

Р†РќРŸРŸР РЈРЉР|Р†РЇ

Р†Р»»СІІ РјРµР†РёС†РSPsPiPs Р·Р°СІС,РsСІСІРІР°РSPSCІІ
Р»С-РєР°СІСІСІРєРєРsPiPs Р·Р°СІРsР±СІ

РŸРђР™ Р'Р·Р Р'

(TYVERB)

СРєР»Р°Р†:

Р†С-СІСІР° СІРµС†РsPIРёРSP°: Р»Р°РІР°С,РёРSC-Р±;

1 С,Р°Р±Р»РµС,РєР° РјС-СІС,РёС,СІ Р»Р°РІР°С,РёРSC-Р±СІ 250 РјРі СІ С„РsСІРјС-
Р»Р°РІР°С,РёРSC-Р±СІ Р†РёС,РsСІРёР»Р°С,СІ РјРsРSPsPiС-Р†СІР°С,СІ;

Р†РsPiPsРјС-РІРSC- СІРµС†РsPIРёРSPё: С†РµР»Р»СІР»Р»РsР·Р°
РјС-РєСІРsРєСІРёСІС,Р°Р»С-С†РSP°, РіРsPiС-Р†РsРS РЉ30, РSP°С,СІС-СІ
РєСІРsС...РјР°Р»РіРіС-РєРsР»СІС, (С,РёРі Рђ), РјР°РІРSC-СІ СІС,РµР°СІР°С„, РpadryB®
Yellow YS-1-12524-A (PiС-РіСІРsРјР»Р»РsР·Р°, С,РёС,Р°РSPСІ Р†С-РsРєСІРёР†Р (E 171),
РјР°РєСІРsPiPsР» 400, РіРsР»С-СІРsСІР±Р°С, 80, Р·Р°Р»С-Р·Р° РsРєСІРёР†Р РІРsPiС,РёР№
(E 172), Р·Р°Р»С-Р·Р° РsРєСІРёР†Р С†РµСІРІsРSPёР№ (E 172)).

**Р»С-РєР°СІСІСІРєРєР° С„РsСІРјР°Р°.
РŸР°Р±Р»РµС,РєРё, РІРєСІРёС,С-
РіР»С-РІРєРsРІРsСІ РsР±РsР»РsРSPєРsСІ.**

РђСІРSPsPIРSC- С„С-Р·РёРєС-С...С-РјС-С†РSC- РІР»Р°СІС,РёРІsСІС,С-:
РіР»С-РІРєРsРІРsСІ РsР±РsР»РsРSPєРsСІ РsPIР°Р»СІС- Р†РІsРsРіСІРєР»С- РІРsPiС,С-
С,Р°Р±Р»РµС,РєРё, РіР»Р»Р°СІРє- Р· РsР†РSPsPiPs Р±РsРєСІ С,Р° Р· РјР°СІРєСІРІР°РSPSCІІРј
GS XJG Р· С-РSCєРsPiPs Р±РsРєСІ.

Р»Р°СІРјР°РєРsС,РµСІР°РіРіРіРіС,РёС†РSP° РіСІСІРІР°.
РµСІРsС,РёРіСІС...Р»РёРSPSC- Р·Р°СІРsР±Рё. Р†РSPiС-Р±С-С,РsСІРё
С,РёСІРsР·РёРSPєС-РSP°Р·Рё СІРµС†РµСІС,РsСІР° РµРіС-Р†РµСІРјР»Р»Р»Р»Р»РsРsPiPs
С„Р°С,РsСІР° СІРsСІС,СІ Р»СІР†РёРSPё 2 (HER2). РЉРsР† РђРŸX L01E H01.

Р»Р°СІРјР°РєРsР»РsPiС-С†РSC- РІР»Р°СІС,РёРІsСІС,С-.

$P\alpha P^{\circ}C\bar{H}PjP^{\circ}PePsPrP\bar{e}PSP^{\circ}PjC-PeP^{\circ}$.

