Curriculum Vitae

Personal Information:

Name and Surname: **Giuseppe Manfroni (PhD)**
Address: **Via del Liceo, 1; 06123 Perugia (Italy)**
Phone: **+39-075-5855126/46**, **+39-338-9484395**
E-mail: **giuseppe.manfroni@unipg.it**
Nationality: **Italian**
Birth date: **23/10/1975**
Actual position: **Assistant Professor (Italian scientific sector CHIM/08, ERC sector LS7) Università degli Studi di Perugia-Department of Pharmaceutical Sciences**

Scientific Metrics:

a)Source SCOPUS (October, 2017)
Total indexed papers: **44**
Total citations: **672**
h-index: **16**
ORCID: orcid.org/0000-0003-0207-3927
b) Source Google Scholar (October, 2017)
Total papers and contributions: **48**
Total citations: **648**
h-index: **18**
First author in 6 papers and **corresponding author in 10** papers (October 2017)

Educational:

2006: Doctorate in Chemistry and Technology of drugs-international profile (PhD degree) at the University of Perugia (XVII cicle-CHIM08). Thesis title: Design and Synthesis of Non-peptidic Molecules for the Control of Hepatitis: Acridones as Anti-HCV Agents**.** Supervisor: Prof. Arnaldo Fravolini

2001: **Degree in Pharmaceutical Chemistry and Technology A.Y. 1999-2000 (with full marks 110/110)**
Thesis title: "Sintesi di Derivati Chinolonici ad Attività anti-HIV". Supervisor: Prof. Arnaldo Fravolini

Work experience:

March-April 2017: three weeks staff training E**RASMUS + experience** at the University of Tuebingen under the supervision of Prof. Stefan Laufer. Topics: microsomial stability of anti-prion compounds and biochemical assays for the evaluation of chinases (p38 alpha, JNK, JAK) inhibition.

2008-till now: Assistant Professor at Department of Pharmaceutical Sciences (Università di Perugia). Lecturer Pharmaceutical Analysis course III at the Faculty of Pharmacy (Università di Perugia).

2005-2007: Postdoc position at the Dipartimento di Chimica e Tecnologia del Farmaco (Università di Perugia)

2005: short period as **"visiting researcher" at the Rega Institute** for Medical Research (Katholieke Universiteit of Leuven, Belgium), headed by Prof. Erik De Clercq. Supervisor: Prof. Johan Neyts.

2006-2007: six months research experience at the Laboratory of Chemoinformatics and Molecular Modeling (Università di Perugia, Italy) headed by Prof. Gabriele Cruciani. Research project: Discovery of novel anti-HCV NS5B polymerase inhibitors by using the program GLUE.

April-July 2001: fixed-term contract with no subordination obligation at the University of Perugia concerning the synthesis of heterogeneous bases for anti-HIV compounds

Institutional/Academic responsibilities:

2016-till now: elected member of the executive board of Italian Chemical Society-Umbria section.

2016-till now: elected member of the board ("Giunta") of Department of Pharmaceutical Sciences

2017-from August to October: member of a commission involved on the realization of a departmental project for the call "Excellence of Italian Academic Departments".

2010-2012: elected member within the Faculty of Pharmacy-Università degli Studi di Perugia

2008-2011: elected member within the Council of the Department of Drug Chemistry and Technology.

Academic Educational Activities at the University of Perugia (Academic Years 2005-2018):

AY 2005-2006: Lecturer in Pharmaceutical Biotechnology (24 hs) at the integrated course of Biotechnological Drugs and Pharmaceutical Biotechnology, course of Pharmaceutical Biotechnology.
AY 2006-2007: Lecturer in Pharmaceutical Biotechnology (32 hs) at the integrated course of Biotechnological Drugs and Pharmaceutical Biotechnology, course of Pharmaceutical Biotechnology.
AY 2007-2008: Lecturer in Pharmaceutical Biotechnology (6 CFU) at the integrated course of Biotechnological Drugs and Pharmaceutical Biotechnology, course of Pharmaceutical Biotechnology

AYs 2008-2009, 2009-2010, 2010-2011: Lecturer in Pharmaceutical Analysis III (5 CFU) at the course of Pharmacy and in Pharmaceutical Biotechnology (6 CFU) at the course of Pharmaceutical Biotechnology.
AYs 2011-2012, 2012-2013, 2013-2014, 2014-2015, 2015-2016, 2016-2017, 2017-2018: Lecturer in Pharmaceutical Analysis III (6 CFU) at the integrated course of Pharmaceutical Analysis III and IV, course of Pharmacy.

