SAN DIEGO, June 25, 2014 /PRNewswire-iReach/ -- SignalRX Pharmaceuticals Inc., focused on developing more effective oncology drugs though molecular design imparting multiple target inhibition, today announced the discovery of patented new molecules such as SF2523 that inhibit kinase targets such as PI3 kinase (PI3K) while also blocking epigenetic targets such as bromodomain proteins. SignalRx's in vivo evidence of efficacy without toxicity in mouse cancer models with SF2523 alleviates potential theoretical safety concerns arising from inhibiting multiple key nodal cancer targets with one drug.

The ability to safely simultaneously inhibit multiple key targets is highly sought after in cancer treatment to maximize efficacy and prevent resistance. Replacing several combinations of drugs with one drug hitting multiple targets is also being driven by exploding oncology drug costs to patients and to the health care system. SignalRx compounds are being developed as next generation PI3K inhibitors and it has now been shown that they also potently inhibit certain bromodomain proteins such as BRD4. SF2523 is a lead dual inhibitor compound and has been demonstrated to: 1) inhibit proliferation across 18 different cancer cell lines; 2) induce apoptosis in neuroblastoma cells, renal cell carcinoma cells, multiple brain cancer cell lines including patient-derived samples; 3) block angiogenic signaling and blood vessel production in vivo; 4) inhibit cancer stem cells in breast and human medulloblastoma patient cells; 5) exhibit potent antitumor efficacy and anti-metastatic effects without toxicity in renal cell carcinoma xenograft models, neuroblastoma mouse models, orthotopic pancreatic cancer model and Lewis lung cancer models.

Bromodomain proteins bind to acetylated lysine groups on chromatin and promote gene transcription. SignalRx's compounds act as acetyl lysine mimetics and prevent the bromodomain protein from binding to chromatin. This mechanism of action is distinct from the compound's PI3K inhibition where the inhibitors bind in the ATP catalytic site of the kinase. This allows for the first time simultaneous control of both the PI3K pathway and the transcription of certain genes mediated by bromodomain proteins. An example of the utility of this approach to solve unmet medical needs is to block the tumor suppressor gene MYC which is a driver in many cancers including CLL and multiple myeloma and for which small molecule inhibitors have been elusive. Inhibition of PI3K increases the cellular degradation of MYC protein while BRD4 inhibition decreases the transcription (production) of MYC protein. Use of SignalRx's dual PI3K/BRD4 inhibitors provides a unique and effective approach to block the action of MYC via two orthogonal mechanisms demonstrated with lead compound SF2523 to be efficacious without toxicity in mouse models.

These new compounds are broadly covered by composition-of-matter U.S. Patent No. 8,557,807 entitled "Thienopyranones as kinase inhibitors" issued October 15, 2013. Additional information on preparation and structure-activity-relationships of these compounds were recently published in the Journal of Medicinal Chemistry (February 14th 2013 issue, volume 56, pages 1922-1939).

"The discovery of these compounds inhibiting both PI3K and BRD4, particularly SF2523, represents a major step forward in designing anticancer agents to be as effective as possible" said Donald L. Durden, MD, PhD, SignalRx President and Chief Executive Officer. "Additionally, the problem of early stage clinical trial evaluation of multiple combinations is solved by this approach by consolidating at least two of the combination partners into one drug. Moreover, because two separate drugs will always suffer from differing cell penetration, metabolism, and pharmacokinetics our approach of one molecule hitting two critical targets in the same cell is the only way to ensure that desired simultaneous blockage of multiple key signaling pathways is achieved in vivo."

About SignalRx Pharmaceuticals Inc.

SignalRx is a privately held corporation developing small molecule inhibitors of key signaling pathways used by cancer and cancer stem cells to evade treatments. Such key signaling pathways include major cell survival mechanisms, epigenetic regulation processes, and DNA repair actions encompassing critical targets such as PI3K, MEK, BRAF, Wnt, HDAC, DNMT, PARP and BET bromodomains. SignalRx is leveraging its expertise in PI3K pathway inhibition to be the leader in developing single molecule therapeutics that selectively inhibit synergistic critical cancer pathways. These designed multi-action therapeutics are expected to exhibit enhanced anticancer effects and are the result of an effort to be both efficacious and cost effective in an evolving price sensitive oncology environment relying increasingly on prohibitively expensive combination treatments.

For additional information please visit our website (www.signalrx.com) or email us at info@signalrx.com