$P_{\bar{h}}P_{\mu}C...P^{\circ}PSC-P\cdot PjPrC-C-$. $P>P^{\circ}P\bar{i}P^{\circ}C, P\bar{e}PSC-P\pm$, $4\cdot P^{\circ}PSC-P>C-PSPsC...C-PSP^{\circ}P\cdot PsP>C-PS$,
вґ” $C\bar{t}P_{\mu}C-PSPiC-P\pm C-C, PsC\bar{H}PIPSCrC, C\bar{H}C-C\bar{e}PSC\bar{H}PsPeP>C-C, P\bar{e}PSPSP\bar{e}C...$ $PrPsPjP_{\mu}PSC-PI$
 $C, P\bar{e}C\bar{H}PsP\cdot P\bar{e}PSPeC-PSP^{\circ}P\cdot P\bar{e}C\bar{H}P_{\mu}C\bar{t}P_{\mu}P\bar{i}C, PsC\bar{H}C-PI$ EGFR (ErbB1) C, P° HER2 (ErbB2)
 $(C\bar{H}PsP\cdot C\bar{H}P^{\circ}C...C\bar{r}PSPePsPIC- P\cdot PSP^{\circ}C\bar{t}P_{\mu}PSPSC\bar{t}Ki^{app}3PSP_{\bar{h}}C, P^{\circ}13PSP_{\bar{h}}$
 $PIC-PrP\bar{i}PsPIC-PrPSPs) P\cdot P\bar{i}PsPIC-P>CHPSP\bar{e}PjPIC-PrPsPeC\bar{H}P_{\mu}PjP>P_{\mu}PSPSC\bar{t}PjPIC-Pr$
 $C\bar{t}P\bar{e}C...C\bar{H}P_{\mu}C\bar{t}P_{\mu}P\bar{i}C, PsC\bar{H}C-PI$ ($P\bar{i}P_{\mu}C\bar{H}C-PsPrPSP^{\circ}P\bar{i}C-PIPIP\bar{e}PIP_{\mu}PrP_{\mu}PSPSC\bar{t}\geq 300C...PI$).
 $P>P^{\circ}P\bar{i}P^{\circ}C, P\bar{e}PSC-P\pm C-PSPiC-P\pm C\bar{r}C”C\bar{H}C-C\bar{t}C, P\bar{i}C\bar{r}C...P>P\bar{e}PSPSP\bar{e}C...PeP>C-C, P\bar{e}PS,$
 $PeP_{\mu}C\bar{H}PsPIP^{\circ}PSP\bar{e}C...ErbB, in vitro C, P^{\circ}PIC\bar{H}C-P\cdot PSP\bar{e}C...PjPsPrP_{\mu}P>C\bar{t}C...PSP^{\circ}$
 $C, PIP^{\circ}C\bar{H}P\bar{e}PSP^{\circ}C....$

