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WNK1 kinase is a serine/threonine protein kinase associated with familial hypertension and has recently been identified as an upregulated signature gene in triple negative breast cancer. It is a drug target for cancer and hypertension, and a homolog WNK3 has been implicated in brain disfunctions including Parkinson's disease and stroke. Using a 230,000 compound high-throughput screen, we identified several compounds that inhibit the kinase activity of WNK1 selectively. From these compounds, molecules that are more potent WNK3 were identified. The crystal structure of SW074925, a novel WNK1 inhibitor scaffold reveals active site binding.