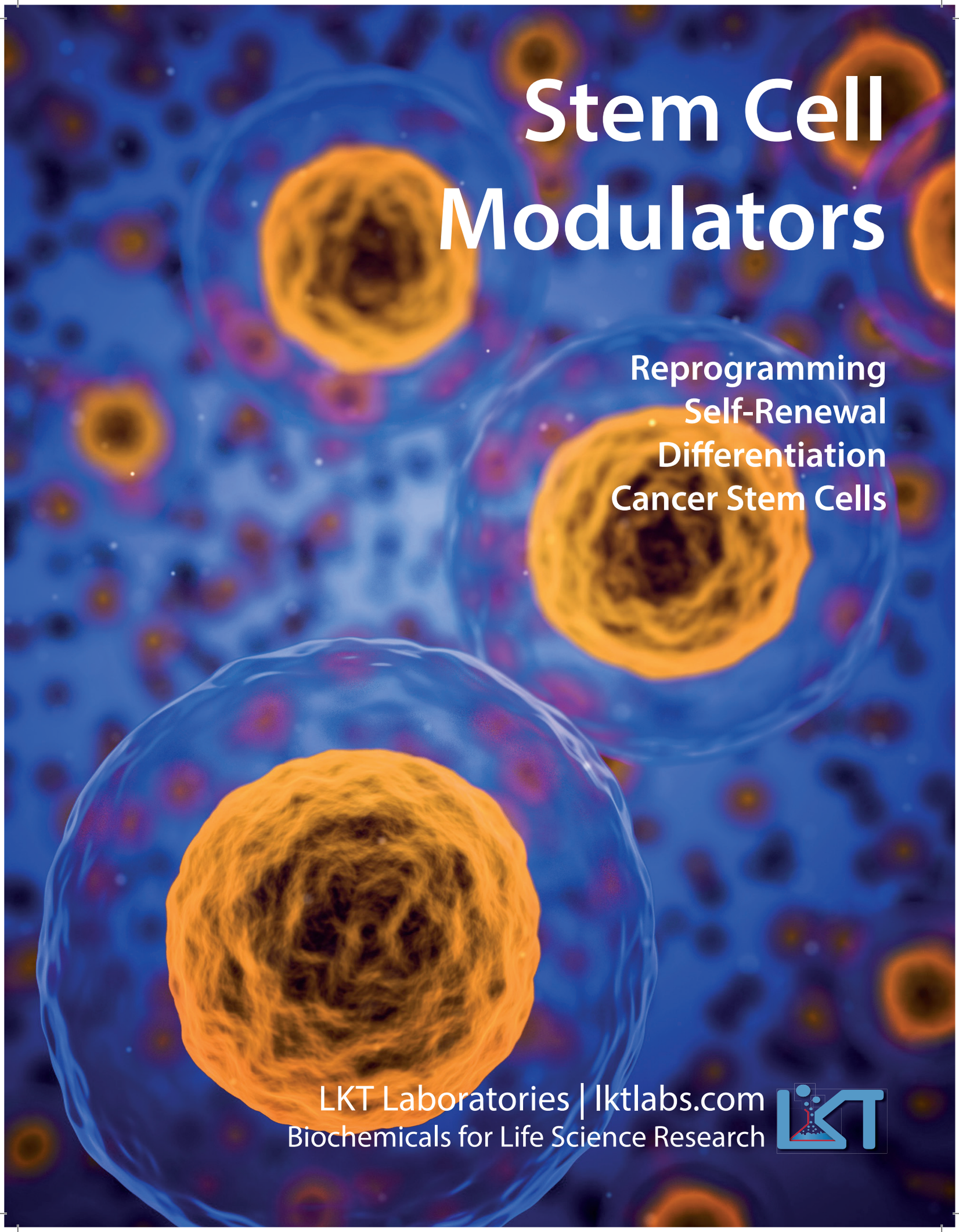
Stem Cell
Modulators
Reprogramming
Self-Renewal
Differentiation
Cancer Stem Cells
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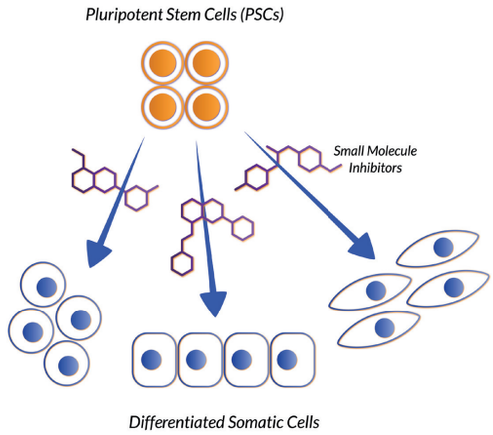
# Influencing Stem Cell Biology with Small Molecules

Small molecules are playing an increasingly important role in the advancement of stem cell research and technology. They are versatile tools that have shown effectiveness in everything from somatic cell reprogramming to stem cell renewal to differentiation of pluripotent stem cells. They have increased the efficiency and speed at which cells move to and from pluripotency, unlocking new avenues of previously cost-prohibitive research. In some cases, small molecules have even helped somatic cells bypass the need to move to pluripotency altogether in a process called transdifferentiation.

