**Table S1.** Profiling of NVP-JAA120 in biochemical and cellular assays.

| Assay | $IC_{50}$ (nmol/L) |
|---|---|
| MET kinase assay | <3 |
| 77 other kinase assays | >2900/>10,000* |
| Proliferation (GTL-16) | 1.6 |
| Proliferation (EBC-1) | 0.7 |
| Proliferation (MKN-45) | 2.9 |
| MET phosphorylation (GTL-16) | 1.4 |
| MET phosphorylation (A549) | 0.9 |
| Proliferation (BaF3 TPR-MET) | <4.6 |
| Proliferation (14 other BaF3 strains) | >10,000 |

Profiling of NVP-JAA120 in biochemical and cellular assays was done as described in (1).

* In a panel of 78 biochemcial kinase assays, 67 assays did not show inhibition by JAA120 at the maximal concentration of 10 μM, while 10 assays gave $IC_{50}$ values between 2.9 and 9.1 μM. MET was inhibited half-maximally below 3 nM.

**Table S2.** Ligand-mediated rescue in 4 MET-dependent cell lines treated with a MET inhibitor. Table of hits from primary screening data with an average transcript Z-score greater than 3 across all lines.

| | Cell line | | | | |
|---|---|---|---|---|---|
| **Gene symbol, Transcript ID** | **GTL-16** | **Hs 746T** | **KP-4** | **MKN-45** | **NCI-H1993** |
| **DGKA** | | | | | |
| NM_201445.1 | | | | | 3.07 |
| **ENPP5** | | | | | |
| NM_021572.4 | | | | 4.45 | |
| **ENTPD5** | | | | | |
| NM_001249 | 4.21 | | | | |
| **FGF16** | | | | | |
| NM_003868 | 29.92 | | | 15.59 | |
| **FGF17** | | | | | |
| NM_003867 | 3.65 | | | | |
| **FGF18** | | | | | |
| NM_003862 | 3.93 | | | 8.56 | |
| **FGF3** | | | | | |
| NM_005247 | 3.34 | | | | |
| **FGF6** | | | | | |
| NM_020996 | 12.37 | 5.07 | | 7.51 | |
| **FGF7** | | | | | |
| NM_002009 | 31.98 | | | 35.47 | |
| **FGF8** | | | | | |
| NM_006119 | 25.67 | 3.72 | | 13.98 | |
| NM_033163 | 16.72 | | | 19.65 | |
| NM_033164 | 3.37 | | | | |
| **FGF9** | | | | | |
| NM_002010 | 34.37 | | | 10.96 | |
| **FJX1** | | | | | |
| NM_014344.3 | | | | 4.93 | |
| **GPX4** | | | | | |
| NM_001039847 | 4.02 | | | | |
| **HBEGF** | | | | | |
| NM_001945 | 11.31 | | | | |
| **IFNA6** | | | | | |
| NM_021002 | 3.09 | | | | |
| **IFNA7** | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| NM_021057 | 3.51 | | | | |
| **IFNB1** | | | | | |
| NM_002176 | 3.07 | | | | |
| **IFNG** | | | | | |
| NM_000619 | 8.18 | | | | |
| **IGF1** | | | | | |
| NM_001111284.1 | | | | | 3.34 |
| **IL4** | | | | | |
| NM_000589 | 3.07 | | | | |
| **LOC255809** | | | | | |
| XM_938361 | 5.90 | | | | |
| **MAPKAPK3** | | | | | |
| NM_004635.3 | | | | 3.62 | |
| **NRG1** | | | | | |
| NM_013956 | 14.78 | | | | |
| NM_013964 | 5.79 | | | 6.78 | |
| **NRG2** | | | | | |
| NM_004883.2 | | | | 12.74 | |
| NM_013981.3 | | | | 8.29 | |
| NM_013982.2 | | | | 9.44 | |
| **OSM** | | | | | |
| NM_020530.3 | | 5.89 | 5.23 | | 4.50 |

**Table S3.** Ligand-mediated rescue in FGFR-dependent KATO III and RT-112 cells treated with FGFR inhibitor. Table of hits from primary screening data with an average transcript Z-score greater than 3 across all lines.

| | Cell Line | |
|---|---|---|
| **Gene symbol, Transcript ID** | **KATO III** | **RT-112** |
| **ASPN** | | |
| NM_017680.4 | 4.30 | |
| **DAND5** | | |
| NM_152654.2 | 3.64 | |
| **HBEGF** | | |
| NM_001945.2 | 6.90 | 9.04 |
| **HGF** | | |
| NM_000601.4 | 6.26 | 12.54 |
| NM_001010932.1 | 5.01 | 15.18 |
| **IL1RN** | | |
| NM_173841.2 | 3.72 | |
| **NRG1** | | |
| NM_013956.3 | 7.87 | 12.93 |
| NM_013957.3 | 12.41 | 11.15 |
| NM_013960.3 | | 7.85 |
| NM_013964.3 | 6.56 | 9.65 |
| **NRG2** | | |
| NM_004883.2 | 3.39 | 7.89 |
| NM_013981.3 | | 10.42 |
| NM_013982.2 | 4.48 | 7.29 |
| **TGFA** | | |
| NM_001099691.1 | | 4.01 |
| NM_003236.2 | | 4.51 |

**Table S4.** Expression of selected RTKs and cognate ligands in cancer cell lines as a basis for selecting models for testing of FGFR/MET inhibitor combinations.

See separate Excel file.

Cell line models were prioritized and ranked for selection (columns: A,B). The ranking was based on gene expression levels of MET mRNA and HGF mRNA as well as all FGFx and FGFRx mRNAs (columns: I-Y). To integrate and balance the individual gene expression levels the following strategy was applied: For each mRNA cell lines were ranked by its expression level. The lowest rank corresponded to the highest expression level. Columns D and E list the ranks of MET and HGF expression, respectively. In case of MET the minimal rank of the two probe sets is reported. Columns G and H list the rank for FGFx and FGFRx expression. Here, only the minimal rank is reported for each family of genes. The final ranking (column B) is defined by the average rank of column E (HGF) and column F (FGFx, FGFRx) while excluding the third of the cell lines with the lowest expression of MET (column D, rank >= 600). Column F reports the rank which is reached by at least one FGFx and one FGFRx (maximum of the columns G and H).

**Table S5.** Anti-tumor effects and assessment of synergy

| | C | A (INC280) | B (BGJ398) | AB (combo) | A/C | B/C | A/C x B/C | AxB/C | Difference | Result |
|---|---|---|---|---|---|---|---|---|---|---|
| **Δ tumor volume** | 309.6 | 333.6 | -16.6 | -67.8 | 1.078 | -0.054 | -0.058 | -0.219 | -0.16 | synergy |

The significance of combination data was assessed using the method presented by Clark (2), which can estimate interactions from limited data. For compound A, B or the combination AB (with control group C), the end values are collected. Antagonism is predicted when the calculation AB/C > A/C x B/C, additive AB/C = A/C x B/C, synergistic interactions are predicted to occur when AxB/C < A/C x B/C.