**Figure Captions**

**a** Number of protein-altering mutations in cancer samples.

**b** Co-occurrence of gene alterations in cancer samples.

**c** Survival probability for LRP1B mutant versus wild-type (WT) samples.

**d** Survival probability for FAM135B mutant versus WT samples.

**e** Gene expression and signaling pathways.

**Cell cycle regulation**
- **CDK2A**
  - 6% 0% 0%
- **CDK4/6**
- **CCND1**
- **MDM2**
  - 4% 15% 0%
- **RBL1**
  - 4% 15% 0%
- **RBL2**
  - 6% 0% 0%
- **RB1**
  - 23% 48% 54%
- **TP53**
  - 84% 66% 73%
- **TP73**
  - 54% 19% 23%
- **E2F**

**Transcriptional regulation**
- **CREBBP**
  - 9% 11% 0%
- **MYCL1**
  - 61% 32% 67%
- **MYCN**
  - 39% 16% 11%
- **EP300**
  - 32% 0% 6%
- **MYC**
  - 57% 42% 93%

**Receptor kinase/PI3K signaling**
- **KIT**
  - 25% 5% 27%
- **IGF1R**
- **FGFR1**
  - 44% 11% 36%
- **IRS2**
  - 47% 16% 54%
- **PIK3CA**
  - 67% 58% 93%
- **PTEN**
  - 7% 11% 11%

**Notch signaling/neuroendocrine differentiation**
- **NOTCH**
  - 28% 11% 5%
- **HESi1/HEY1**
  - 48% 11% 50%
- **ASCL1**
  - 48% 11% 50%
- **DLK1**

**G1/S transition, proliferation, cell survival**

**Growth, translation**

**Chromatin modifications**
- **Cell cycle progression, cell growth**

**Survival probability**
- **Time**
  - 0 50 100 150 200
- **Survival probability**
  - 0.0 0.2 0.4 0.6 0.8 1.0
- **P-value:** 0.12; HR: 0.614
- **LRP1B Mutant v/s WT**
- **FAM135B Mutant v/s WT**
- **P-value:** 0.278; HR: 1.51