Supplementary teaching activities for undergraduate students: Pharmaceutical Analysis III (course of Pharmacy), Medicinal Chemistry II (course of Pharmacy), Pharmaceutical Biotechnology (course of Pharmaceutical Biotechnology).
Support activities for students and assessment: thesis supervisor for both compilation and experimental thesis, member of the examining boards for Pharmaceutical Analysis III (Pharmacy course), Pharmaceutical Analysis (CTF course), Pharmaceutical Biotechnology, Laboratory Structural Modeling (course of Pharmaceutical Biotechnology) and Medicinal Chemistry II (course of Pharmacy).

Research activities and main skills:

Giuseppe Manfroni is involved on the design, synthesis and discovery of new chemical entities with defined biological activity (see publications). In particular, his research is focused on the identification and optimization of new hit/lead compounds. The main skills are: (i) rational design of new compounds also through the use of basic computational methods, (ii) planning and optimization of synthetic routes, including the use of the microwave synthesis and parallel synthesis, for the preparation of new chemical entities, (iii) chemical characterization of the synthesized compounds by instrumental techniques such as NMR, IR, UV, HRMS and purification of the compounds through chromatographic separation methods, (iv) bibliographic study and selection of new "drugable targets" for innovative antiviral therapies. Giuseppe Manfroni has particularly experience on the synthesis of heterocyclic compounds such as: quinolones, acridones, benzothiazines, pyrazolobenzothiazines, dibenzothiazines.

Main research topics:

1. Design, synthesis and chemical characterization of compounds active against HIV, HCV, virus Dengue (DENV) and West Nile virus (WNV).

2. Design, synthesis, and chemical characterization of quinolones with anti-tumour activity acting *via* miRNA mediated gene silencing.

3. Design, synthesis, and chemical characterization of anti-prion agents.

4. Design, synthesis, and chemical characterization of p38alpha MAPK inhibitors for the treatment of inflammatory and immune diseases.

Personal Scientific Collaborations:
Dr. Emiliano Biasini: Istituto Mario Negri, Milan, Italy

Prof. Martino Bolognesi: Università degli Studi di Milano, Italy
Prof. Helena Danielson: Uppsala University, Sweden
Prof. Stefan Laufer: University of Tuebingen, Germany
Prof. Johan Neyts: Rega Institute For Medical Research, Katholieke Universiteit Leuven
Prof. Neerja Kaushik-Basu: New Jersey Medical School- Rutgers University, USA
Dr. Mario Milani and Dr. Eloise Mastrangelo: CNR Milano, Italy
Dott. Gilles Querat: Aix Marseille Université-Emergenges des Pathologies Virales, Marseille, Italy.

Referee For The Following Indexed Journals:
Antiviral Research
Bioorganic Medicinal Chemistry Letters
Emerging Microbes and Infections (Nat. Publishing group)
European Journal of Medicinal Chemistry
Journal of Enzyme Inhibition and Medicinal Chemistry
Journal of Medicinal Chemistry
Scientific Reports (Nature Publishing Group)

Founded projects:

2017: Fondazione Cassa di Risparmio di Perugia, project code 2017.0277.021 Ricerca scientifica e Tecnologica. Title: "Riduzione della neurotossicità indotta dalla proteina prionica con molecole a struttura eterociclica: implicazioni nella malattia di Alzheimer. **Principal Investigator**.

2014: MIUR-SIR, project code RBSI14C78S. Title: "Anti-viral drug discovery strategies: structure-based development of Dengue virus RNA-dependent RNA polymerase inhibitors." **Member of the unit, local principal investigator**.

2010-2011: MIUR-PRIN, project code: 2010W2KM5L_004. Title: "Bloccare la replicazione di HIV-1 attraverso un approccio rivolto verso diversi bersagli molecolari." **Member of local unit**.

2008: MIUR-PRIN, project code: 2008CE75SA_002. "Inibitori della regolazione trascrizionale dell'HIV. **Member of local unit**.