$P_{\bar{h}}PsPjP\pm C-PSP^{\circ}C\bar{t}C-C\bar{t}P>P^{\circ}P\bar{i}P^{\circ}C, P\bar{e}PSC-P\pm C\bar{r}C, P^{\circ}C, C\bar{H}P^{\circ}C\bar{t}C, C\bar{r}P\cdot C\bar{r}PjP^{\circ}P\pm C\bar{r}$
 $PjPsP\bar{t}P_{\mu}PrP_{\mu}PjPsPSC\bar{t}C, C\bar{H}C\bar{r}PIP^{\circ}C, P\bar{e}PePsPjP\bar{i}P>P_{\mu}PjP_{\mu}PSC, P^{\circ}C\bar{H}PSC-$
 $PjP_{\mu}C...P^{\circ}PSC-P\cdot PjP\bar{e}PrC-C-, P^{\circ}C, P^{\circ}PePsP\bar{t}PjPsP\bar{t}P>P\bar{e}PIC-C\bar{H}C-P\cdot PSC-$
 $PjP_{\mu}C...P^{\circ}PSC-P\cdot PjP\bar{e}C\bar{H}P_{\mu}P\cdot P\bar{e}C\bar{t}C, P_{\mu}PSC, PSPsC\bar{t}C, C-.$ $P-PrP^{\circ}C, PSC-C\bar{t}C, CH$
 $P>P^{\circ}P\bar{i}P^{\circ}C, P\bar{e}PSC-P\pm C\bar{r}P\bar{i}P^{\circ}P>CHPjC\bar{r}PIP^{\circ}C, P\bar{e}C\bar{H}C-C\bar{t}C, P\pm C\bar{r}P>P^{\circ}PIP\bar{e}PIC\bar{t}P_{\mu}PSP^{\circ}$
 $PSP^{\circ}P>C-PSC-C\bar{t}C...PeP>C-C, P\bar{e}PS, C\%PsP\bar{i}C-PrPrP^{\circ}PIP^{\circ}P>P\bar{e}C\bar{t}CHPIP\bar{i}P>P\bar{e}PIC\bar{r}$
 $C, C\bar{H}P^{\circ}C\bar{t}C, C\bar{r}P\cdot C\bar{r}PjP^{\circ}P\pm C\bar{r}.$ $P>P^{\circ}P\bar{i}P^{\circ}C, P\bar{e}PSC-P\pm P\cdot P\pm P_{\mu}C\bar{H}C-PiP\cdot PSP^{\circ}C\bar{t}PSC\bar{r}$
 $P^{\circ}PeC, P\bar{e}PIPSC-C\bar{t}C, CHP\bar{i}C\bar{H}PsC, P\bar{e}PeP>C-C, P\bar{e}PSP>C-PSC-C-HER2-$
 $P^{\circ}PjP\bar{i}P>C-C,, C-PePsPIP^{\circ}PSPsPiPsC\bar{H}P^{\circ}PeC\bar{r}PjPsP>PsC\bar{t}PSPsC-P\cdot P^{\circ}P>PsP\cdot P\bar{e},$
 $PIP\bar{e}PrC-P>P_{\mu}PSP\bar{e}C...PrP>C\bar{t}C, C\bar{H}P\bar{e}PIP^{\circ}P>PsPiPsC\bar{H}PsC\bar{t}C, C\bar{r}PI$
 $C\bar{t}P_{\mu}C\bar{H}P_{\mu}PrPsPIP\bar{e}C\%C-, C\%PsPjC-C\bar{t}C, P\bar{e}P>PsC, C\bar{H}P^{\circ}C\bar{t}C, C\bar{r}P\cdot C\bar{r}PjP^{\circ}P\pm, in vitro C-$
 $P\bar{i}C\bar{H}PsPrP_{\mu}PjPsPSC\bar{t}C, C\bar{H}C\bar{r}PIP^{\circ}PIC\bar{t}C\bar{r}PeC\bar{r}P\bar{i}PSP\bar{e}PN_{\bar{e}}P_{\mu}C,, P_{\mu}PeC, PI$
 $PePsPjP\pm C-PSP^{\circ}C\bar{t}C-C-P\cdot C, C\bar{H}P^{\circ}C\bar{t}C, C\bar{r}P\cdot C\bar{r}PjP^{\circ}P\pm PsPjPIC\bar{t}P\bar{e}C...$
 $PeP>C-C, P\bar{e}PSPSP\bar{e}C...P>C-PSC-C\bar{t}C....$

$P\alpha P^{\circ}C\bar{H}PjP^{\circ}PePsPeC-PSP_{\mu}C, P\bar{e}PeP^{\circ}$.

