Curriculum Vitae

Personal Information:
Name and Surname: **Giuseppe Manfroni (PhD)**
Address: **Via del Liceo, 1; 06123 Perugia (Italy)**
Phone: **+39-075-5855126/46, +39-393-0144393**
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_3) Università degli Studi di Perugia-Department of Pharmaceutical Sciences**

Scientific Metrics:
a)Source SCOPUS (April, 2018)
Total indexed papers: **47**
Total citations: **740**
h-index: **18**
ORCID: orcid.org/0000-0003-0207-3927
b) Source Google Scholar (April, 2018)
Total papers and contributions: **51**
Total citations: **865**
h-index: **18**
First author in 6 papers and **corresponding author in 12** papers (April 2018)

Education/training:

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

2008 (February, 18-24): 7th Laboratory of Synthetic Methodologies in Medicinal Chemistry-patronized by Italian Society of Chemistry

AYs 2002-2005 (XVII cycle): 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 (titled acquired on February 2006)

2004,2005,2006: European School of Medicinal Chemistry (ESMEC) for PhD students.

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

Professional experience:

2008-till now: Assistant Professor at Department of Pharmaceutical Sciences (Università di Perugia). Lecturer in 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 PhD student 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 heterocyclic bases for anti-HIV compounds

Career interruption:

Sept. 2001-Sept. 2002: Compulsory Military Service-Italian Army (Infantry)-Caporal-health assistant of medical officer.

Institutional/Academic appointments:

2017-current: co-supervisor of a PhD thesis. Doctorate student: Maria Sole Burali (XXXIII cycle-Doctorate in Pharmaceutical Sciences (international-industrial)). Thesis title: *Fighting (re)emerging viruses: hit discovery and hit-to-lead optimization.*

2016-current: elected member of the executive committee of the Italian Chemical Society-Umbria section.

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

2017: Italian National Habilitation (MIUR-ANVUR) as Associate Professor obtained on July, the 31st. Duration date: from July, 31, 2017 to July, 31, 2023.

2017-from August to October: member of a commission involved in the realization of the departmental project DEPLHI for the call "Excellence of Italian Academic Departments"- DEPLHI has been awarded with a grant of 8 million euros by MIUR (Italian Ministry of Education, University and Research)

2013: supervisor of a research contract committed to Dr. Sabatini Roberta and funded by Regione Umbria (*POR UMBRIA FSE 2007-2013 Asse IV "Capitale Umano", Obiettivo specifico "l")*. Title of the research: *Lotta all'epatite C: progettazione, sintesi e valutazione pre-clinica di nuovi agenti antivirali.*

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

2008-2011: elected member within the board ("giunta") of the Department of Drug Chemistry and Technology.

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

AY 2017-2018: **High educational training to doctorate students** (2 CFU-24 hrs frontal lessons) on biotechnological methods and chemical biology in drug discovery.

AY 2017-2018: Lecturer 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.

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.

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

Supplementary teaching activities for undergraduate students: Pharmaceutical Analysis III (course of Pharmacy), Medicinal Chemistry II (course of Pharmacy), Pharmaceutical Biotechnology (course of Pharmaceutical Biotechnology).

Students examination and assessment: 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).

Supervisor or co-supervisor of 40 thesis of undergraduate student at the course of Pharmacy, Pharmaceutical Biotechnology, Pharmaceutical Chemistry and Technology.

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 (hit explosion, hit-to-lead optimization). 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) structure-activity relationship studies around a defined chemical class, (v) bibliographic study and selection of new "drugable targets" for innovative antiviral therapies. Giuseppe Manfroni has particularly experience with the synthesis of heterocyclic compounds such as: quinolones, acridones, benzothiazines, pyrazolobenzothiazines, dibenzothiazines and on the preparation of biotinylated compounds for chemical biology studies.

Main research topics:

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

2. Design, synthesis, and chemical characterization of quinolones with anti-tumor 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*: University of Trento-CIBIO, Trento, Italy. Topic: anti-prion/anti-Alzheimer compounds

-*Prof. Martino Bolognesi*: Università degli Studi di Milano, Italy. Topic: anti-flavivirus compounds

-*Prof. Helena Danielson*: Uppsala University, Sweden. Topic: anti-HCV compounds

-*Prof. Francesca Fallarino*: University of Perugia, Department of Experimental Medicine, Italy. Topic: anti-multiple sclerosis compounds

-*Prof. Francesco Galli*: University of Perugia, Department of Pharmaceutical Sciences, ITALY. Topic: inhibitors of p38 alpha MAPK.