Oral communications and participation to organizing committees:

Relatore presentante una comunicazione orale da 30 minuti (keynote, CP-03) al XXXV TUMA 2016, Giulianova 25-27 Settembre 2016 dal titolo: "Identification, hit explotion, and mechanism of action of pyrididobenzothiazoles as anti-flavivirus compounds" come desumibile dal sito ufficiale del congresso:http://www.tuma2016.univaq.it/images/DOCUMENTI/Programma_XXXV_TUMA2016_def.pdf.

Comunicazione orale Enzymology……..

Relatore presentante una comunicazione orale da 20 minuti al XXIV National Meeting in Medicinal Chemistry dal titolo "Pyridobenzothiazoles efficiently inhibit flavivirus replication in cells: combining structural biology and virology studies to investigate the mechanism of action" come desumibile dal sito ufficiale del congresso http://nmmc2016.chimfarm.unipg.it/index.php/rdpa-m/programme

Membro del comitato organizzatore del XXIV National Meeting in Medicinal Chemistry-10° Young Medicinal Chemists' Symposium (NPCF) come desumibile dalla pagina web ufficiale del sito (http://nmmc2016.chimfarm.unipg.it/index.php/rdpa-m/committees) e dal documento allegato, estratto dal libro dei riassunti (vedi allegato pfd)- 11/09/2016-14/09/2016

Membro del comitato organizzatore del congresso internazionale "International Conference on Enzymology" 20-21 Marzo 2017-Roma, come si evince dal sito ufficiale http://enzymology.conferenceseries.com/organizing-committee.php

List of publications: *= corresponding author

1. Cannalire, R.; Tarantino, D.; Astolfi, A.; Barreca, M. L.; Sabatini, S.; Massari, S.; Tabarrini, O.; Milani, M.; Querat, G.; Mastrangelo, E.; **Manfroni, G.;*** Cecchetti, V. Functionalized 2,1-benzothiazine 2,2-dioxides as new inhibitors of Dengue NS5 RNA-dependent RNA-polymerase. *Eur. J. Med. Chem*. 2017, doi: 10.1016/j.ejmech.2017.10.064, *just accepted article*.
2. Astolfi, A.; Felicetti, T.; Iraci, N.; **Manfroni, G**.; Massari, S.; Pietrella, D.; Tabarrini, O.; Kaatz, G. W.; Barreca, M. L.; Sabatini, S.; Cecchetti, V. Pharmacophore-Based Repositioning of Approved Drugs as Novel Staphylococcus aureus NorA Efflux Pump Inhibitors. *J. Med. Chem.* **2017**, *60*, 1598-1604.
3. Sabatini, S.; Piccioni, M.; Felicetti, T.; De Marco, S.; **Manfroni, G.**; Pagiotti, R.; Nocchetti, M.; Cecchetti, V.; Pietrella, D. Investigation on the effect of known potent: S. aureus NorA efflux pump inhibitors on the staphylococcal biofilm formation. *RSC Advances*, **2017**, 7, 37007-37014.
4. Cannalire, R.; Machado, D.; Felicetti, T.; Santos Costa, S.; Massari, S.; **Manfroni G**.; Barreca, M.L.; Tabarrini, O.; Couto, I.; Viveiros, M.; Sabatini, S.; Cecchetti V. Natural isoflavone biochanin A as a template for the design of new and potent 3-phenylquinolone efflux inhibitors against Mycobacterium avium. *Eur. J. Med. Chem.* **2017**, *140*, 321-330.
5. Desantis, J.; Nannetti, G.; Massari, S.; Barreca, M.L.; **Manfroni, G**.; Cecchetti, V.; Palù, G.; Goracci, L.; Loregian, A.; Tabarrini O. Exploring the cycloheptathiophene-3-carboxamide scaffold to disrupt the interactions of the influenza polymerase subunits and obtain potent anti-influenza activity. *Eur. J. Med. Chem.* **2017**, *138*, 128-139.
6. Felicetti, T.; Cannalire, R.; Burali, M. S.; Massari, S.; **Manfroni, G**.; Barreca, M. L.; Tabarrini, O.; Schindler, B. D.; Sabatini, S.; Kaatz, G. W.; Cecchetti V. Searching for Novel Inhibitors of the S. aureus NorA Efflux Pump: Synthesis and Biological Evaluation of the 3-Phenyl-1,4-benzothiazine Analogues. *ChemMedChem.* **2017**, 12, 1293-1302.

