. In this regard I extend my gratitude to Vaishali Madam, Heenaben, Praghnesh, Chandrkant for being very kind and considerate in material procurements, accounting etc. I sincerely thank all the non-teaching staff for the smallest help they have offered.

I express my special thanks to Mr. Imran Vhora, as my companion in many academic and research activities and supplying valuable deliberations to work out on selected research methodology. I also thank all my colleague and co-researchers Rohan Lalani, Priyanka Bhatt, Jitendra Amrutiya, Hinal Patel for their dynamic support as friend as well as in conducting the experimental work in planned manner. My deep appreciation goes out to my friend Rajeev Mudakavi (IISC, Bangalore) for sharing his experiences and valuable suggestions in undertaking cell line studies.

I am grateful to all my lab seniors Mr. Atul kolte, Dipesh Bardiya, Girish Kore, Chetan Yewale for their support and sharing their valuable previous experiences providing glimpse of the anticipated challenges and furnishing viable solutions to them which helped me develop better research methodology.

I am thankful to Mrs. Saritha Gupta, Co-coordinator DBT-ILSPAIR for providing requisite facility such as NanoDrop, FACS, Confocal imaging etc. I am also thankful to staff at Vikram Sarabhai Central Instrumentation Facility, DBT-ILSPAIR, for providing necessary support and guidance in carrying out cell line studies.

I sincerely acknowledge the support by Sophisticated Analytical Instrumentation Facility (SAIF), Panjab University, Chandigarh for carrying out NMR studies. I am also thankful to facility at SICART, Vallabh Vidhyanagar and Sun Pharmaceuticals, Vadodara for their help in TEM studies.

I am indebted to my colleague from chemistry lab: Mahesh Shidore, Mahesh Baramade, Mayank Sharma for helping me with synthetic set-up, reagents and data interpretation. I am also thankful to my friends Ridhish Patadiya, Jatin Macchi who were always so helpful and provided me their assistance in numerous ways during various stages of my dissertation.

Lastly, I express hearty thanks to my beloved parents for their love, patience, and understanding as their support, encouragement and blessings helped me to pursue my interests. I hope with my hard work and dedication, I would be able to translate all their dreams into reality.