

FACT SHEET

Media:	Charlotte Arnold	(650) 467-6800
Advocacy:	Sonali Padhi	(650) 467-0842
Investor:	Karl Mahler	011 41 61 687 8503
	Thomas Kudsk Larsen	(650) 467-2016

MetMab and Non-Small Cell Lung Cancer

MetMab is a novel, investigational, monovalent (one-armed), monoclonal antibody designed to block a certain type of Met signaling that can occur in tumor cells.

About Met

Met, a protein on the surface of cells, is a receptor for the protein Hepatocyte Growth Factor/Scatter Factor (HGF/SF). HGF/SF binding to Met causes Met molecules to come together, or dimerize with each other. This process “activates” Met and initiates a signaling cascade that is believed to play an important role in cell proliferation, survival and spread to other parts of the body.^{1,2}

Met and Cancer

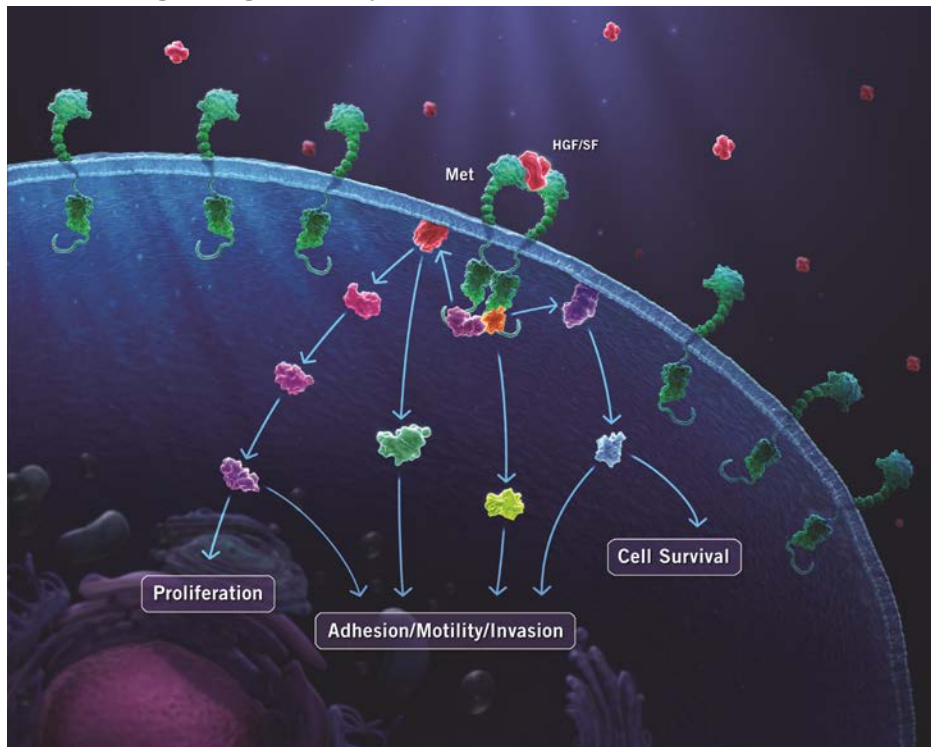
Increased levels of Met or its binding partner, HGF/SF, can lead to increased Met signaling and are associated with a worse prognosis in many types of cancer.³ For example, approximately half of all non-small cell lung cancer (NSCLC) tumors have high levels of Met on the cell surface, which can result in cell proliferation, spread to other parts of the body and escape from the therapeutic effects of chemotherapy, radiotherapy and targeted medicines.⁴⁻⁸

According to the American Cancer Society, lung cancer is the second most commonly diagnosed cancer in both men and women in the United States and the leading cause of cancer deaths. Each year, more people die from lung cancer than from breast, colon and prostate cancers combined. NSCLC accounts for 85 percent of all lung cancers.⁹

How MetMab Works (Proposed Mechanism of Action)

- MetMab is designed to block the cancer-driving effects of HGF/SF binding to Met
 - MetMab binds to Met on the cell surface
 - HGF/SF is unable to bind to Met when MetMab is bound to Met
 - This prevents HGF/SF from causing Met dimerization and activation
- MetMab is being developed with a companion diagnostic test to identify NSCLC patients whose tumors have high levels of Met