As stem cell research tools, small molecules offer a variety of inherent benefits. They offer a high degree of control to researchers, as they are able to reversibly alter the function of target proteins at precise points in time. Their synthesis routes are well developed and the compounds are well characterized, meaning that they are high in purity and low in variability between batches, both key factors in reproducibility. They are cost-effective relative to growth factors, and they are safer than using viral vectors that can introduce unwanted genetic material. Small molecules are playing an integral role in improving our understanding of stem cells, and enabling advancements in stem cell technology.




# Reprogramming Somatic Cells With Small Molecules

| ID | Name | Class | Description | Purity |
|---|---|---|---|---|
| A001001 | A 83-01 | TGF-β inhibitor | Enables Oct4-induced reprogramming in mouse fibroblasts. | ≥98% |
| A9602 | Azacitidine (5-azacytidine) | DNMT inhibitor | Accelerates transition to pluripotency in some cell types. | ≥98% |
| A9603 | 5-Aza-2'-deoxycytidine (Decitabine) | DNMT inhibitor | DNMT inhibiton may enhance reprogramming efficiency, diminishing the number of cells that only reach partially reprogrammed states. | ≥98% |
| B349921 | BIX-01294 TriHCl | HMT inhibitor | Enables reprogramming of some mouse cells to iPSCs without c-Myc and SOX2. | ≥98% |
| F5668 | Forskolin | cAMP activator | In combination with other compounds, induces pluripotent stem cells from somatic cells in mice. | ≥98% |
| K1655 | Kenpaullone | Inhibitor of GSK-3, CDK | Functionally replaces the reprogramming factor Klf4 while still yielding induced PSCs indistinguishable from murine ESCs. | ≥95% |
| P1202 | PD-325901 | MEK/ERK inhibitor | Promotes and increases efficiency of reprogramming in human somatic cells. | ≥98% |
| Q8016 | Quercetin Dihydrate | Flavonoid | Promotes reprogramming of somatic cells. | ≥95% |
| R0161 | Rapamycin | mTOR inhibitor | May enhance reprogramming efficiency. | ≥98% |
| R2400 | RG-108 | DNMT inhibitor | Accelerates transition to pluripotency in some cell types. | ≥98% |
| T6903 | Tranylcypromine HCl | MAO inhibitor | Enables Oct4-induced reprogramming in mouse fibroblasts. | ≥98% |
| T6933 | Trichostatin A | HDAC inhibitor | Establishes a ground state pluripotency in mouse iPS cells, erasing prior cell lineage "memory". | ≥98% |
| V0147 | Valproic Acid Sodium | HDAC inhibitor | Enables Oct4 and Sox2 induced reprogramming in primary human fibroblasts, bypassing oncogenes c-Myc and Klf4. | ≥98% |
| V5734 | Vorinostat (SAHA) | HDAC inhibitor | Promotes and increases efficiency of reprogramming in human and somatic cells in mice. | ≥98% |

Reprogramming cells from a somatic state to a pluripotent one using methods that bypass the need for oncogenes and viral vectors has been a boon to the research community. Small molecules have been useful on two fronts when it comes to reprogramming. First, they have made the process itself faster and more efficient, making it easier to generate desired cell types in vitro for disease modeling and other applications. This has been accomplished with epigenetic modifiers such as histone deacetylase inhibitors and DNA methyltransferase inhibitors. Small molecule antioxidant compounds reduce genome instability during reprogramming, when oxidative stress levels are elevated, improving efficiency. Secondly, small molecules have been useful in helping researchers understand the underlying mechanisms of pluripotency itself, unlocking new possibilities for the treatment of disease.