7. Machado, D.; Fernandes, L.; Costa, S. S.; Cannalire, R.; **Manfroni, G**.; Tabarrini, O.; Couto, I.; Sabatini, S.; Viveiros, M. Mode of action of the 2-phenylquinoline efflux inhibitor PQQ4R against *Escherichia coli*. *PeerJ*. **2017**, 5, e3168.
8. Tarantino D, Cannalire R, Mastrangelo E, Croci R, Querat G, Barreca ML, Bolognesi M, **Manfroni G**,* Cecchetti V, Milani M. Targeting flavivirus RNA dependent RNA polymerase through a pyridobenzothiazole inhibitor. *Antiviral. Res*. **2016**, *134*, 226-235.
9. Kaushik-Basu N, Ratmanova NK, Manvar D, Belov DS, Cevik O, Basu A, Yerukhimovich MM, Lukyanenko ER, Andreev IA, Belov GM, **Manfroni G**, Cecchetti V, Frick DN, Kurkin AV, Altieri A, Barreca ML. Bicyclic octahydrocyclohepta[*b*]pyrrol-4(1*H*)one derivatives as novel selective anti-hepatitis C virus agents. *Eur. J. Med. Chem.* **2016**, *122*, 319-25.
10. Corona A, Desantis J, Massari S, Distinto S, Masaoka T, Sabatini S, Esposito F, **Manfroni G**, Maccioni E, Cecchetti V, Pannecouque C, Le Grice SF, Tramontano E, Tabarrini O. Studies on Cycloheptathiophene-3-carboxamide Derivatives as Allosteric HIV-1 Ribonuclease H Inhibitors. *ChemMedChem* **2016**, 11, 1709-1720.
11. Cannalire, R.; Barreca, M.L.; **Manfroni, G.**;* Cecchetti, V. A Journey around the medicinal chemistry of hepatitis C virus inhibitors targeting NS4B: from target to preclinical drug candidates. *J. Med. Chem.* **2016**, *59*, 16-41.
12. Machado D, Cannalire R, Santos Costa, S.; **Manfroni G**, Tabarrini O, Cecchetti V, Couto I, Viveiros M, Sabatini S. Boosting Effect of 2-Phenylquinoline Efflux Inhibitors in Combination with Macrolides against Mycobacterium Smegmatis and Mycobacterium Avium. *ACS Infect. Dis.* **2015**, *1*, 593-603.
13. Franci, G.; **Manfroni, G.;*** Cannalire, R.; Felicetti, T.; Tabarrini, O.; Salvato, A.; Barreca, M.L.; Altucci, L.;Cecchetti, V. Tumour cell population growth inhibition and cell death induction of functionalized 6-aminoquinolone derivatives. *Cell Prolif.* **2015**, *48*, 705-717.
14. Sabatini, S.; **Manfroni, G.**;* Barreca, M.L.; Bauer, S.M.; Gargaro, M.; Cannalire, R.; Astolfi, A.; Brea, J.; Vacca, C.; Pirro, M.; Massari, S.; Tabarrini, O.; Loza, M.I.; Fallarino, F.; Laufer, S.A.; Cecchetti, V. The pyrazolobenzothiazine core as a new chemotype of p 38 alpha mitogen-activated protein chinase inhibitors. *Chem. Biol. & Drug Des*. **2015**, *86*, 531-545.
15. Astolfi, A.; Iraci, N.; **Manfroni, G.**; Barreca, M.L.; Cecchetti, V. A comprehensive structural overview of p38 MAPK in complex with type I inhibitors. *ChemMedChem*, **2015**, *10*, 957-969.
16. Andreev, I.A.; Manvar, D.; Barreca, M. L.; Belov, D.S.; Basu, A.; Sweeny, N.L.; Ratmanova, N.K.; Lukyanenko, E.R.; **Manfroni, G.**; Cecchetti, V.; Frick, D.N.; Altieri, A.; Kaushik-Basu, N.; Kurkin, A.V. Discovery of the 2-phenyl-4,5,6,7-tetrahydro-1H-indole as a novel anti-hepatitis C virus targeting scaffold. *Eur. J. Med. Chem.* **2015**, *96*, 250-258.
17. Massari, S.; Nannetti, G.; Desantis, J.; Muratore, G.; Sabatini, S.; **Manfroni, G.**; Mercorelli, B.; Cecchetti, V.; Palù, G.; Cruciani, G.; Loregian, A.; Goracci, L.; Tabarrini, O. A Broad Anti-influenza Hybrid Small Molecule That Potently Disrupts the Interaction of Polymerase Acidic Protein-Basic Protein 1 (PA-PB1) Subunits. *J. Med. Chem.* **2015**, *58*, 3830-3842.