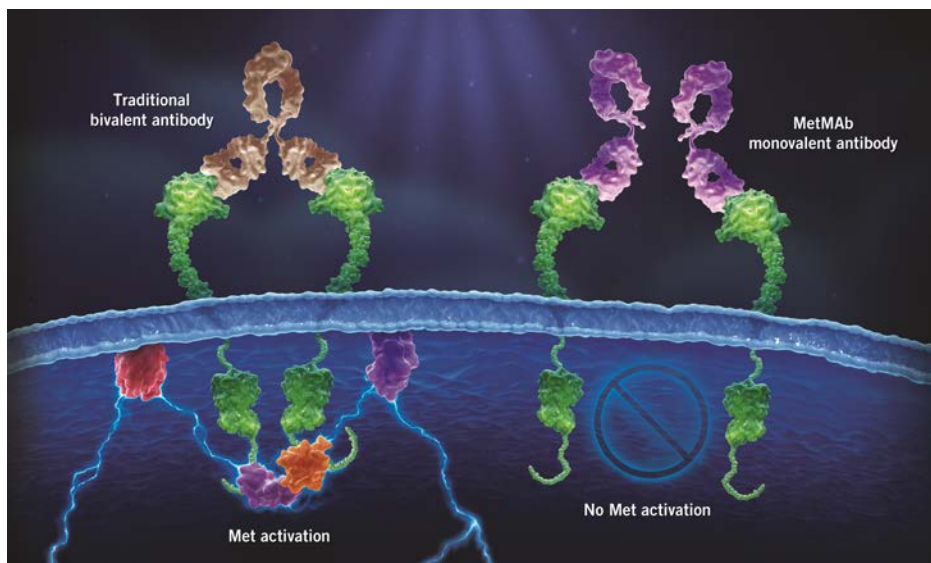
The Met Signaling Pathway¹⁻³



HGF/SF binds to and activates Met on the cell surface, leading to cell proliferation, survival and spread to other parts of the body.

MetMab: A Novel One-Armed Design

Preclinical studies of Met revealed that conventional two-armed (bivalent) antibodies can cause Met dimerization and activation. To address this problem, Genentech researchers created a novel one-armed (monovalent) antibody that blocks HGF/SF from binding to Met without causing Met to dimerize.^{6,10}



MetMAB Clinical Studies and Development Program

- A Phase II study of MetMAB in combination with erlotinib in people with advanced NSCLC has been completed
- More information about MetMAB clinical trials can be found at <http://www.clinicaltrials.gov>

For additional information on MetMAB, please visit <http://www.biooncology.com>.

References

1. Peruzzi B, Bottaro DP. Targeting the c-Met signaling pathway in cancer. *Clin Cancer Res.* 2006;12(12):3657-3660.
2. Eder JP, Vande Woude GF, Boerner SA, LoRusso PM. Novel Therapeutic inhibitors of the c-Met signaling pathway in cancer. *Clin Cancer Res.* 2009;15(7):2207-2214.
3. Lengyel E, Prechtel D, Resau JH, et al. C-Met overexpression in node-positive breast cancer identifies patients with poor clinical outcome independent of Her2/neu. *Int J Cancer.* 2005;113(4):678-682.
4. Cipriani NA, Abidoye OO, Vokes EE, et al. MET as a target for treatment of chest tumours. *Lung Cancer.* 2009;63(2):169-179.
5. Tsao M, Liu N, Chen J, et al. Differential expression of Met/hepatocyte growth factor receptor in subtypes of non-small cell lung cancer. *Lung Cancer.* 1998;20:1-16.
6. Birchmeier C, Birchmeier W, Gherardi E, Vande Woude GF. Met, metastasis, motility and more. *Mol Cell Biol.* 2003;4:915-925.
7. Engelman JA, Janne PA. Mechanisms of acquired resistance to epidermal growth factor receptor tyrosine kinase inhibitors in non-small cell lung cancer. *Clin Cancer Res.* 2008;14(1):2895-2899.
8. Fan S, Meng Q, Laterra JJ, Rosen EM. Role of Src signal transduction pathways in scatter factor-mediated cellular protection. *J Biol Chem.* 2009;284:7561-7577.
9. American Cancer Society. Cancer Facts and Figures 2010. <http://www.cancer.org/acs/groups/content/@epidemiologysurveillance/documents/document/acspc-026238.pdf>. Accessed March 29, 2011.
10. Martens T, Schmidt N-O, Echerich C, et al. A novel one-armed anti-c-Met antibody inhibits glioblastoma growth in vivo. *Clin Cancer Res.* 2006;12:6144-6152.

BIO0000417600

###