# Small Molecules Enhance Self Renewal

| ID | Name | Class | Description | Purity |
|---|---|---|---|---|
| A2420 | A-769662 | AMPK activator | Maintains naïve pluripotent state in mouse ESCs through AMPK activation. | ≥98% |
| A0918 | N-Acetyl-L-Cysteine | Antioxidant | Reduces genome instability of iPSCs in combination with other antioxidants. | ≥98% |
| A3208 | AICAR | AMPK activator | Maintains naïve pluripotent state in mouse ESCs through AMPK activation. | ≥98% |
| C9710 | Cyclopamine | Hedgehog signaling inhibitor | Decreases proliferation in human mesenchymal stem cells, demonstrating the importance of Hh signaling during hMSC proliferation. | ≥98% |
| G7443 | GSK-429286A | ROCK inhibitor | Increases cloning efficiency of human PSCs. Improves cell maintenance by increasing resistance to senescence. | ≥98% |
| N3310 | Nicotinamide | N-methyltransferase inhibitor | Activates senescent muscle stem cells. | ≥98% |
| P327212 | Pifithrin-α-cyclic HBr | p53 inhibitor | Enhances proliferation of hematopoietic stem cells. | ≥98% |
| P698583 | Prostaglandin E2 | EP activator | Improves survival and self-renewal of hematopoietic stem cells in mice. | ≥99% |
| T3132 | Thiazovivin | ROCK inhibitor | Enhances survival of human ESCs, potentially through the stabilization of E-cadherin signaling. | ≥98% |
| Y1000 | Y27632 2HCl | ROCK inhibitor | Reduces dissociation-induced apoptosis in embryonic and neural stem cells. Increases cloning efficiency. | ≥98% |

In order to support the expanding stem cell research field, improving the methodologies and technologies for maintaining stem cells in defined culture systems is critical. Additionally, research on the mechanisms of self-renewal and stem cell preservation will enable the development of new stem cell applications. Small molecules have demonstrated the ability to improve the long term maintenance of stem cells, while others have shown the potential to stimulate self-renewal. Small molecules might also improve stem cell survival by preventing apoptosis caused by imperfect stem cell manufacturing processes through the manipulation of signaling pathways.

# Small Molecules Promote Differentiation

| ID | Name | Class | Description | Purity |
|---|---|---|---|---|
| C291342 | CHIR-99021 | GSK3 inhibitor | Promotes differentation in human PSCs to cardiomyocytes. | ≥98% |
| D0260 | DAPT | Notch inhbitor | Promotes differentiation in PSCs to insulin producing beta cells. Also shown to promote neuronal differentiation. | ≥98% |
| D1693 | Dexamethasone | Glucocorticoid | Promotes differentiation in human mesenchymal cells to multiple lineage types. | ≥97% |
| F5668 | Forskolin | cAMP activator | Improves transdifferentiation of human adult peripheral T cells into neurons. | ≥98% |
| G1652 | Genistein | Isoflavone phytochemical | Inhibits differentiation of adipocytes, possibly due to interactions with AMPK. | ≥98% |
| I9060 | IWP-2 | Inhibitor of PORCN, WNT | Promotes differentation in human PSCs to cardiomyocytes. Increases conversion of ES cells. | ≥98% |
| K9600 | KY-0211 | WNT inhibitor | Promotes differentation in human PSCs to cardiomyocytes. | ≥98% |
| N3310 | Nicotinamide | N-methyltransferase inhibitor | Promotes differentiation in human iPSCs, as well as in ES cells to mature neurons. | ≥98% |
| P8370 | Purmorphamine | Hedgehog activator | Promotes differentiation in induced PSCs to spinal motor neurons. Also promotes differentiation from human mesenchymal cells. | ≥98% |
| R1885 | Reversine | Inhibitor of MEK, AurK | Promotes differentiation in porcine stem cells to germ-like cells. | ≥98% |
| S0500 | SB-203580 | p38 MAPK inhibitor | Promotes differentiation in human and mouse ES cells to cardiomyocytes. | ≥98% |
| S0400 | SB-431542 | TGF-β inhibitor | Improves neuronal differentiation in vitro from human PSCs. Also enhances cardiomyocyte differentiation from mouse and human PSCs. | ≥98% |
| S3343 | Silibinin | Phytoestrogen flavonoid | Induces vascular differentiation from mouse ESCs, potentially by way of PI3K, STAT3, and AKT activation. | ≥97% |
| R1780 | trans-Retinoic Acid | RAR activator | Retinoids are involved in the regulation of differentiation. Promotes differentiation in induced PSCs to motoneurons. | ≥98% |
| X0384 | XAV-939 | Inhibitor of TNKS, WNT | Promotes differentation of cardiomyocytes from human PSCs. | ≥95% |

Manipulating developmental signaling pathways to induce differentiation in stem cells has far reaching implications in cancer research, neuroscience, and regenerative medicine. Key factors of successful induced differentiation include efficiency, reliability, and reproducibility. By this measure, small molecules give researchers an excellent tool to maintain control over stem cells as they transition to other cell lineages of interest. Numerous signaling pathways have proven to be important in differentiation, including WNT, Notch, Hedgehog, and TGF-β. This process is rife with variables, including the choice of initial pluripotent cell and desired cell lineage, the method of directing differentiation, the timing of introducing differentiation inducing tools, and potential combination effects with other small molecules. Understanding and optimizing differentiation is an ongoing effort.

