

**Géraldine Gontier, Ph.D.**

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## **TRANSLATIONAL PHARMACOLOGY & BIOMARKER STRATEGY | IN VIVO PHARMACOLOGY | PRECLINICAL DEVELOPMENT**

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### **PROFESSIONAL SUMMARY**

PhD scientist with 5+ years of biotechnology drug-development experience and 17+ years in neuroscience, aging, and disease biology. Extensive hands-on mouse pharmacology experience, including in vivo dosing, stereotaxic procedures, blood and tissue collection, necropsy, and downstream histology. Specializes in preclinical study design, PK/PD, translational biomarkers, and integration of exposure, target-engagement, efficacy, and safety data to guide candidate selection and program decisions. Experienced in both direct study execution and leadership of internal and CRO studies, from discovery through IND-enabling development and early clinical translation.

### **SELECTED TRANSLATIONAL PHARMACOLOGY & PROGRAM IMPACT**

- Integrated in vivo pharmacology, PK/PD, exposure-response, target-engagement, efficacy, and safety data across neuroscience and metabolic programs to inform candidate selection, dosing strategy, therapeutic-window assessment, and program progression.
- Designed and interpreted pharmacology studies across mouse, rat, and non-human primate models, defining dose levels, treatment schedules, sampling strategies, tissue/biofluid collection, pharmacodynamic endpoints, and exposure-response analyses.
- Established GPNMB as a translational pharmacodynamic biomarker of PIKfyve inhibition, progressing the biomarker from preclinical qualification across cellular, animal, and human ex vivo systems into clinical evaluation in ALS.
- Developed pharmacodynamic strategies for CD38 inhibition, integrating exposure with NAD<sup>+</sup>, NAM, and ADPR responses across blood and disease-relevant tissues to characterize target engagement, dose response, duration of pharmacological activity, and cross-species translation.
- Evaluated complex pharmacology and biomarker datasets to identify scientific gaps, assay limitations, model constraints, and development risks, recommending experiments and analyses needed to support program decisions.
- Directed externally executed pharmacology and bioanalytical studies, partnering with CROs on experimental design, protocol development, assay implementation, troubleshooting, data quality, interpretation, and delivery against program milestones.
- Communicated integrated scientific assessments and recommendations to multidisciplinary teams and leadership, translating preclinical findings into implications for candidate progression, dose selection, biomarker strategy, and IND-enabling development.

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### **EDUCATION**

Ph.D. in Physiology and Physiopathology, Pierre et Marie Curie University, Paris, France (2009–2013)

M.Sc. in Biology and Pharmacology of Aging, Pierre et Marie Curie University, Paris, France (2007–2009)

B.Sc. in Biomedicine, Descartes University, Paris, France (2006–2007)

## PROFESSIONAL EXPERIENCE

### Independent Consultant, In Vivo Pharmacology & Translational Biomarkers

SELF-EMPLOYED | San Francisco, CA | 2026-Present

- Provide independent scientific consulting in in vivo pharmacology, PK/PD, translational biomarkers, and preclinical development for biotechnology clients.
- Evaluate preclinical study designs, pharmacology and biomarker datasets, assay strategies, and development plans to identify scientific gaps and support data-driven decision-making.
- Advise on biomarker qualification, pharmacodynamic strategy, assay and matrix selection, exposure-response analysis, and preclinical study design supporting IND-enabling programs.

