G. Leslie Burnett

Menlo Park, CA 94025 glesliebburnett@gmail.com

Qualifications

- Driven scientific leader in drug discovery with 9 years of experience in structure-based drug design (SBDD) and lead optimization in the bRo5 space targeting "difficult to drug" proteins
- Led the chemistry development of the $KRAS^{G12D}$(ON) clinical candidate zoldonrasib (RMC-9805) and mTORC1 clinical candidate RMC-5552
- Strong experience leading chemistry teams utilizing internal as well as external resources, including teams of >80 external FTEs
- Experienced medicinal chemist in SAR analysis and rapid optimization of leads (physicochemical properties, SBDD, PK, pharmacology, toxicology)
- Excellent communication skills interacting within project teams and across multidisciplinary departments

Experience

Director – Revolution Medicines 2/2023 – Present

- Project Team Lead (PTL) for an undisclosed RAS(ON) project
- Led the development of immuno-oncology (IO) tool compounds that enabled a collaboration with Aethon Therapeutics for the development of bispecific antibodies

Associate Director – Revolution Medicines 2/2022 – 2/2023

- Project Qualification Team Lead for an undisclosed RAS(ON) project
- Led the design and screening of novel tri-complex inhibitor (TCI) DNA Encoded Libraries (DEL)
- Initiated the $KRAS^{G12R}$(ON) program as interim lead chemist
- Managed and mentored 5 direct reports (MS and PhD)

Senior Scientist I – Revolution Medicines 3/2019 – 2/2022

- Lead chemist for the $KRAS^{G12D}$(ON) program through DC nomination of zoldonrasib (RMC-9805)
  - Led the development of an oral, RAS(ON) G12D-selective, covalent tri-complex inhibitor
  - Developed the first aspartate selective covalent warhead
  - Partnered with structural biology and computation chemistry teams to enable an iterative SBDD workflow
  - Promoted cross-functional collaboration with biology, DMPK, pharmacology, and toxicology teams to advance lead compounds through the testing funnel and to derisk the safety and tolerability profile of a novel class of covalent warheads both *in vitro* and *in vivo*
  - Enabled chemistry knowledge transfer to the PR&D team
  - Collaborated with the legal team to coordinate an IP filing strategy
- Disclosed the structure of RMC-5552 at the New Drugs on the Horizon session of the 2021 AACR Annual Meeting
- Managed 2 international CROs (80 FTEs) and 4 direct reports (MS and PhD)

Scientist II – Revolution Medicines 9/2016 – 3/2019

- Lead Chemist for the 4EBP1 program through DC nomination and IND submission of RMC-5552
  - Led the development of a bRo5 mTORC1 selective bi-steric inhibitor
  - Enabled chemistry knowledge transfer to the PR&D team
- Scaled-up and optimized the synthesis of RMC-4630 leading up to DC nomination for the SHP2 program
- Managed domestic and international CROs (30 FTEs) and 1 direct report (MS)

Postdoctoral Research Associate – Materials Department, University of California, Santa Barbara 1/2014 – 7/2016

- Developed a method to synthesize sterically hindered small molecule amines under ATRP-like conditions
- Quantified methylene bridge crosslinking within chloromethylated polystyrene-divinylbenzene resins utilizing solid-state NMR
- Partnered with Dow Water & Process Solutions to functionalize crosslinked resins
- Profiled metal binding affinities of functionalized resins with inductively coupled plasma (ICP-AES)
- Collaborated with the NAVY (Naval Surface Warfare Center) to provide NMR, FTIR, and GPC-MALS polymer characterization

Lecturer – Department of Chemistry, University of California, Santa Barbara 9/2013 – 12/2013

- Chem 109B: Organic Chemistry – Structure, Reactivity, and Synthesis of Organic Molecules

Graduate Research Assistant – University of California, Santa Barbara 6/2008 – 6/2013

- Developed enantioselective access to late-stage chiral 2,5-cyclohexadienone intermediates en route to scyphostatin analogues through the dearomatization of substituted tyrosines
- Accessed the core of the marine natural product paecilospirone utilizing an inverse demand Diels–Alder reaction of an *ortho*-quinone methide and enol ether