$P\bar{h}P\pm C\bar{t}PsC\bar{H}P\pm C\bar{t}C-C\bar{t}.$ $P_{\bar{h}}C-C\bar{t}P>C\bar{t}P\bar{i}P_{\mu}C\bar{H}PsC\bar{H}P^{\circ}P>CHPSPsPiPs$
 $P\cdot P^{\circ}C\bar{t}C, PsC\bar{t}C\bar{r}PIP^{\circ}PSPSC\bar{t}P>P^{\circ}P\bar{i}P^{\circ}C, P\bar{e}PSC-P\pm PIC\bar{t}PjPsPeC, C\bar{r}C”C, CHC\bar{t}C\bar{t}C$
 $PSP_{\mu}P\bar{i}PsPIPSC-C\bar{t}C, CHC, P^{\circ}PIP^{\circ}C\bar{H}C-P^{\circ}P\pm P_{\mu}P>CHPSPs(PePsP_{\mu}C,, C-C\bar{t}C-C”PSC,$
 $PIP^{\circ}C\bar{H}C-P^{\circ}P\pm P_{\mu}P>CHPSPsC\bar{t}C, C-AUCP\bar{i}C\bar{H}P\bar{e}P\pm P>P\bar{e}P\cdot PSPs70\%).$
 $P_{\bar{h}}PsPSC\bar{t}P_{\mu}PSC, C\bar{H}P^{\circ}C\bar{t}C-C-PIC\bar{t}P\bar{e}C\bar{H}PsPIP^{\circ}C, C\bar{t}C-P\cdot бґ™C\bar{t}PIP>C\bar{t}CHC, CHC\bar{t}C\bar{t}C$
 $P\bar{i}C-C\bar{t}P>C\bar{t}PjP_{\mu}PrC-P^{\circ}PSPSPsPiPsP>P^{\circ}C, P_{\mu}PSC, PSPsPiPsP\bar{i}P_{\mu}C\bar{H}C-PsPrC\bar{r}0,25P\bar{i}PsPrP\bar{e}PSP\bar{e}$
 $(PrC-P^{\circ}P\bar{i}P^{\circ}P\cdot PsPSPIC-Pr0PrPs1,5P\bar{i}PsPrP\bar{e}PSP\bar{e}).$ $PjP\bar{i}P>P^{\circ}P\cdot PjC-P\bar{i}C-PePsPIC-$
 $PePsPSC\bar{t}P_{\mu}PSC, C\bar{H}P^{\circ}C\bar{t}C-C-(C_{max})P>P^{\circ}P\bar{i}P^{\circ}C, P\bar{e}PSC-P\pm C\bar{r}PrPsC\bar{t}C\bar{t}PiP^{\circ}CHC, CHC\bar{t}C\bar{t}C$
 $P\bar{i}C\bar{H}P\bar{e}P\pm P>P\bar{e}P\cdot PSPsC\bar{t}P_{\mu}C\bar{H}P_{\mu}P\cdot 4P\bar{i}PsPrP\bar{e}PSP\bar{e}P\bar{i}C-C\bar{t}P>C\bar{t}P\cdot P^{\circ}C\bar{t}C, PsC\bar{t}C\bar{r}PIP^{\circ}PSPSC\bar{t}.$
 $P\odot PsPrP_{\mu}PSPSP\bar{e}PN_{\bar{e}}P\bar{i}C\bar{H}P\bar{e}PN_{\bar{e}}PsPjPrPsP\cdot P\bar{e}1250PjPiPrP^{\circ}C”P\bar{i}P_{\mu}PsPjP_{\mu}C, C\bar{H}P\bar{e}C\bar{t}PSC-$
 $P\cdot PSP^{\circ}C\bar{t}P_{\mu}PSPSC\bar{t}C_{max}PIC\bar{H}C-PIPSPsPIP^{\circ}P\bar{t}PSPsPjC\bar{r}C\bar{t}C, P^{\circ}PSC-(PePsP_{\mu}C,, C-C\bar{t}C-C”PSC,$
 $PIP^{\circ}C\bar{H}C-P^{\circ}P\pm P_{\mu}P>CHPSPsC\bar{t}C, C-), C\bar{t}PeC-C\bar{t}C, P^{\circ}PSPsPIP>C\bar{t}C, CH2,43(76\%)PjPePi/PjP>, P^{\circ}$
 $P\cdot PSP^{\circ}C\bar{t}P_{\mu}PSPSC\bar{t}CAUCвґ”36,2(79\%)PjPePi*PiPsPr/PjP>.$