### Principal Scientist | Associate Principal Scientist

VERGE GENOMICS | South San Francisco, CA | 2022 – 2025

- Served as preclinical pharmacology lead for small-molecule programs across ALS, Parkinson's disease, obesity, and metabolic disease, integrating in vivo pharmacology, PK/PD, biomarker, efficacy, and safety data to support candidate selection and development decisions.
- Independently designed and interpreted PK/PD, target-engagement, efficacy, and dose-response studies, selecting animal models, dosing regimens, sampling schedules, biological matrices, tissues, and pharmacodynamic endpoints based on program hypotheses and development questions.
- Performed hands-on mouse pharmacology studies, including oral (PO), intraperitoneal (IP), and subcutaneous (SC) dosing, blood collection by cardiac puncture, tissue collection, and necropsy.
- Built exposure-response relationships linking systemic and tissue drug exposure with pharmacodynamic activity to characterize dose response, duration of target modulation, and pharmacologically active exposure ranges.
- Led preclinical PK/PD strategy supporting development-candidate nomination, integrating pharmacology, biomarker, exposure, and safety findings to compare compounds and inform candidate selection.
- Established GPNMB as a translational pharmacodynamic biomarker for PIKfyve inhibition, integrating evidence from cellular systems, animal models, human whole blood/PBMC studies, and PK/PD analyses; the biomarker subsequently progressed into clinical evaluation in ALS.
- Developed and qualified NAD<sup>+</sup>, NAM, and ADPR pharmacodynamic biomarkers for CD38 inhibition, evaluating dose- and exposure-dependent responses across blood and disease-relevant tissues and across species to inform dosing and translational strategy.
- Qualified translational biomarkers by evaluating biological relevance, fit-for-purpose assay performance, matrix selection, sampling feasibility, and exposure-response relationships to support preclinical and clinical translation.
- Partnered with Translational Medicine, Clinical, DMPK, Toxicology, Bioanalytical, and Discovery teams to evaluate biomarker feasibility, assay readiness, clinically relevant matrices, sampling strategies, and pharmacology findings supporting early clinical-development planning.
- Directed CRO-executed pharmacology and bioanalytical studies from experimental planning through protocol review, execution, troubleshooting, data QC, analysis, and interpretation, ensuring datasets were scientifically robust and decision-ready.
- Developed and qualified standardized LC-MS workflows for NAD metabolite quantification, improving assay robustness and reproducibility and enabling implementation across multiple CROs.
- Mentored scientists and research associates in experimental design, data interpretation, and scientific communication and contributed to manuscripts, reports, and regulatory-supporting documentation.

### Scientist

UNITY BIOTECHNOLOGY | South San Francisco, CA | 2020 – 2022

- Designed and interpreted in vivo pharmacology studies for senolytic ASO programs in neurodegenerative disease models, aligning study design, dosing, endpoints, and biomarker readouts with program hypotheses and milestones.
- Executed hands-on mouse studies with IP and SC dosing, stereotaxic injections, ALZET osmotic pumps for ASO delivery, cardiac puncture, tissue collection, and necropsy.
- Integrated efficacy, molecular, and immunohistology findings to evaluate pharmacological activity, mechanism, and proof-of-concept.

- Performed immunohistochemistry (IHC) and tissue imaging using epifluorescence and confocal microscopy to assess molecular and histological endpoints.
- Evaluated study outcomes and remaining pharmacology and biomarker gaps and recommended follow-up experiments to project teams.
- Communicated integrated, data-driven scientific assessments to project teams and leadership to inform experimental priorities and program strategy.
- Mentored research associates and interns in study planning, execution, data interpretation, and scientific rigor.

## **Postdoctoral Fellow**

**UCSF, SAUL VILLEDIA Lab | San Francisco, CA | 2014 – 2020**

- Designed and led in vivo studies of brain aging, neurogenesis, cognition, epigenetic regulation, and systemic drivers of brain function, integrating behavioral, molecular, cellular, and histological endpoints.
- Conducted hands-on mouse studies, including IP and SC dosing, stereotaxic injection of siRNA, cardiac puncture, tissue collection, and necropsy.
- Investigated disease-relevant mechanisms and therapeutic hypotheses using complex mouse studies and multidisciplinary experimental approaches.
- Performed immunohistochemistry (IHC) and epifluorescence and confocal microscopy to characterize molecular and cellular outcomes.
- Coordinated collaborative research programs involving multiple experimental techniques and investigators, managing study timelines and experimental dependencies.
- Mentored technicians and graduate students and contributed to scientific strategy, experimental rigor, and interpretation.
- Research resulted in multiple first- and co-author publications, including Cell Reports, Science, and Nature Medicine.

## **Graduate Student**

**PIERRE ET MARIE CURIE UNIVERSITY Martin Holzenberger Lab | Paris, France | 2009 – 2013**

- Investigated IGF-1 receptor signaling in Alzheimer's disease and aging, designing and executing in vivo and molecular studies to evaluate disease mechanisms and therapeutic hypotheses.
  - Integrated behavioral, biochemical, molecular, and histological endpoints to characterize the effects of IGF signaling on Alzheimer's disease pathology and aging.
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## SCIENTIFIC & DRUG-DEVELOPMENT EXPERTISE

**In Vivo Pharmacology:** Preclinical study design | Animal models | Dose-response | Efficacy | Tissue pharmacology | Cross-species translation

**Hands-on Mouse Techniques:** PO, IP, SC dosing | Stereotaxic injection | ALZET osmotic pumps | Cardiac puncture | Tissue collection and necropsy | IHC | Epifluorescence and confocal microscopy | Behavior

**Translational Pharmacology:** PK/PD | Exposure-response analysis | Target engagement | Pharmacodynamic activity | Dose selection | Therapeutic-window assessment

**Biomarker Strategy:** Translational and pharmacodynamic biomarkers | Biomarker qualification | Assay selection and readiness | Matrix selection | LC-MS biomarkers | Clinical translation