Undergraduate Research Assistant – Temple University 1/2007 – 5/2008

- Developed a seven-step route for the synthesis of *N*-hydroxyhomophthalimide analogues for testing as influenza endonuclease inhibitors
- Project lead for a team of 10 undergraduate researchers

Education

Ph.D., Organic Chemistry, University of California, Santa Barbara, CA 9/2008 – 6/2013

- Dissertation: "A Synthetic Approach Towards Paecilospirone"
- Advisor: Professor Thomas R. R. Pettus

B.S., Chemistry with Distinction, Temple University, Philadelphia, PA 9/2004 – 5/2008

- Advisor: Professor Scott McN. Sieburth

Publications

- Mahauad-Fernandez, W. D.; Yang, Y. C.; Lai, I.; Park, J.; Yao, L.; Evans, J. W.; Atibalentja, D. F.; Chen, X.; Kanakaveti, V.; Zhao, Z.; **Burnett, G. L.**; Lee, B. J.; Dinglasan, N.; Shifrin, N. T.; Ahler, E.; Quintana, E.; Gill, A. L.; Smith, J. A. M.; Singh, M.; Felsher, D. W. Targeting the MYC oncogene with a selective bi-steric mTORC1 inhibitor elicits tumor regression in MYC-driven cancers. *Cell Chem. Biol*. **2025**, *32*, 994–1012.e11.
- Weller, C.†; **Burnett, G. L.**†; Jiang, L.†; Chakraborty, S.; Zhang, D.; Vita, N. A.; Dilly, J.; Kim, E.; Maldonato, B.; Seamon, K.; Eilerts, D. F.; Milin, A.; Marquez, A.; Spradlin, J.; Helland, C.; Gould, A.; Ziv, T. B.; Dinh, P.; Steele, S. L.; Wang, Z.; Mu, Y.; Chugh, S.; Feng, H.; Hennessey, C.; Wang, J.; Roth, J.; Rees, M.; Ronan, M.; Wolpin, B. M.; Hahn, W. C.; Holderfield, M.; Wang, Z.; Koltun, E. S.; Singh, M.; Gill, A. L.; Smith, J. A. M.; Aguirre, A. J.; Jiang, J.; Knox, J. E.; Wildes, D. A Neomorphic Protein Interface Catalyzes Covalent Inhibition of RAS G12D Aspartic Acid in Tumors. *Science* **2025**, *389*, eads0239. †Co-first author
- **Burnett, G. L.***; Yang, Y. C.; Aggen, J. B.; Pitzen, J.; Gliedt, M. K.; Semko, C. M.; Marquez, A.; Evans, J. W.; Wang, G.; Won, W. S.; Tomlinson, A. C. A.; Kiss, G.; Tzitzilonis, C.; Thottumkara, A. P.; Cregg, J.; Mellem, K. T.; Choi, J. S.; Lee, J. C.; Zhao, Y.; Lee, B. J.; Meyerowitz, J. G.; Knox, J. E.; Jiang, J.; Wang, Z.; Wildes, D.; Wang, Z.; Singh, M.; Smith, J. A. M.; Gill, A. L.* Discovery of RMC-5552, a Selective Bi-Steric Inhibitor of mTORC1, for the Treatment of mTORC1-Activated Tumors. *J. Med. Chem.* **2023**, *66*, 149–169. *Co-corresponding author
- Lee, B. J.; Boyer, J. A.; **Burnett, G. L.**; Thottumkara, A. P.; Tibrewal, N.; Wilson, S. L.; Hsieh, T.; Marquez, A.; Lorenzana, E. G.; Evans, J. W.; Hulea, L.; Kiss, G.; Liu, H.; Lee, D.; Larsson, O.; McLaughlan, S.; Topisirovic, I.; Wang, Z.; Wang, Z.; Zhao, Y.; Wildes, D.; Aggen, J. B.; Singh, M.; Gill, A. L.; Smith, J. A. M.; Rosen, N. Selective inhibitors of mTORC1 activate 4EBP1 and suppress tumor growth. *Nat. Chem. Biol.* **2021**, *17*, 1065–1074.
- Feng, Z.-G.; **Burnett, G. L.**; Pettus, T. R. R. A Biomimetic Synthesis of des-Hydroxy Paecilospirone. *Synlett* **2018**, *29*, 1517–1519.

