opnMe.com: a digital initiative for sharing tools with the biomedical research community

Andreas Gollner[1], Markus Köster[2], Paul Nicklin[3], Thomas Trieselmann[3], Elliott Klein[4], Jaromir Vlach[4], Claudia Heine[3], Marc Grundl[3], Jürgen Ramharter[1], David Wyatt[3], Menorca Chaturvedi[2], Alessio Ciulli[5], Katharine C. Carter[6], Susanne Müller[7], Daniel Bischoff[3], Peter Ettmayer[1], Eric Haaksma[8], Jürgen Mack[3], Darryl McConnell[1], Dirk Stenkamp[9], Harald Weinstabl[1], Matthias Zentgraf[3], Clive R. Wood[9] and Florian Montel[3]✉

Pharmacological probes are important tools for exploring disease biology and discovering new therapies. Often molecules of insufficient quality are used instead, leading to spurious and misleading results. The Boehringer Ingelheim open innovation portal opnMe.com addresses this deficiency by sharing extensively validated pharmacological probes with the scientific community.

[1]*Discovery Research, Boehringer Ingelheim RCV GmbH & Co KG, Vienna, Austria.*

[2]*Discovery Research, Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany.*

[3]*Discovery Research, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riss, Germany.*

[4]*Discovery Research, Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, USA.*

[5]*University of Dundee, James Black Centre, Dundee, UK.*

[6]*Univeristy of Strathclyde, Glasgow, Scotland.*

[7]*Structural Genomics Consortium, Frankfurt am Main, Germany.*

[8]*Animal Health Global Innovation, Boehringer Ingelheim GmbH, Ingelheim am Rhein, Germany.*

[9]*C.H. Boehringer Sohn AG & Co. KG, Ingelheim am Rhein, Germany.*

✉*e-mail: florian.montel@boehringer-ingelheim.com*

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'Open innovation' initiatives that engage the research community through precompetitive and collaborative platforms can address wide-ranging challenges in biomedical research. One key challenge is the limited availability of high-quality pharmacological probes to investigate disease biology and provide a basis for drug candidate development. Most research focuses on a small proportion of proteins with readily available probes, despite genetic evidence that the poorly understood fraction of the proteome is important in human disease. Studies that rely on low-quality probes still dominate the scientific literature, undermining research advances[1]. Furthermore, pharmaceutical companies rarely disclose the probes they develop for drug discovery projects, which could help address such issues.

Despite these challenges, there has been a recent increase in impactful biological research based on validated, high-quality, publicly available chemical probes. As a seminal example, the Structural Genomics Consortium (SGC), a public–private partnership founded in 2004, provides information and links to suppliers of 165 chemical probes free-of-cost to scientists. Here, we describe opnMe.com, an online portal established by Boehringer Ingelheim in 2017 to provide easy access to industry-quality pharmacological probes and facilitate communication between internal and external scientists. We also highlight selected key outputs to date.

opnMe.com

As of 28 February 2022, opnMe.com has 3,381 unique registered users from 1,907 institutions in 85 countries (Supplementary Fig. 1). Two asset-sharing arms for both small-molecule and biologic-based probes were featured as part of the launch: Molecules to Order (M2O), and Molecules for Collaboration (M4C). M2O provides unrestricted, cost-free access to high-quality, validated probes to any scientist with an affiliation at a public, private or industrial research institution. M4C invites external scientists to apply for access to innovative, in-house tool compounds developed during ongoing preclinical research and, in some cases, funding for their projects.

Molecules to Order (M2O). The M2O programme began in November 2017 with 20 well-characterized small molecules made available through opnMe.com. Compounds are added continuously. By 28 February 2022, 68 small-molecule probes were available, including their negative controls. M2O provides probes from Boehringer Ingelheim's inventory of published tool compounds, as well as internal compounds that have not previously been publicly disclosed and tool compounds developed by academic partners. Among the most-ordered probes are five proteolysis-targeting chimera (PROTAC) compounds originating from Alessio Ciulli at the University of Dundee and developed with the Boehringer Ingelheim PROTAC collaboration (see Supplementary Table 1 for compounds ranked by batches shipped). Each compound is accompanied by a comprehensive data package of in vitro and, in most cases, in vivo studies, well-characterized negative control compounds and protein–compound co-crystal structures. All probes and available negative controls have been screened on a standard assay panel to provide a complete picture of off-target selectivity. Site users may also request access to formulation data or any missing critical data. While Boehringer Ingelheim retains intellectual property rights for each probe, external scientists retain exclusive rights to their own research.

The user-friendly platform makes searching for and ordering M2O compounds as simple as possible. In most cases, M2O orders are shipped within days after an order is placed. In the period between M2O's launch and 28 February 2022, we received 1,433 orders for 4,235 unique batches of our probes from 1,060 unique registered portal users (Supplementary Fig. 2). The large number of orders has facilitated a range of scientific publications from scientists, independent of Boehringer Ingelheim's research network. Through 15 March 2022, external scientists published 50 peer-reviewed studies that used opnMe.com probes and a further 17 books and review articles referenced the platform. Internal scientists also published 20 papers on opnMe.com probes.