-*Prof. Stefan Laufer*: University of Tuebingen, Germany. Topic: inhibitors of p38 alpha MAPK.
-*Prof. Johan Neyts*: Rega Institute For Medical Research, Katholieke Universiteit Leuven. Topic: anti-HCV compounds.
-*Prof. Neerja Kaushik-Basu*: New Jersey Medical School- Rutgers University, USA. Topic: anti-HCV compounds.
-*Dr. Mario Milani and Dr. Eloise Mastrangelo*: CNR Milano, Italy. Topic: anti-flavivirus compounds
-*Dr. Gilles Querat*: Aix Marseille Université-Emergenges des Pathologies Virales, Marseille, France. Topic: anti-flavivirus compounds
-*Prof. Subhash Vasudevan*: Department of Microbiology & Immunology, Duke-NUS Medical School, Singapore. Topic: anti-flavivirus compounds.
-*Prof. Giuseppe Servillo*, University of Perugia, Department of Experimental Medicine, Italy. Topic: anti-tumor quinolone compounds acting as enhancer of miRNA gene silencing.

Referee for the following indexed journals:

Antiviral Research, Bioorganic Medicinal Chemistry Letter; Bioorganic and Medicinal Chemistry; 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).

Editorial activities: Member of the editorial board of Pharmaceutical Science and Technology, Science Publishing Group.

Awards: 2017-recipient of MIUR-FFABR fund for basic research addressed to 75% of Italian academic researchers with positive evaluation of their research.

Funded projects:

- **2018: AIRC Investigator Grant** - IG 2017. Project title: *"Tackling Interleukin 4 Induced 1, IL4i1, as a novel target enzyme for tumor immunotherapy"*. **Member of the research unit**. *Peer reviewed project*

- **2017**: **National Multiple Sclerosis Society, New York (USA)**. Pilot Grant-Project title: "*Targeting cellular prion protein in multiple sclerosis*". **Member of the research unit**. *Peer reviewed project.*

- **2017: Pilot project-Fondazione Ricerca Fibrosi Cistica**. Project title: *"Identification of new efflux pumps inhibitors able to contrast nontuberculous mycobacterial infections in cystic fibrosis patients"*, project code: FFC#17/2017. **Member of the research unit**. *Peer reviewed project*

- **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** (Scientific Independence of young Researchers), project code RBSI14C78S. Title: "*Anti-viral drug discovery strategies: structure-based development of Dengue virus RNA-dependent RNA polymerase inhibitors*." **local project leader**. *Peer reviewed project.*

- **2010**: **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**. *Peer reviewed project.*

- **2009: Fondazione Cassa di Risparmio di Perugia**, project code "*Lotta all'epatite C: la ricerca di base come strumento per l'identificazione di nuovi agenti antivirali*". Project code: 2009.010.00413 Bando a tema Ricerca di Base 2009. **Member of the research unit**.

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

Oral communications and participation to organizing committees:

1. **XXXV TUMA 2016**, Giulianova 25-27 September 2016: "*Identification, hit explotion, and mechanism of action of pyrididobenzothiazoles as anti-flavivirus compounds*" Key lecture.

2. **2nd International Conference on Enzymology and Molecular Biology** March, 20-21, 2017-Rome: "*Inhibition of the RNA-dependent RNA polymerase activity of Flavivirus NS5 by heterocyclic compounds*." Published in *Journal of Biotechnology and Biomaterials*, **2017**, *7*, 44. Oral communication.

3. **XXIV National Meeting in Medicinal Chemistry and 10th YOUNG Medicinal Chemistry symposium NPCF**- September, 11-14, 2016, Perugia.: "*Pyridobenzothiazoles efficiently inhibit flavivirus replication in cells: combining structural biology and virology studies to investigate the mechanism of action*". Oral communication.

a) Member of the organizing committee of the XXIV National Meeting in Medicinal Chemistry-10° Young Medicinal Chemists' Symposium (NPCF). September, 11-14, 2016, Perugia.

b) Member of the organizing committee of the "2nd International Conference on Enzymology" March, 20-21th, 2017-Roma.