- Poelma, S. O.; Oh, S. S.; Helmy, S.; Knight, A. S.; **Burnett, G. L.**; Soh, H. T.; Hawker, C. J.; Read de Alaniz, J. Controlled Drug Release to Cancer Cells from Modular One-Photon Visible Light-Responsive Micellar System. *Chem. Commun.* **2016**, *52*, 10525–10528.
- Poelma, S. O.; **Burnett, G. L.**; Discekici, E. H.; Mattson, K. M.; Treat, N. J.; Luo, Y.; Hudson, Z. M.; Shankel, S. L.; Clark, P. G.; Kramer, J. W.; Hawker, C. J.; Read de Alaniz, J. Chemoselective Radical Dehalogenation and C–C Bond Formation on Aryl Halide Substrates Using Organic Photoredox Catalysts. *J. Org. Chem.* **2016**, *81*, 7155–7160.
- **Burnett, G. L.**; Rohanna, J. C.; Rosenberg, S.; Schultz, A. K.; Read de Alaniz, J. Determination of Methylene Bridge Crosslinking in Chloromethylated PS-DVB Resins. *J. Polym. Sci. Part A: Polym. Chem.* **2016**, *54*, 1955–1960.
- Fisher, D.; **Burnett, G. L.**; Velasco, R.; Read de Alaniz, J. Synthesis of Hindered α-Amino Carbonyls: Copper-Catalyzed Radical Addition with Nitroso Compounds. *J. Am. Chem. Soc.* **2015**, *137*, 11614–11617.
- Green, J. C.; **Burnett, G. L., IV**; Pettus, T. R. R. New Strategies for Natural Products Containing Chroman Spiroketals. *Pure Appl. Chem.* **2012**, *84*, 1621–1631.
- Cha, J. Y.; **Burnett, G. L., IV**; Huang, Y.; Davidson, J. B.; Pettus, T. R. R. A Strategy for the Late-Stage Divergent Syntheses of Scyphostatin Analogues. *J. Org. Chem.* **2011**, *76*, 1361–1371.

