LIST OF PUBLICATIONS

Part of this thesis:

Maarten L.J. Doornbos, Sophie C. Vermond, Hilde Lavreysen, Gary Tresadern, Adriaan P. IJzerman, Laura H. Heitman. *Impact of allosteric modulation: exploring the binding kinetics of glutamate and other orthosteric ligands of the metabotropic glutamate receptor 2.* Biochemical Pharmacology 155 (**2018**) 356–365. doi:10.1016/j.bcp.2018.07.014.

Maarten L J Doornbos, Ilse Van der Linden, Liesbeth Vereyken, Gary Tresadern, Adriaan P IJzerman, Hilde Lavreysen, Laura H Heitman. *Constitutive activity of the metabotropic glutamate receptor 2 explored with a whole-cell label-free biosensor.* Biochemical Pharmacology 152 (**2018**) 201–210. doi:10.1016/j.bcp.2018.03.026.

Maarten L. J. Doornbos, Xuesong Wang, Sophie C. Vermond, Luc Peeters, Laura Pérez-Benito, Andrés A. Trabanco, Hilde Lavreysen, José María Cid, Laura H. Heitman, Gary Tresadern, Adriaan P. IJzerman. *A covalent allosteric probe for the metabotropic glutamate receptor 2: Design, synthesis and pharmacological characterization.* Journal of Medicinal Chemistry. Publication Date (Web) March 1, **2018**. doi:10.1021/acs.jmedchem.8b00051.

Maarten L. J. Doornbos, José María Cid, Jordi Haubrich, Alexandro Nunes, Jasper W. van de Sande, Sophie C. Vermond, Thea Mulder-Krieger, Andrés A. Trabanco, Abdellah Ahnaou, Wilhelmus H Drinkenburg, Hilde Lavreysen, Laura H. Heitman, Adriaan P. IJzerman, Gary Tresadern. *Discovery and Kinetic Profiling of 7-Aryl-1,2,4-triazolo[4,3-a]pyridines: Positive Allosteric Modulators of the Metabotropic Glutamate Receptor 2.* Journal of Medicinal Chemistry 60 (**2017**) 6704–6720. doi:10.1021/acs.jmedchem.7b00669.

Maarten L J Doornbos, Laura Pérez-Benito, Gary Tresadern, Thea Mulder Krieger, Ilse Biesmans, Andrés A Trabanco, Jose María Cid, Hilde Lavreysen, Adriaan P IJzerman, Laura H Heitman. *Molecular mechanism of positive allosteric modulation of the metabotropic glutamate receptor 2 by JNJ-46281222.* British Journal of Pharmacology 173 (**2016**) 588–600. doi:10.1111/bph.13390.

Not part of this thesis:

Maarten L.J. Doornbos and Laura H. Heitman. *Protocol for a Label-free impedance-based whole cell assay to study GPCR pharmacology.* Manuscript submitted; invitation from Methods in Cell Biology.

Laura Pérez-Benito, Maarten L.J. Doornbos, Arnau Cordomí, Luc Peeters, Hilde Lavreysen, Leonardo Pardo, Gary Tresadern. *Molecular Switches of Allosteric Modulation of the Metabotropic Glutamate 2 Receptor*. Structure 25 (**2017**) 1–10. doi: 10.1016/j.str.2017.05.021.

João F.S. Carvalho, Julien Louvel, Maarten L.J. Doornbos, Elisabeth Klaasse,Zhiyi Yu, Johannes Brussee, Adriaan P. IJzerman. *Strategies to reduce HERG K+ channel blockade. Exploring heteroaromaticity and rigidity in novel pyridine analogues of dofetilide.* Journal of Medicinal Chemistry 56 (**2013**) 2828–40. doi: 10.1021/jm301564f.

Annelien J.M. Zweemer, Indira Nederpelt, Hilde Vrieling, Sarah Hafith, Maarten L.J. Doornbos, Henk de Vries, Jeffrey Abt, Raymond Gross, Dean Stamos, John Saunders, Martine J. Smit, Adriaan P. IJzerman, Laura H. Heitman. *Multiple binding sites for small-molecule antagonists at the CC chemokine receptor 2*. Molecular Pharmacology 84 (**2013**) 551–61. doi: 10.1124/mol.113.086850.