18. Sardella, R.; Carotti, A.; **Manfroni, G.**; Tedesco, D.; Martelli, A.; Bertucci, C; Cecchetti, V.; Natalini, B. Enantioresolution, stereochemical characterization and biological activity of a chiral large-conductance calcium-activated potassium channel opener. *J. Chromatog. A.* **2014**, *1363*, 162-168.
19. Sancineto, L.; Iraci, N.; Barreca, M.L.; Massari, S.; **Manfroni, G.**; Corazza, G.; Cecchetti, V.; Marcello, A.; Daelemans, D.; Pannecouque, C.; Tabarrini, O. Exploiting the anti-HIV 6-desfluoroquinolones to design multiple ligands. *Bioog. Med. Chem.* **2014**, *22*, 4658-4666.
20. Donalisio, M.; Massari, S.; Argenziano, M.; **Manfroni, G.**; Cagno, V.; Civra, A.; Sabatini, S.; Cecchetti, V.; Loregian, A.; Cavalli, R.; Lembo, D.; Tabarrini, O. Ethyl 1,8-Naphthyridone-3-carboxylates Downregulate Human Papillomavirus-16 E6 and E7 Oncogene Expression. *J. Med. Chem.* **2014**, 57, 5649-5663.
21. **Manfroni, G.**; Manvar, D.; Barreca, M.L.; Kaushik-Basu, N.; Leyssen, P.; Paeshuyse, J.; Cannalire, R.; Iraci, N.; Basu, A.; Chudaev, M.; Zamperini, C.; Dreassi, E.; Sabatini, S.; Tabarrini, O.; Neyts, J.; Cecchett,i V. New Pyrazolobenzothiazine Derivatives as Hepatitis C Virus NS5B Polymerase Palm Site I Inhibitors. *J. Med. Chem.* **2014**, *57*, 3247-3262.
22. Barreca, M. L., Iraci, N.; **Manfroni, G**.; Gaetani, R.; Guercini, C.; Sabatini, S., Tabarrini, O., Cecchetti, V. Accounting for Target Flexibility and Water Molecules by Docking to Ensembles of Target Structures: The HCV NS5B Palm Site I Inhibitors Case Study. *J Chem. Inf. Model.* **2014**, 54, 481-497.
23. **Manfroni, G.;*** Cannalire, R.; Barreca, M.L.; Kaushik-Basu, N.; Leyssen, P.; Winquist, J.; Iraci, N.; Manvar, D.; Paeshuyse, J.; Guhamazumder, R.; Basu, A.; Sabatini, S.; Tabarrini, O.; Danielson, U.H.; Neyts, J.; Cecchetti, V. The Versatile Nature of the 6-Aminoquinolone Scaffold: Identification of Submicromolar Hepatitis C Virus NS5B Inhibitors. *J. Med. Chem.* **2014**, 57, 1952-1963.
24. Massari, S.; Nannetti, G.; Goracci, L., Sancineto, L., Muratore, G., Sabatini, S., **Manfroni G**., Mercorelli, B., Cecchetti, V.; Facchini, M., Palù, G.; Cruciani, G.; Loregian, A.; Tabarrini, O. Structural investigation of cycloheptathiophene-3-carboxamide derivatives targeting influenza virus polymerase assembly. *J. Med. Chem.* **2013**, *56*, 10118-10131.
25. Sancineto, L.; Iraci, N.; Massari, S.; Attanasio, V.; Corazza, G.; Barreca, M. L.; Sabatini, S.; **Manfroni, G**.; Avanzi, N. R.; Cecchetti, V.; Pannecouque, C.; Marcello, A.; Tabarrini, O. Computer-aided design, synthesis and validation of 2-phenylquinazolinone fragments as CDK9 inhibitors with anti-HIV-1 Tat-mediated transcription activity. *ChemMedChem*, **2013**, *8*, 1941-1953.
26. Blasi, P.; Schoubben, A.; Traina, G.; **Manfroni, G**.; Barberini, L.; Alberti, P.F.; Cirotto, C.; Ricci, M. Lipid nanoparticles for brain targeting III. Long-term stability and in vivo toxicity. *Int. J. Pharm.* **2013**, 454, 316-323.
27. Sabatini, S.; Gosetto, F.; Iraci, N.; Barreca, M. L.; Massari, S.; Sancineto, L.; **Manfroni G.**; Tabarrini, O.; Dimovska, M.; Kaatz, G. W.; Cecchetti, V. Re-evolution of the 2-phenylquinolines: ligand-based design, synthesis, and biological evaluation of a potent new class of Staphylococcus aureus NorA efflux pump inhibitors to combat antimicrobial resistance. *J. Med. Chem.*, **2013**, *56*, 4975–4989.
28. Martelli, A.; **Manfroni, G.;*** Sabbatini, P.; Barreca, M. L.; Testai L., Novell,i M.; Sabatini, S.; Massari, S.; Tabarrini, O.; Masiello, P.; Calderone, V.; Cecchetti, V. 1,4-