Patents

- Knox, J. E.; Koltun, E. S.; Latimer, B. K.; Madej, B. D.; Parsons, D. E.; Thompson, S.; Tomlinson, A.; Buckl, A.; **Burnett, G. L.**; Cregg, J.; Gill, A. L.; Luu, N. H. Q. RAS inhibitors. WO2025171296, 2025
- Gill, A. L.; Buckl, A.; Koltun, E. S.; Aay, N.; Tambo-ong, A. A.; Thompson, S.; Gliedt, M. J.; Knox, J. E.; Cregg, J.; Edwards, A. V.; Liu, Y.; **Burnett, G. L.** Bicyclic Heteroaryl Compounds and Uses Thereof. US Patent US 12,258,366 B2, March 25, 2025.
- **Burnett, G. L.**; Cregg, J.; Edwards, A. V.; Gill, A. L.; Knox, J. E.; Koltun, E. S.; Pitzen, J.; Semko, C. RAS Inhibitors. US Patent 12,252,497 B2, March 18, 2025.
- Knox, J. E.; Koltun, E. S.; Liu, Y.; **Burnett, G. L.**; Cregg, J.; Edwards, A. V.; Gill, A. L.; Buckl, A.; Semko, C. RAS Inhibitors. US Patent 12,202,845 B2, January 21, 2025.
- Semko, C. M.; Wang, G.; **Burnett, G. L.**; Aggen, J. B.; Kiss, G.; Cregg, J. J.; Gliedt, M. J. E.; Pitzen, J.; Lee, J. C.; Won, W.; Thottumkara, A. P.; Gill, A. L. C26-Linked Rapamycin Analogs as mTOR Inhibitors. US Patent 12,187,746 B2, January 7, 2025.
- **Burnett, G. L.**; Cregg, J.; Gill, A. L.; Gliedt, M. J.; Knox, J. E.; Koltun, E. S.; Latimer, B. K.; Madej, B. D.; Parsons, D. E.; Thompson, S.; Tomlinson, A.; Aay, N.; Buckl, A.; Luu, N. H. Q. Condensed Macrocyclic compounds as RAS inhibitors. WO 2024/211663, 2024.
- Koltun, E. S.; Knox, J. E.; Luu, N. H. Q.; Parsons, D. E.; Thompson, S.; Tomlinson, A.; Tye, M.; Wu, K. Y.; Buckl, A.; **Burnett, G. L.**; Cregg, J.; Edwards, A. V.; Gill, A. L. Condensed Macrocyclic compounds as RAS inhibitors. WO 2024/211712, 2024.
- **Burnett, G. L.**; Aggen, J. B.; Pitzen, J. C40-, C28-, and C-32-linked rapamycin analogs as mTOR inhibitors. US Patent 12,048,749 B2, July 30, 2024.
- **Burnett, G. L.**; Edwards, A. V.; Gill, A. L.; Gliedt, M. J.; Knox, J. E.; Koltun, E. S.; Aggen, J.; Buckl, A.; Pitzen, J.; Semko, C. Compounds, complexes, and methods for their preparation and of their use. WO 2024/102421 A3, 2024.
- Aggen, J.; **Burnett, G. L.**; Pitzen, J.; Gill, A. L.; Koltun, E. S.; Cregg, J.; Buckl, A.; Edwards, A. V.; Knox, J. E. RAS Inhibitors. US Patent 11,739,074 B2, August 29, 2023.
- Aay, N.; **Burnett, G. L.**; Cregg, J.; Gill, A. L.; Knox, J. E.; Koltun, E. S.; Liu, Y.; Buckl, A.; Lee, B. J.; Wildes, D. E.; Rice, M. A.; Singh, M. Ras Inhibitors. US Patent 11,690,915 B2, July 4, 2023.
- Koltun, E. S.; Cregg, J.; Gill, A. L.; Knox, J. E.; Liu, Y.; **Burnett, G. L.** RAS Inhibitors. WO 2023/133543 A1, 2023.
- Semko, C. M.; Wang, G.; **Burnett, G. L.**; Aggen, J. B.; Kiss, G.; Cregg, J. J.; Gliedt, M. J. E.; Pitzen, J.; Lee, J. C.; Won, W.; Thottumkara, A. P.; Gill, A. L. C26-Linked Rapamycin Analogs as mTOR Inhibitors. US Patent 11,685,749 B2, June 27, 2023.
- Buckl, A.; **Burnett, G. L.**; Cregg, J.; Edwards, A. V.; Gill, A. L.; Knox, J. E.; Koltun, E. S.; Liu, Y.; Semko, C. RAS Inhibitors. WO 2023/060253 A1, 2023
- Buckl, A.; **Burnett, G. L.**; Cregg, J.; Edwards, A. V.; Gill, A. L.; Knox, J. E.; Koltun, E. S.; Pitzen, J.; Semko, C. RAS Inhibitors for the Treatment of Cancer. US 2022/0396589 A1, 2022.
- Koltun, E. S.; Cregg, J.; Gill, A. L.; Knox, J. E.; Liu, Y.; **Burnett, G. L.** RAS Inhibitors. US 2023/0106174 A1, 2022.
- **Burnett, G. L.**; Edwards, A. V.; Gill, A. L.; Knox, J. E.; Koltun, E. S.; Pitzen, J. Covalent RAS Inhibitors and Uses Thereof. WO 2022/235866 A1, 2022.

