# Candidate Pediatric Molecular Target List

Pursuant to section 505B(m)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), the table labeled "automatic waivers" lists the "molecular targets of new cancer drugs and biological products in development for which pediatric cancer study requirements under [section 505B of the FD&C Act] will be automatically waived" (section 505B(m)(1)(B)). All other tables list "molecular targets considered, on the basis of data the secretary determines to be adequate, to be substantially relevant to the growth or progression of a pediatric cancer, and that may trigger the requirements under [section 505B of the FD&C Act]" (section 505B(m)(1)(A)).

## A) Gene Abnormality

| Target Symbol | Gene Abnormality |
|---|---|
| ABL1/2 | ABL1/2 gene fusions (BCR-ABL1, etc.) |
| ACVR1 | ACVR1 |
| ALK | ALK and ALK gene fusions |
| ASCL1 | ASCL1 gene |
| BRAF | BRAF |
| BRD3-NUTM1 | BRD3-NUTM1 |
| BRD4-NUTM1 | BRD4-NUTM1 |
| CCND1,2 | CCND1,2 |

| | |
|---|---|
| CDK12 | EWSR1-FLI1 |
| c-KIT or KIT | c-KIT or KIT |
| CSF1R | CSF1R gene fusions |
| CTNNB1 (β-catenin) | CTNNB1 |
| DDX3X | DDX3X |
| DOT1L | MLL gene fusions |
| EGFR | EGFR |
| ERK | BRAF, MAP2K1 |
| ETS gene fusions | ETS fusions (ERG, FLI1, ETV1) |
| EWSR1-FLI1 | EWSR1-FLI1 |
| EZH2 | SMARCB1, SMARCA4 |
| FGFR | FGFR and FGFR gene fusions |
| FLT3 | FLK2, STK1, CD135 |
| Gamma secretase | NOTCH1 and FBXW7 |
| GFI1 | GFI1 |
| GFI1B | GFI1B |
| Histone 3 G34R/V | Histone 3 G34R/V |

| | |
|---|---|
| Histone 3 K27M | Histone 3 K27M |
| IDH1 and IHD2 | IDH1 and IDH2 |
| JAK1, 2, and 3 | JAK1, 2, and 3 |
| LIN28B | LIN28B |
| MDM2 | MDM2, TP53 |
| MEK | BRAF and BRAF gene fusions, MAP2K1, NF1 |
| Menin | MLL gene fusions |
| MET | MET |
| MLL | MLL gene fusions (MLL-AF4/AF9/AF10/ENL/ELL/AF1p/AFX/FKHRL1/SEPT6/GAS7/EEN/CBP/PTD) |
| mTOR | TSC1, TSC2 |
| MYC | MYC translocations and amplification |
| MYCN | MYCN amplification |
| Neoantigens | MSH2, MLH1, MSH6, PMS2 POLE, and POLD1 |
| NFkappaB | RELA fusion |
| NOTCH1 | NOTCH1, FBXW7 |

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|---|---|
| NSD3-NUTM1 | NSD3-NUTM1 |
| NT5C2 | NT5C2 |
| NTRK | NTRK gene fusions |
| ODC1 | MYC target gene |
| PARP | BRCA1/2, PALB2, ATM, BRIP1, CHEK2, RAD51, etc. |
| PAX-FOXO1 | PAX-FOXO1 |
| PDGFRA/B | PDGFRA/B gene fusions |
| PI3Kα | PIK3CA |
| PML-RARα | PML-RARα |
| PPM1D (WIP1) | PPM1D (WIP1) |
| RAS | RAS |
| RET | RET |
| SH2B3 | SH2B3 |
| SHP2 | SHP2 |
| Smoothened | PATCH1, SMO |
| STAT2,3 | STAT2,3 |

| | |
|---|---|
| SYT-SSX | SYT-SSX |
| TERT | TERT |
| TORC1/2 as distinct from mTOR | TORC1/2 |
| TrkB | TrkB |
| TP53 | TP53 |
| TYK2 | TYK2 |
| ZNF532-NUTM1 | ZNF532-NUTM1 |

## B) Cell Lineage

| Target Symbol | | | |
|---|---|---|---|
| AKR1C3 | CD70 | GPNMB | PTEN |
| BCOR | CD79b | ERBB2 (HER2/Neu) | SYK |
| BTK | CD123/IL3RA | IL6 | WT1 |
| CD7 | CD276 (B7-H3) | IL13RA2 | YAP1 |
| CD19 | Cereblon CBL (E3 Ubiquitine protein ligase) | LRRC15 | |
| CD20 | DLL3 | MAGE-A3 | |
| CD22 | DLK1 | MSLN (mesothelin) | |
| CD30 | EGFRvIII | NR5A1 (Steroidogenic factor-1) | |
| CD33 | EPHA2 | NY-ESO-1 | |
| CD37 | GD2 | Olig2 | |

| | | | |
|---|---|---|---|
| CD38 | GPC2 | PIK3CD (PI3 kinase delta) | |
| CD56 | GPC3 | PRAME | |

## C) Tumor Microenvironment and immunotherapy

| Target Symbol | |
|---|---|
| B7H3 | OX40 |
| CD40 | PD-1/PD-L1 |
| CD47 | RELA |
| CD52 | RIG-I |
| CXCR4 | STEAP1 |
| CXCL10 | STING |
| CTLA4 | TIM3/TIM4 |
| GM-CSF | VEGF |
| IDO1 | VEGFR |
| IFN-gamma | |
| IL-2 | |
| LAG3 | |

## D) Others

| Target Symbol | | | |
|---|---|---|---|
| AKT | CDK9 | MCT1 (monocarboxylate transporter 1) | PRMT2 |
| ATM | CK1 | MEK | PRMT5 |
| ATR | CK2 (casein kinase 2) | MIZ1 | Proteasome |
| ATRX | CREBBP/EP300 | MGMT | PTPN (protein tyrosine phosphatase) |
| AURKA (Aurora kinase A) | DNA (alkylators) | MLL5 | RPA3 |

| | | | |
|---|---|---|---|
| AURKB (Aurora kinase B) | DNA-PK | MYST3 (MYST histone acetyltransferase (monocytic leukemia) | SHP2 |
| AXL | DNMT (DNA methyl transferase) | NAMPT | SMYD3 |
| A1/BFL | FAK | NEDD8 activating enzyme (NAE) | Somatostatin Receptor |
| BAK | FOLR1 (folate receptor 1) | PARP | Survivin (BIRC5) |
| BAX | GSK-3 | PDK-1 (3-phosphoinositide-dependent protein kinase 1) | SUZ12 |
| BCL2 family members (Bcl-2, Bcl-XL, Mcl-1, A1/BFL, BAK, BAX) | HDAC | PI3Kdelta | SWI/SNF |
| BET bromodomain family | HIF1A | PIM1 | TET2 |
| BMPR | Hippo pathway (YAP, TAZ, TEADs) | PKA | TGF-beta |
| Brd1 | Hsp90 | PKC | Thymidylate synthase |
| Brd4 | IAPs (inhibitor-of-apoptosis) | PLK1 | Topoisomerase I/II |
| CDK4/6 | IGFR-1 | POL1 | TRAIL |
| CHK1 | KDM4A | PRDM1 | Tubulin |
| CDK2 | LSD1 | PRDM8 | XPO1 (Exportin) |
| CDK7 | MCL1 | PRDM10 | WDR5 |
| | | | WEE1 |