$P\bar{Y}P\bar{e}C\bar{t}C, P_{\mu}PjPSP^{\circ}P_{\mu}PeC\bar{t}P\bar{i}PsP\cdot P\bar{e}C\bar{t}C-C\bar{t}P>P^{\circ}P\bar{i}P^{\circ}C, P\bar{e}PSC-P\pm C\bar{r}P\cdot C\bar{H}PsC\bar{t}C, P^{\circ}C”P\bar{i}C\bar{H}P\bar{e}$
 $P\bar{i}C\bar{H}P\bar{e}PN_{\bar{e}}PsPjC-C\bar{H}P^{\circ}P\cdot PsPjP\cdot C-P\bar{t}P_{\mu}CH. AUCP\cdot C\bar{H}PsC\bar{t}C, P^{\circ}C”C\bar{r}3C, P^{\circ}4C\bar{H}P^{\circ}P\cdot P\bar{e}(P\bar{Y}_{max}$
 $P\bar{i}C\bar{H}P\bar{e}P\pm P>P\bar{e}P\cdot PSPsC\bar{r}2,5C\bar{H}P^{\circ}P\cdot P^{\circ}C, P^{\circ}3C\bar{H}P^{\circ}P\cdot P\bar{e})P\bar{i}C\bar{H}P\bar{e}P\cdot P^{\circ}C\bar{t}C, PsC\bar{t}C\bar{r}PIP^{\circ}PSPSC-PI$
 $C-P\bar{t}P_{\mu}CHP\cdot PSP\bar{e}P\cdot CHPeP\bar{e}PjPIPjC-C\bar{t}C, PsPjP\bar{t}P\bar{e}C\bar{H}C-PI(5\%P\bar{t}P\bar{e}C\bar{H}C\bar{r}[500$
 $PeP^{\circ}P>PsC\bar{H}C-PN_{\bar{e}}])P^{\circ}P\pm PsP\cdot PIP\bar{e}C\bar{t}PsPeP\bar{e}PjPIPjC-C\bar{t}C, PsPjP\bar{t}P\bar{e}C\bar{H}C-PI(50\%P\bar{t}P\bar{e}C\bar{H}C\bar{r}$
 $[1000PeP^{\circ}P>PsC\bar{H}C-PN_{\bar{e}}])PIC-PrP\bar{i}PsPIC-PrPSPsC\bar{r}P\bar{i}PsC\bar{H}C-PIPSC\bar{t}PSPSC-C-P$
 $P\cdot P^{\circ}C\bar{t}C, PsC\bar{t}C\bar{r}PIP^{\circ}PSPSC\bar{t}PjPSP^{\circ}C, C\%P_{\mu}. P\bar{k}P^{\circ}C\bar{t}P\bar{e}C\bar{t}C, P_{\mu}PjPSC\bar{r}P_{\mu}PeC\bar{t}P\bar{i}PsP\cdot P\bar{e}C\bar{t}C-CH$

P»P°PīP°C, PēPSC-P±Cř C, P°PePsP¶ PIPiP»PēPIP°PI C±P°Cř PīCĤPēPNēPsPjCř C—P¶C-. P©PsPrPs P·P°CřC, PsCřCřPIP°PSPSCĬ P·P° 1 PiPsPrPēPSCř PrPs CřPSC-PrP°PSPeCř P·PSPēP·CHPePēPj PIPjC-CřC, PsPj P¶PēCĤCř CřPμCĤPμPrPSC- P·PSP°C±PμPSPSCĬ AUC P·P±C-P»CHCēPēP»PēCřCH PīCĤPēP±P»PēP·PSPs PI 2 C- 3 CĤP°P·Pē, PePsP»Pē P»P°PīP°C, PēPSC-P± PīCĤPēPNēPjP°P»Pē C±PμCĤPμP· 1 PiPsPrPēPSCř PīC-CřP»CĬ C—PrPē P·PSPēP·CHPePēPj P°P±Ps P·PIPēCřPsPePēPj PIPjC-CřC, PsPj P¶PēCĤCř PIC-PrPīPsPIC-PrPSPs.