- Pitzen, J.; **Burnett, G. L.**; Aggen, J. C40-, C28-, and C-32-Linked Rapamycin Analogs as mTOR Inhibitors. US Patent 11,364,300 B2, June 21, 2022.
- Aay, N.; **Burnett, G. L.**; Cregg, J.; Gill, A. L.; Knox, J. E.; Koltun, E. S.; Liu, Y.; Buckl, A.; Lee, B. J.; Wildes, D. E.; Rice, M. A.; Singh, M. Ras Inhibitors. US 2022/0105185 A1, 2022.
- Pitzen, J.; Aggen, J.; **Burnett, G. L.**; Gill, A. L.; Semko, C.; Edwards, A. V.; Gliedt, M. J.; Kiss, G.; Jogalekar, A.; Knox, J. E.; Buckl, A.; Koltun, E. S. Covalent RAS Inhibitors and Uses Thereof. WO 2021/108683 A1, 2021.
- Gill, A. L.; Buckl, A.; Koltun, E. S.; Aay, N.; Tambo-ong, A. A.; Thompson, S.; Gliedt, M. J.; Knox, J. E.; Cregg, J.; Edwards, A. V.; Liu, Y.; **Burnett, G. L.** Bicyclic Heteroaryl Compounds and Uses Thereof. US Patent 11,168,102 B1, November 9, 2021.
- Koltun, E. S.; Cregg, J.; Aay, N.; Buckl, A.; Gill, A. L.; Aggen, J.; **Burnett, G. L.**; Pitzen, J.; Whalen, D. M.; Knox, J. E.; Liu, Y. RAS Inhibitors. US 2021/0130369 A1, 2021.
- Koltun, E. S.; Cregg, J.; Gill, A. L.; Aggen, J.; **Burnett, G. L.**; Pitzen, J.; Buckl, A.; Knox, J. E.; Liu, Y. RAS Inhibitors. US 2021/0130303 A1, 2021.
- Aggen, J.; **Burnett, G. L.**; Pitzen, J.; Gill, A. L.; Koltun, E. S.; Cregg, J.; Buckl, A.; Edwards, A. V.; Semko, C.; Gliedt, M. J.; Knox, J. E. RAS Inhibitors. US 2021/0130326 A1, 2021.
- Pitzen, J.; Gliedt, M. J. E.; **Burnett, G. L.**; Aggen, J. B.; Kiss, G.; Cregg, J. J.; Semko, C. M.; Won, W.; Wang, G.; Lee, J. C.; Thottumkara, A. P.; Gill, A. L.; Mellem, K. T. C40-, C28-, and C-32-Linked Rapamycin Analogs as mTOR Inhibitors. US Patent 10,980,889 B1, April 20, 2021.
- Semko, C. M.; Wang, G.; **Burnett, G. L.**; Aggen, J. B.; Kiss, G.; Cregg, J. J.; Gliedt, M. J. E.; Pitzen, J.; Lee, J. C.; Won, W.; Thottumkara, A. P.; Gill, A. L. C26-Linked Rapamycin Analogs as mTOR Inhibitors. WO 2019/212991 A1, 2019.
- Semko, C.; Pitzen, J.; Wang, G.; Tibrewal, N.; Aggen, J. B.; Thottumkara, A.; **Burnett, G. L.**; Kiss, G.; Won, W.; Lee, J. C.; Gill, A. L. Rapamycin analogs as mTOR inhibitors. US 2021/0094975 A1, 2018.
- **Burnett, G. L.**; Read De Alaniz, J.; Rohanna, J. C.; Schultz, A. K.; Rosenberg, S. Vinyl Aromatic Resin. WO 2017/222980 A1, 2017.