Benzothiazine ATP-sensitive potassium channel openers: modifications at the C-2 and C-6 positions. *J. Med. Chem.*, **2013**, *56*, 4718–4728.

29. Barreca M.L., **Manfroni, G.**;* Leyssen, P.; Winquist, J.; Kaushik-Basu, N.; Paeshuyse, J., Krishnan, R.; Iraci, N.; Sabatini, S.; Tabarrini, O.; Basu, A.; Danielson, U. H.; Neyts, J.; Cecchetti, V. Structure-based discovery of pyrazolobenzothiazine derivatives as inhibitors of hepatitis C virus replication. *J. Med. Chem.* **2013**, *56*, 2270-2282.
30. Sabatini, S.; Gosetto, F.; Serritella, S.; **Manfroni, G.**; Tabarrini, O.; Iraci, N.; Brincat, J.P.; Carosati, E.; Villarini, M.; Kaatz, G.W.; Cecchetti, V. Pyrazolo[4,3-c][1,2]benzothiazines 5,5-Dioxide: A Promising New Class of Staphylococcus aureus NorA Efflux Pump Inhibitors. *J. Med. Chem*. **2012**, 55, 3568-3572.
31. **Manfroni, G.;*** Meschini, F.; Barreca, M.L.; Leyssen, P.; Samuele, A.; Iraci, N.; Sabatini, S.; Massari, S.; Maga, G.; Neyts, J.; Cecchetti, V. Pyridobenzothiazole derivatives as new chemotype targeting the HCV NS5B polymerase. *Bioorg. Med. Chem.* **2012**, *20*, 866-876.
32. Sabatini, S.; Gosetto, F.; **Manfroni, G.**; Tabarrini, O.; Kaatz, G. W.; Patel, D.; Cecchetti, V. Evolution from a natural flavones nucleus to obtain 2-(4-propoxyphenyl)quinoline derivatives as potent inhibitors of the S. aureus NorA efflux pump. *J. Med. Chem.* **2011**, *54*, 5722–5736.
33. Brincat, J.P.; Carosati, E.; Sabatini, S.; **Manfroni, G**.; Fravolini, A.; Raygada, J.L.; Patel, D.; Kaatz, G.W.; Cruciani, G. Discovery of novel inhibitors of the NorA multidrug transporter of Staphylococcus aureus. *J. Med. Chem.* **2011**, *54*, 354-365.
34. **Manfroni, G.;*** Meschini, F.; Costantino, F.; Tabarrini, O.; Cecchetti, V. N-Benzoyl-N-methylsulfonylanthranilates: unexpected cyclization reaction to 4-alkoxy-2,1-benzothiazines. *Arkivoc* **2011**, (ix), 165-176.
35. Tabarrini, O.; Massari, S.; Sancineto, L.; Daelemans, D.; Sabatini, S.; **Manfroni, G.**; Cecchetti, V.; Pannecouque, C. Structural investigation of the naphthyridone scaffold: identification of a 1,6-naphthyridone derivative with potent and selective anti-HIV activity. *ChemMedChem* **2011**, *6*, 1249–1257.
36. Barreca, M.L.; Iraci, N.; **Manfroni, G.**; Cecchetti, V. Allosteric inhibition of the hepatitis C virus NS5B polymerase: in silico strategies for drug discovery and development. *Future Med. Chem.* **2011**, *3*, 1027–1055.
37. Tabarrini, O.; Massari, S.; Daelemans, D.; Meschini, F.; **Manfroni, G.;** Bottega, L.; Gatto, B.; Palumbo, M.; Pannecouque, C.; Cecchetti, V. Studies of anti-HIV transcription inhibitor quinolones: identification of potent *N*1-vinyl derivatives. *ChemMedChem* **2010**, *5*, 1880-92.
38. Massari, S.; Daelemans, D.; **Manfroni, G**.; Sabatini, S.; Tabarrini, O.; Pannecouque, C.; Cecchetti, V. Studies on anti-HIV quinolones: new insights on the C-6 position. *Bioorg. Med. Chem.* **2009**, *17*, 667-674.
39. **Manfroni, G.**; Gatto, B.; Tabarrini, O.; Sabatini, S.; Cecchetti, V.; Giaretta, G.; Parolin, C.; Del Vecchio, C.; Calistri, A.; Palumbo, M.; Fravolini, A. Synthesis and biological evaluation of 2-phenylquinolones targeted at Tat/TAR recognition. *Bioorg. Med. Chem. Letters* **2009**, *19*, 714-717.
40. Spogli, R.; Sabatini, S.; **Manfroni, G**.; Tabarrini, O.; Cecchetti, V. Synthesis of 2-(Arylamino)ethanethiols via Lewis acid catalyzed aminolysis of 2,2-