**Drug Development:** Candidate selection | IND-enabling pharmacology | Early clinical translation | Regulatory-supporting documentation | Scientific risk assessment

**Leadership:** Independent scientific assessment | Cross-functional decision-making | CRO/vendor oversight | Scientific communication | Mentoring

**Therapeutic Areas:** ALS | Parkinson's disease | Alzheimer's disease | FTD | Obesity | Metabolic disease | Aging

**Modalities:** Small molecules | ASOs

**Species & Systems:** Mouse | Rat | Non-human primate | Human ex vivo blood/PBMC systems

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## HONORS & AWARDS

Keystone Symposia Future of Science Fund Scholarship | AFAR Transition Award | Philippe Foundation Grant | French Foundation for Medical Research Fellowship | France Alzheimer Research Grant

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## PATENTS

- U.S. Patent No. 62/633041: Therapeutics invoking epigenetic changes for treating neurological conditions (2018)

## PUBLICATIONS

### Peer-reviewed Articles:

- Gontier G., Kim G. \*, Wang C., Zhu K., Gau R., Zhang N., Naphade S., Stewart A., Schmidt M.J., Galembo R., Shook B., Tarachandani A., Choi I., Raines S., Scannevin R.H., Grievink H.W., Smits L.M.G., Kremer P.H.C., Cadavid D. Glycoprotein Non-Metastatic Melanoma Protein B (GPNMB): A Translational Pharmacodynamic Biomarker for PIKfyve Inhibition with VRG50635. *Clinical and Translational Science*. (\*co-first author)
- Zhang N., Blockus H., Gontier G., Madero-Perez J., Ayhan F., Wong N., Viera Ortiz A., Gau R., Wang C., Heinrich L., Dhara M., Modan S., Taylor P., Andreoletti G., Shah K., Dulcey A., Shook B., Frank C., Choi I., Scannevin R.H. Inhibition of CD38 with VRG201 rescues multiple pathophysiological features of obesity and metabolic disorders in preclinical models. *Manuscript submitted*.
- Pratt K.J.B., Shea J.M., Remesal-Gomez L., Bieri G., Smith L.K., Couthouis J., Chen C.P. , Roy I.J., Gontier G. \*, Villeda S.A.\* (2022) Loss of neuronal Tet2 enhances hippocampal-dependent cognitive function. *Cell reports* (\*co-last author)
- Lin K., Bieri G., Gontier G., Müller S., Smith L.K., Snethlage C.E., White C.W., Maybury-Lewis S.Y., Villeda S.A. (2021) MHC class I H2-Kb negatively regulates neural progenitor cell proliferation by inhibiting FGFR signaling. *PLoS biology*
- Horowitz A.M., Fan X., Bieri G., Smith L.K., Sanchez-Diaz C., Schroer A.B., Gontier G., et al. (2020). *Blood factors transfer beneficial effects of exercise on neurogenesis and cognition to the aged brain*. *Science*.
- Gontier G., Iyer M., Shea J.M., Bieri G., et al. (2018). *Tet2 rescues age-related regenerative decline and enhances cognitive function in adult mouse brain*. *Cell Reports*.
- George C., Gontier G., Lacube P., et al. (2017). *The Alzheimer's disease transcriptome mimics the neuroprotective signature of IGF-1 receptor-deficient neurons*. *Brain*.
- Gontier G., George C., Chaker Z., et al. (2015). *Blocking IGF signaling in adult neurons alleviates Alzheimer's disease pathology through amyloid- $\beta$  clearance*. *Journal of Neuroscience*.
- Smith L.K., He Y.B., Park J.S., et al. (2015).  *$\beta$ 2-microglobulin is a systemic pro-aging factor that impairs cognitive function and neurogenesis*. *Nature Medicine*.
- Gontier G., Xu J., Chaker Z., et al. (2014). *Longevity effect of IGF-1R $\pm$  mutation depends on genetic background-specific receptor activation*. *Aging Cell*.
- Gontier G., Lukaszewicz A.C., Faivre V., et al. (2012). *Elevated production of reactive oxygen species by polymorphonuclear neutrophils in cerebrospinal fluid infection*. *Ann Intensive Care*.

### Reviews and Commentaries:

- Gontier G., Lin K., Villeda S.A. (2015). *Fat Chance for Neural Stem Cells in Alzheimer's Disease*. *Cell Stem Cell*. (Commentary)
- Gontier G., Holzenberger M. (2010). *IGF and insulin signaling pathways in longevity*. *Biol Aujourd'hui* [French].

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## REFERENCES