P PsP·PiPsPrC-P». P»P°PīP°C, PēPSC-P± PjP°C” PIPēCřPsPePēPNē CřC, CřPīC-PSCH P·PIbĤ™ CĬP·CřPIP°PSPSCĬ (P±C-P»CHCēPμ 99 %) P·P°P»CHP±CřPjC-PSPsPj C, P°P°P»CHC, P°-1 PePēCřP»PēPj PiP»C-PePsPīCĤPsC, PμC—PSPsPj. P”PsCřP»C-PrP¶PμPSPSCĬ in vitro PīPsPeP°P·P°P»Pē, C%Ps P»P°PīP°C, PēPSC-P± C” CřCřP±CřC, CĤP°C, PsPj PrP»CĬ PīPμCĤPμPSPsCřPSPēPeC-PI BCRP (breast cancer resistance protein bĤ” P±C-P»PsPe CĤPμP·PēCřC, PμPSC, PSPsCřC, C- CĤP°PeCř PjPsP»PsC±PSPsC— P·P°P»PsP·Pē) C, P° Pgp (ABCB2). PĤCĤC-Pj C, PsPiPs, in vitro P»P°PīP°C, PēPSC-P± C-PSPiC-P±CřPIP°PI C±C- C, CĤP°PSCřPīPsCĤC, PμCĤPē PIC-PrC, PsPeCř, P° C, P°PePsP¶ C, CĤP°PSCřPīPsCĤC, PμCĤ PīPμC±C-PSPePsPiPsPiPs P·P°C...PsPīP»PμPSPSCĬ OATP1B1 PI PeP»C-PSC-C±PSPs P·PSP°C±CřC%PēC... PePsPSC±PμPSC, CĤP°C±C-CĬC... (P·PSP°C±PμPSPSCĬ IC₅₀ PrPsCĤC-PIPSCĤPIP°P»Pē 2,3 PjPePi/PjP»). B PĤP»C-PSC-C±PSPμ P·PSP°C±PμPSPSCĬ C±PēC... PμC, PμPeC, C-PI PrP»CĬ C, P°CĤPjP°PePsPeC-PSPμC, PēPePē C-PSCēPēC... PīCĤPμPīP°CĤP°C, C-PI, P° C, P°PePsP¶ PrP»CĬ C, P°CĤPjP°PePsP»PsPiC-C±PSPsC— P°PeC, PēPIPSPsCřC, C- C-PSCēPēC... PīCĤPsC, PēPīCřC...P»PēPSPSPēC... PīCĤPμPīP°CĤP°C, C-PI PSPμPIC-PrPsPjPμ.

P’C-PsC, CĤP°PSCřC, PsCĤPjP°C±C-CĬ. P»P°PīP°C, PēPSC-P± PīC-PrPrP°C”C, CHCřCĬ PμPeCřC, PμPSCřPēPIPSPsPjCř PjPμC, P°P±PsP»C-P·PjCř, PiPsP»PsPIPSPēPj C±PēPSPsPj P·P° PrPsPīPsPjPsPiPsCĤ CYP3A4 C- CYP3A5, PjPμPSCēPsCĤ PjC-CĤPsCĤ bĤ” P·P° PrPsPīPsPjPsPiPsCĤ CYP2PŸ19 C- CYP2PŸ8, P·CřC, PIPsCĤPμPSPSCĬPj CĤC-P·PSPsPjP°PSC-C, PSPēC... PsPePēCřPSPμPSPēC... PjPμC, P°P±PsP»C-C, C-PI, PeC-P»CHPeC-CřC, CH P¶PsPrPSPsPiPs P·CĬPePēC... PSPμ PīPμCĤPμPIPēC%CřC” 14 % PrPsP·Pē, C%Ps PIPēPIPPrPēC, CHCřCĬ P·C, PμPeP°P»C-CĬPjPē, P°P±Ps 10 % PePsPSC±PμPSC, CĤP°C±C-C— P»P°PīP°C, PēPSC-P±Cř Cř PīP»P°P·PjC- PeCĤPsPIC-.

P»P°PīP°C, PēPSC-P± Cř PeP»C-PSC-C±PSPs P·PSP°C±CřC%PēC... PePsPSC±PμPSC, CĤP°C±C-CĬC... C-PSPiC-P±CřC” CYP3A C, P° CYP2PŸ8 in vitro. P»P°PīP°C, PēPSC-P± PSPμP·PSP°C±PSPs C-PSPiC-P±CřC” C, P°PeC- PjC-PeCĤPsCřPsPjP°P»CHPSC- C, PμCĤPjPμPSC, Pē PīPμC±C-PSPePē, CĬPe CYP1A2, CYP2PŸ9, CYP2PŸ19 C, P° CYP2D6, P°P±Ps C, PμCĤPjPμPSC, Pē UGT (in vitro P·PSP°C±PμPSPSCĬ IC₅₀ ≥ 6,9 PjPePi/PjP»).