Probes on opnMe.com allowed several external scientists to conduct research in areas that previously lacked adequate probes or data. Here we highlight several articles that exemplify the range of impact (see Supplementary Table 2 for a complete list of articles that use opnMe.com probes). Słabicki et al. published an article on the mechanism of action of BI-3802, a BCL6 degrader developed by Boehringer Ingelheim that opens new directions in the field of 'molecular glue' research[2]. Ermondi et al. evaluated in silico methods for predicting drug properties of protein degraders including MZ1 and other opnMe.com PROTACs using data provided on the platform[3]. Ferraro et al. used a fatty acid synthesis (FAS) inhibitor to investigate the role of FAS in breast cancer brain metastasis in a novel use of a probe that was originally designed for our metabolic disease discovery programme (BI99179)[4]. Finally, Ricciardiello et al. reported an enhanced effect of the pan-RAS inhibitor BI-2852 in combination with hexosamine biosynthetic pathway inhibition, suggesting a novel combination therapy for pancreatic ductal adenocarcinoma[5].

Molecules for Collaboration (M4C). M4C publicly reveals protein targets from ongoing therapeutic projects and shares novel, unpublished tool compounds. The compounds chosen for M4C include small molecules, therapeutic antibodies and viral vectors. They are suitable for both in vitro and in vivo studies on targets for which high-quality, well-characterized tool compounds are not available.

M4C calls provide detailed in vitro and in vivo data profiles of the compounds, allowing researchers to immediately identify whether these compounds are appropriate tools for their research. Boehringer Ingelheim research scientists review all collaboration proposals, and all researchers receive detailed feedback on their proposals. Selected projects enter negotiations to ensure a fair and transparent collaboration. In addition to providing external researchers with internal expertise and compounds, including additional probes with differential properties, some projects also receive funding.

M4C has led to 48 new research collaborations with external scientists and helped to broaden several projects in Boehringer Ingelheim's discovery research portfolio. In April 2017, we piloted M4C prior to the official web launch with a challenge brokered through InnoCentive and NineSigma. Since the release of opnMe.com, there have been an additional 10 calls for proposals, the last of which began on 7 February 2022. Future calls will be released approximately twice per year as part of Boehringer Ingelheim's long-term research and external collaboration strategy. As M4C's reputation grew, we received a steady increase in the number of proposals, which was accompanied by an increase in high-quality collaborations (Supplementary Fig. 3). The complete calls received a total of 820 research proposals from 760 researchers. Of these, we selected 77 for further review and subsequently initiated negotiations for 54 projects, 89% of which led to collaboration agreements.

Outlook

An overview of the pharmaceutical tool-sharing landscape one year into opnMe.com's launch is shown in Supplementary Fig. 4. The opnMe.com initiative filled a key role in this landscape and continues to seek to accelerate biomedical research by lifting the barriers between academic researchers and high-quality, industrial technology (see Supplementary Fig. 5 for results of a user survey). We view opnMe.com as an opportunity for us to enhance our contribution to research and innovation from the research community at large. We are committed to ongoing growth through the addition of new challenges to M4C and compounds and additional supporting data packages to M2O. In March 2020, we launched a third arm, opn2EXPERTS, where we seek advice from biologists on strategies to address unmet patient needs.

With this publication, we hope to encourage others in industry to share tools from their research programmes and to provide a potential blueprint for such efforts. The popularity and impact of opnMe.com is evidence of the value in providing open tools with as few restrictions as possible to as many researchers as possible.

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Author contributions
M.C., A.G., M.G., C.H., E.K., M.K., P.N., J.R., T.T. and J.V. analysed user data, created figures and wrote the article, and are part of the opnMe core team. F.M. leads the opnMe.com team. A.G. and C.H. run the M2O arm. T.T., M.G., J.R., P.N., D.W., M.K., E.K. and J.V. run the M4C arm. M.K. and M.C. run the communication. D.B., P.E., E.H., J.M., D.M., D.S., H.W., M.Z. and C.R.W. are originators, supporters or sponsors of the open innovation initiative of Boehringer Ingelheim; they also commented on and reviewed this article. A.C. offered compounds for the M2O programme, K.C.C. was selected to get probe compounds to validate biological hypothesis, and S.M. is our collaborator for the chemical programme at SGC. A.C., K.C.C. and S.M. also contributed to article writing.

Competing interests
M.C., A.G., M.G., C.H., E.K., M.K., P.N., J.R., T.T., J.V., D.W., D.B., P.E., E.H., J.M., D.M., D.S., H.W., M.Z., C.R.W. and F.M. are all employees of Boehringer. A.C., K.C.C. and S.M. declare no competing interests.

Supplementary information
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