dimethylthiirane as precursors of the 1,4-benzothiazine Nucleus. *Synthesis* **2009**, *9*, 1513-1519.

41. **Manfroni, G.**; Paeshuyse, J.; Massari, S.; Zanoli, S.; Gatto, B.; Maga, G:, Tabarrini, O.; Cecchetti, V.; Fravolini, A.; Neyts J. Inhibition of subgenomic hepatitis C virus RNA replication by acridone derivatives: identification of an NS3 helicase inhibitor. *J. Med. Chem.* **2009**, *52*, 3354-3365.
42. Calderone, V.; Spogli, R.; Martelli, A.; **Manfroni, G**.; Testai, L.; Sabatini, S.; Tabarrini, O.; Cecchetti, V. Novel 1,4-benzothiazine derivatives as large conductance Ca2+-activated potassium channel openers. *J. Med. Chem.* **2008**, *51*, 5085-5092.
43. Tabarrini, O.; Massari, S.; Daelemans, D.; Stevens, M.; **Manfroni, G**.; Sabatini, S.; Balzarini, J.; Cecchetti, V.; Pannecouque, C.; Fravolini, A. Structure-activity relationship study on anti-HIV 6-desfluoroquinolones. *J. Med. Chem.* **2008**, *51*, 5454-5458.
44. Tabarrini, O.; **Manfroni, G**.; Fravolini, A.; Cecchetti, V.; Sabatini, S.; De Clercq, E.; Rozenski, J.; Canard, B.; Dutartre, H.; Paeshuyse, J.; Neyts, J. Synthesis and Anti-BVDV Activity of Acridones As New Potential Antiviral Agents. *J. Med. Chem.* **2006**, *49*, 2621-2627.
45. Tabarrini, O.; Stevens, M.; Cecchetti, V.; Sabatini. S.; Dell'Uomo, M.; **Manfroni, G**.; Palumbo, M.; Pannecouque, C.; De Clercq, E.; Fravolini, A. Structure Modifications of 6-Aminoquinolones with Potent Anti-HIV activity. *J. Med. Chem.* **2004**, *47*, 5567-5578.

Perugia, October the 31th 2017