# Targeting Cancer Stem Cells With Small Molecules

| ID | Name | Class | Description | Purity |
|---|---|---|---|---|
| A6234 | Apigenin | Flavonoid | Supresses stemness traits in TNBC cells, possibly due to decreased YAP/TAZ activity. | ≥98% |
| C0267 | Carnosol | Diterpene | Targets c-Met dependent pancreatic CSCs, down regulating pluripotency maintaining genes. | ≥98% |
| C2947 | Chlorpromazine HCl | Antipsychotic | Supresses stemness traits in breast cancer CSCs, possibly due to the degradation of YAP (yes-associated protein). | ≥98% |
| D5898 | Doxycycline Monohydrate | Tetracycline antibiotic | Targets metabolic pathways by impairing mitochondrial function. Certain metabotypic phenotypes may have a causitive role in maintaining stem traits in CSCs. | ≥97% |
| E6234 | Epigallocatechin Gallate | Flavonoid found in green tea | Inhibits the transcription and translation of genes that encode stemness markers such as Nanog, Oct4, Sox2, and CD44, thereby inhibiting CSC self-renewal. | ≥98% |
| G4580 | Glucosamine Hydrochloride | Inhibitor of STAT3 | Reduces stemness of breast cancer CSCs by inhibiting the STAT3 pathway. STAT3 signaling contributes to the regulation of breast cancer CSCs. | ≥96% |
| J3204 | E-JIB-04 | Inhibitor of Jumonji histone demethylases | Selectively targets colorectal cancer stem cells, reducing the self-renewal and stemness of those cells, perhaps due to interaction with WNT/β-catenin signaling. | ≥98% |
| J3205 | Z-JIB-04 | Inhibitor of Jumonji histone demethylases | Selectively targets colorectal cancer stem cells, reducing the self-renewal and stemness of those cells, perhaps due to interaction with WNT/β-catenin signaling. | ≥98% |
| M2076 | Metformin HCl | AMPK activator | Targets metabolic pathways by inhibiting glycolysis. Certain metabotypic phenotypes may have a causitive role in maintaining stem traits in CSCs. | ≥98% |
| P0270 | Parthenolide | Sesquiterpene lactone | Induces apoptosis in CSCs of nasopharyngeal carcinoma, perhaps due to COX-2 inhibition. | ≥98% |
| S0168 | Saractinib | Src inhibitor | Combined MEK-Src inhibition decreases tumor-initiating ovarian cancer cells. | ≥98% |
| S1846 | Selumetinib | MEK inhibitor | Combined MEK-Src inhibition decreases tumor-initiating ovarian cancer cells. | ≥98% |
| V1769 | Verapamil HCl | Calcium channel blocker | Inhibits pancreatic cancer tumor growth by targeting stem-like side population cells, and has a pro-apoptotic effect in gemcitabine resistant cells. | ≥98% |
| W3576 | Withaferin A | Steroid lactone | Targets c-Met dependent pancreatic CSCs, down regulating pluripotency maintaining genes. | ≥98% |

The concept of cancer stem cells (CSCs) is a relatively new idea in cancer research. Among all cancer cells found within a given tumor, some fraction exhibit stem-like traits and are responsible for tumor progression and maintenance. These cells are CSCs, and have the ability to generate the other cancer cell types. CSCs may be the first cancer cells to develop, and could be the driving force behind metastasis and drug resistance. This would make CSCs crucial targets in combating cancer and explain why some cancer treatments fail. Although there is increasing evidence that CSCs exist, identifying and targeting them remains a challenge. The same signaling pathways that have been studied for their utility in stem cell research (WNT, Notch, Hedgehog, etc.) can be useful in understanding and eliminating the stem-like qualities of CSCs. Other methods, such as targeting CSC metabolism, have also been explored. Small molecules targeting these pathways and functions will play an important role in providing clarity and solutions to this developing field.

## About Us

LKT Labs is focused on the production and distribution of high purity biochemicals for all types of life science research, including cancer biology, immunology, cardiovascular studies, microbiology, and neuroscience. Our product library includes a wide variety of compounds that can be used for a broad spectrum of in vitro and in vivo research applications.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