List of publications:
(**total IF= 210.201**, **overage IF= 4.472**, **overage citation *per* article= 15.7**, *= corresponding author, IFs are referred to 2017)

1. Cannalire, R.; Tiecco, M.; Cecchetti, V.; Germani, R.; **Manfroni, G.*** Advantageous use of ionic liquids for the synthesis of pharmaceutically relevant quinolones. *Eur. J. Org. Chem.* **2018**, *accepted article-article in press*: *doi.org/10.1002/ejoc.201800415*. (IF= 2.834)

2. Astolfi, A.; **Manfroni, G.**; Cecchetti, V.; Barreca, M.L. A Comprehensive Structural Overview of p38α Mitogen-Activated Protein Kinase in Complex with ATP-Site and Non-ATP-Site Binders. *ChemMedChem*, **2018**, *13*, 7-14. (IF= 3.225)
3. 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*. **2018**, *143*, 1667-1676. (IF= 4.519)
4. 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. (IF= 6.259)
5. 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. (IF= 3.108)
6. 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. (IF= 4.519)
7. 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. (IF= 4.519)
8. 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. (IF= 3.225)
9. 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. (IF= 2.177)
10. 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. *Antivir. Res*. **2016**, *134*, 226-235. (IF= 4.271)
11. 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. (IF= 4.519)

12. 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. (IF= 3.225)
13. 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. (IF= 6.259)
14. 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. (IF= 3.600)
15. 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. (IF= 4.112)
16. 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. (IF= 2.396)
17. 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. (IF= 3.225)
18. 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. (IF= 4.519)
19. 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. (IF= 6.259)
20. 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. (IF= 3.981)
21. 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. (IF= 2.930)
22. 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. (IF= 6.259)

23. **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. (IF= 6.259)
24. 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. (IF= 3.760)
25. **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. (IF= 6.259)
26. 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. (IF= 6.259)
27. 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. (IF= 3.225)
28. 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. (IF= 3.649)
29. 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. (IF= 6.259)
30. 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. (IF= 6.259)
31. 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. (IF= 6.259)

32. 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. (IF= 6.259)
33. **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. (IF= 2.930)
34. 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. (IF= 6.259)
35. 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. (IF= 6.259)
36. **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. (IF= 1.031)
37. 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. (IF= 3.225)
38. 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. (IF= 3.556)
39. 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. (IF= 3.225)
40. 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. (IF= 2.930)
41. **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. (IF= 2.454)
42. 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. (IF= 2.650)
43. **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. (IF= 6.259)

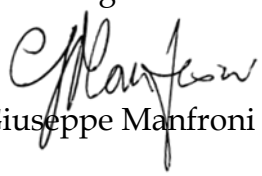
44. Calderone, V.; Spogli, R.; Martelli, A.; **Manfroni, G**.; Testai, L.; Sabatini, S.; Tabarrini, O.; Cecchetti, V. Novel 1,4-benzothiazine derivatives as large conductance Ca2+-activated potassium channel openers. *J. Med. Chem.* **2008**, *51*, 5085-5092. (IF= 6.259)
45. Tabarrini, O.; Massari, S.; 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. (IF= 6.259)
46. 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. (IF= 6.259, *personal top cited paper: 60 citations*)
47. 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. (IF= 6.259)

Book writing activities:

1 chapter book**: Manfroni, G;*** Cannalire, R. *Evolution of NS4B inhibitors*, volume II section II in "*HCV: The Journey from Discovery to a Cure*", Editor: Michael J. Sofia, Editorial office: Springer-Nature, book in realization. Chapter approved by editor.

Perugia, May, the 14th, 2018

Signed



Giuseppe Manfroni

For Italian law: Per gli usi consentiti dalla legge Italiana: autorizzo il trattamento dei miei dati personali ai sensi del Decreto Legislativo 30 giugno 2003, n. 196 "Codice della privacy" e della previgente Legge 675 del 1996.