Presentations

- **Burnett, L.** *Advancing bRo5 Chemical Matter to the Clinic*, MEDI Awards Sessions, ACS Fall 2025 National Meeting & Exposition, Washington DC, August 18, 2025.
- **Burnett, L.** *Advancing bRo5 Chemical Matter to the Clinic,* Philip S. Portoghese *Journal of Medicinal Chemistry*/*ACS Medicinal Chemistry Letters*/Division of Medicinal Chemistry Joint Lectureship Award, webinar June 12, 2025.
- **Burnett, G. L.** *Discovery of RMC-9805, an Oral, RAS(ON) G12D-Selective, Covalent, Tri-Complex Inhibitor*, Bay Area Chemistry Symposium, San Francisco, CA October 25, 2024.
- **Burnett, G. L.** *Discovery of RMC-5552, a selective bi-steric inhibitor of mTORC1 that suppresses 4EBP1 phosphorylation, for the treatment of mTORC1-activated tumors including RAS pathway escape*, 7th World Chemistry Conference and Exhibition, Lisbon, Portugal, September 16, 2024.
- **Burnett, G. L.**; Gliedt, M.; Semko, C. M.; Jiang, J.; Yang, Y. C.; Schulze, C. J.; Marquez, A.; Evans, J. W.; Wilson, S. L.; Hsieh, T.; Wang, Z. C.; Lee, B. J.; Choy, T. J.; Reyes, D. F.; Zhao, Y.; Wildes, D.; Wang, Z. P.; Singh, M.; Smith, J. A. M.; Gill, A. L. *Discovery of RMC-5552, a selective bi-steric inhibitor of mTORC1 that suppresses 4EBP1 phosphorylation, for the treatment of mTORC1-activated tumors including RAS pathway escape*, Frontiers in Medicinal Chemistry, Vienna, Austria, April 5, 2023.
- **Burnett, G. L.** *RMC-9805, a First-in-Class, Orally Bioavailable, Tri-Complex Covalent KRAS^{G12D}(ON) Inhibitor*, Discovery on Target, Boston, MA, October 18, 2022.
- **Burnett, G.L.**; Pitzen, J.; Gliedt, M.; Semko, C. M.; et al. *Discovery of RMC-5552, a selective bi-steric inhibitor of mTORC1 that suppresses 4EBP1 phosphorylation, for the treatment of mTORC1-activated tumors including RAS pathway escape*, ACS Fall 2021 National Meeting, Atlanta, GA, Hybrid Meeting, August 23, 2021.
- **Burnett, G.L.**; Pitzen, J.; Gliedt, M.; Semko, C. M.; et al. *Discovery of RMC-5552, a selective bi-steric inhibitor of mTORC1 that suppresses 4EBP1 phosphorylation, for the treatment of mTORC1-activated tumors including RAS pathway escape*, New Drugs on the Horizon session of the American Association for Cancer Research Annual Meeting 2021, Virtual Meeting, April 12, 2021.
- **Burnett, G. L.**; Cregg, J. J.; Koltun, E. S.; Nichols, R. J.; et al. *Discovery of Small Molecule Inhibitors of Oncogenic Mutants of RAS*, Third Rock's Beyond Great Scientific Poster Session, San Francisco, CA, June 26, 2019.
- **Burnett, L.** *New Materials as Tunable Chelants*, DowMI Workshop, UCSB, Santa Barbara, CA, March 19, 2015.
- **Burnett, L.**; Read de Alaniz, J. *Development of New Chelating Resins*, Dow Chemical, Midland, MI, July 9, 2014.

- **Burnett, G. L.** *Studies Towards the Synthesis of Paecilospirone*, 239th ACS National Meeting, San Francisco, CA, March 22, 2010.
- **Burnett, G. L.**; Yan, L.; Chen, P.; Dhabaria, A.; Sharkan, N.; Patel, H.; Shah, P.; Patel, J.; Chehab, C.; Sieburth, S. M.; Nicholson, A. W.; Waring, R. B. *N-Hydroxyhomophthalimide Analogs as Ribozyme Inhibitors*, 8th Annual ACS Philadelphia Poster Session, Philadelphia, PA, January 2, 2008.
- Yan, L.; **Burnett, L.**; Chen, P.; Dhabaria, A.; Finn, P.; Patel, H.; Shah, P.; Sharkan, N.; Sieburth, S. M.; Nicholson, A. W.; Waring, R. B. *N-Hydroxyhomophthalimides and Analogs as Two-Metal-Ion Dependent Nuclease Inhibitors*, 39th Middle Atlantic Regional Meeting of the American Chemical Society, Collegeville, PA, May 17, 2007.

Awards

- Philip S. Portoghese *Journal of Medicinal Chemistry* / Division of Medicinal Chemistry Joint Lectureship Award 2025

Professional Development

- Insights Discovery 2023
- Leading in a Matrix Team – The Leadership Edge 2022
- Situational Leadership Training – Incite Partners Consulting 2019
- From the Laboratory to Leadership – The Leadership Edge 2018
- ResMed – Residential School on Medicinal Chemistry and Biology in Drug Discovery 2017
- Biotech Primer – 2-Day Drug Development Immersion, South San Francisco, CA 2016