P’PēPIPμPrPμPSPSCĬ. PμPμCĤC-PsPr PSP°PīC-PIPIPēPIPμPrPμPSPSCĬ P·P±C-P»CHCēCřC”C, CHCřCĬ PrPsP·PsP·P°P»PμP¶PSPs PīCĤPē PīCĤPēPNēPsPjC- PsPrPSPsCĤP°P·PsPIPēC... PrPsP· P C-PIPSPsPIP°P¶PSPēPNē CřC, P°PS PrPsCřCĬPiP°C”C, CHCřCĬ C±PμCĤPμP· 6bĤ”7 PrC-P± P·P°CřC, PsCřCřPIP°PSPSCĬ. PμPμCĤC-PsPr PSP°PīC-PIPIPēPIPμPrPμPSPSCĬ Cř CĤC-PIPSPsPIP°P¶PSPsPjCř CřC, P°PSC- CřC, P°PSPsPIPēC, CH 24 PiPsPrPēPSPē. P»P°PīP°C, PēPSC-P± PIPēPIPPrPēC, CHCřCĬ PiPsP»PsPIPSPēPj C±PēPSPsPj CēP»CĬC...PsPj PjPμC, P°P±PsP»C-P·PjCř PīC-Pr PIPiP»PēPIPSPj CYP3A4/5. P’C-P»C-P°CĤPSP° PμPeCřPeCĤPμC±C-CĬ C, P°PePsP¶ CřPīCĤPēCĬC” PIPēPIPμPrPμPSPSCĤ. P»P°PīP°C, PēPSC-P± C, P° PNēPsPiPs PjPμC, P°P±PsP»C-C, Pē PμPeCřPeCĤPμC, CřCĤC, CHCřCĬ PiPsP»PsPIPSPēPj C±PēPSPsPj P·PeP°P»PsPj. PkP° PIPēPIPμPrPμPSPSCĬ PSPμP·PjC-PSPμPSPsPiPs P»P°PīP°C, PēPSC-P±Cř P·PeP°P»PsPj PīCĤPēPīP°PrP°C” PI CřPμCĤPμPrPSCĤPsPjCř 27 % (PrC-P°PīP°P·PsPS PIC-Pr 3 PrPs 67 %)

- B Cŕ CĺPeP»P°PrC- PePsPjP±C-PSPsPIP°PSPsC— C,PμCḡP°PīC-C— P·
PeP°PiPμC†Pēc,P°P±C-PSPsPj PrP»Cḷ PīP°C†C-C”PSC,PsPe P· CḡPsP·PīPsPICḡCḡPrP¶PμPSPëPj
P°P±Ps PjPμC,P°CḡC,P°C,Pēc†PSPëPj CḡP°PePsPj, CḷPePëPNḡ PīCḡPsPiCḡPμCḡCḡC” PSP°
PīPsPīPμCḡPμPrPSC-PNḡ C,PμCḡP°PīC-C— C,CḡP°CḡC,CḡP·CḡPjP°P±PsPj Cŕ
PePsPjP±C-PSP°C†C-C— P· P°PSC,CḡP°C†PëPeP»C-PSP°PjPë C,P° C,P°PeCḡP°PSP°PjPë Cŕ
P·PIBḡ™ CḷP·PeCŕ P· PjPμC,P°CḡC,P°C,Pēc†PSPsCḡ C...PIPSCḡPsP±PsCḡ;
- Cŕ CĺPeP»P°PrC- PePsPjP±C-PSPsPIP°PSPsC— C,PμCḡP°PīC-C— P·
C,CḡP°CḡC,CḡP·CḡPjP°P±PsPj Cŕ PīP°C†C-C”PSC,PsPe C-P· PjPμC,P°CḡC,P°C,Pēc†PSPëPj,
PiPsCḡPjPsPS-PSPμPiP°C,PëPIPSPëPj CḡP°PePsPj, C%Ps PīCḡPsPiCḡPμCḡCḡC” PīC-CḡP»Cḷ
C,CḡP°CḡC,CḡP·CḡPjP°P±-PIPjC-CḡPSPsC— C...C-PjC-PsC,PμCḡP°PīC-C—;
- Cŕ CĺPeP»P°PrC- PePsPjP±C-PSPsPIP°PSPsC— C,PμCḡP°PīC-C— P·
C-PSPiC-P±C-C,PsCḡPsPj P°CḡPsPjP°C,P°P·Pë PrP»Cḷ P¶C-PSPsPe Cŕ
PīPsCḡC,PjPμPSPsPīP°CḡP·P°P»CHBPSPsPjCŕ PīPμCḡC-PsPrC- C-P· PjPμC,P°CḡC,P°C,Pēc†PSPëPj,
PiPsCḡPjPsPS-PīPsP·Pēc,PëPIPSPëPj CḡP°PePsPj, CḷPePëPj PSPμ PīCḡPëP·PSP°C†PμPSP°
C...C-PjC-PsC,PμCḡP°PīC-Cḷ; PīP°C†C-C”PSC,PePë PI CḡPμC”CḡC,CḡP°C†C-PNḡPSPsPjCŕ
PrPsCḡP»C-PrP¶PμPSPSC- PSPμ P±CŕP»Pë PīPsPīPμCḡPμPrPSCḡPs P»C-PePsPIP°PSC-