CURRICULUM VITAE

Maarten Doornbos was born in Leiden on the 10th of May in 1989. After graduating from pre-university education at the Stedelijk Gymnasium Leiden in 2007 he started studying Bio-Pharmaceutical Sciences at Leiden University. The bachelor was finished with a research internship at the division of Medicinal Chemistry under supervision of Dr. Annelien Zweemer. The project focused on the molecular pharmacology of diverse ligands of the CC chemokine receptor 2 (CCR2). In September 2011 Maarten started the master Bio-Pharmaceutical Sciences. He performed a 9-month research internship at the division of Medicinal Chemistry which comprised two projects that were supervised by Dr. João Carvalho and Dr. Julien Louvel. The first project focused on the synthesis of novel molecules to gain molecular understanding of hERG channel blockade. The project resulted in a publication in the Journal of Medicinal Chemistry. The second project was focused on the synthesis of novel antagonists for the Adenosine A_1 receptor. From February 2013 onwards Maarten performed a 6-month research internship at the division of Neuroscience Discovery at Janssen Research and Development in Beerse, Belgium under supervision of Luc Peeters and Dr. Hilde Lavreysen. There he worked on a project focused on the mapping of the allosteric binding pocket of the metabotropic glutamate receptor 2 ($mGlu_2$) using a receptor-mutagenesis approach. The results obtained in this project are part of a publication in Structure.

After obtaining his master degree in September 2013 he started as a PhD candidate at the division of Medicinal Chemistry under supervision of Dr. Laura Heitman and Prof. Dr. Ad IJzerman. The project was a joined effort with the division of Neuroscience Discovery at Janssen Research and Development and was funded by the Vlaams Agentschap Innoveren & Ondernemen. Throughout his PhD studies Maarten presented parts of the work described in this thesis at several national and international conferences. He was invited speaker at various occasions, including the FIGON Dutch Medicines Days 2016 and 2017.

From May to September 2017 he worked as interim assistant professor in the division of Medicinal Chemistry. Currently, Maarten works as project manager at Catalyze in Amsterdam.

Ad & Laura

Gary
Hilde
Ilse
Lieve
Luc
Ilse
Laura
José
Pim
Abdel
Andrès
Liesbeth

Julien
Miriam
Dong
Maris
Annelien
Zhiyi
Rongfang
Arnault
Bart
Indira
Julia
Gerard
Thea
Henk
Jaco
Daan
Elaine

Isaura
Lia
Lance
Andrea
Marjolein
Natalia
Anna
Xue
Xuesong
Tasia
Brandon
Huub
Lindsey
Shardul
Willem
Xuhan

Alexandro
Jordi
Xuesong
Sophie
Dorrit
Huub

Bruno
Emy
Jasper
Miranda
Just

ACKNOWLEDGEMENTS

The work presented in this thesis does not in any way describe the great experience that the last years have been. It especially lacks to show the input and support of so many others: students, colleagues, collaborators, supervisors, friends and family.

In the first place I want to thank my promotor and co-promotor **Ad** and **Laura**. You have shown me the way through this joyful adventure. The lessons that you have taught me will remain useful throughout my career and personal life. I am especially thankful for the confidence that you have given me while standing in for Laura during her maternity leave.

Over the last years I have had the opportunity to collaborate with great people from Neuroscience Discovery at Janssen. I want to especially thank the IWT-team **Hilde**, **Gary**, **Lieve** and **Ilse** for the very fine collegiality. It has always been a great pleasure to work with you.

A big thanks to all the colleagues that have provided support and great fun during the work in the labs, conferences, coffee breaks, lab outings, weekends, dinners, movie nights, borrels, and so many more events. Special thanks to my office mates **Indira**, **Julia**, **Zhiyi**, **Andrea**, **Lance** and **Natalia** for all work related conversations and non-work related fun. A special thanks to **Thea** and **Henk** for support, collaboration and good conversations.

I am thankful to all the students that have contributed to this work. Especially **Alexandro**, **Jordi**, **Xuesong** and **Sophie**. Your work has greatly contributed to various chapters of this thesis and during your master internships you have been of great inspiration while making me think about the project from different angles.

Anna and **Rongfang**, thanks for being my paranimphs. I am happy to have you on my side during this special day.

I finish with the most important person, **Manon**.