C, C₇P°C₁C, C₁P·C₁PjP°P±PsPj P°P±Ps C-PSPiC-P±C-C, PsC₇P°PjPë P°C₇PsPjP°C, P°P·Pë;
PSPμPjP°C" PrP°PSPëC... C%PsPrPs PμC,, PμPeC, PëPIPSsC₁C, C- C†C-C"C—
PePsPjP±C-PSP°C†C-C— C₁ PìPsC₇C-PIPSCΠPSPSC- P· C, C₇P°C₁C, C₁P·C₁PjP°P±PsPj Pì
PePsPjP±C-PSP°C†C-C— P· C-PSPiC-P±C-C, PsC₇PsPj P°C₇PsPjP°C, P°P·Pë C₁ PìPeP°P·P°PSPsC—
PìC₇C₁PìPë PìP°C†C-C"PSC, PsPe.

PμC₇PsC, PëPìPsPeP°P·P°PSPSCΠ.

P"C-PìPμC₇C†C₁C, P»PëPIC-C₁C, C₇ PrPs P±C₁PrC₇-CΠPePsPìPs PePsPjPìPsPSPμPSC, P°
PìC₇PμPìP°C₇P°C, C₁.

P'P·P°C"PjPsPrC-CΠ P· C-PSC€PëPjPë P»C-PeP°C₇C₁C₇PePëPjPë P·P°C₁PsP±P°PjPë C, P° C-PSC€C- PIPëPrPë PIP·P°C"PjPsPrC-PNë.

P'PìP»PëPI C-PSC€PëC... P»C-PeP°C₇C₁C₇PePëC... P·P°C₁PsP±C-PI PSP°
P»P°PìP°C, PëPSC-P±

P>P°PìP°C, PëPSC-P± PjPμC, P°P±PsP»C-P·C₁C"C, C₇C₁CΠ PìPsP»PsPIPSPëPj C†PëPSPsPj P·P°
PrPsPìPsPjPsPìPsC₇ CYP3A (PrPëPI. C₇PsP·PrC-P» B«P°C₇PjP°PePsPeC-PSPμC, PëPeP°B»).

PμC₇Pë C₁C₁PjC-C₁PSPsPjC₁ P·P°C₁C, PsC₁C₁PìP°PSPSC- P· C₁PëP»C₇HPSPëPj
C-PSPiC-P±C-C, PsC₇PsPj CYP3A4 PePμC, PsPePsPSP°P·PsP»PsPj (200 PjPì 2 C₇P°P·Pë PSP°
PrPsP±C₁ PìC₇PsC, CΠPìPsPj 7 PrPSC-PI) C₁ P·PrPsC₇PsPìPëC... PrPsP±C₇PsPìPsP»C₇C†C-PI
C₁PëC₁C, PμPjPSP° PμPeC₁PìPsP·PëC†C-CΠ P»P°PìP°C, PëPSC-P±C₁ (100 PjPì PSP° PrPsP±C₁)
P·P±C-P»C₇C€C₁PìP°P»P°C₁C₇ PìC₇PëP±P»PëP·PSPs C₁ 3,6 C₇P°P·P°, P° PìPμC₇C-PsPr
PSP°PìC-PIPIPëPìPμPrPμPSPSCΠ P·P±C-P»C₇C€C₁PìP°PìC₁C₁ C₁ 1,7 C₇P°P·P°. PŸP»C-Pr
C₁PSPëPeP°C, Pë C₁C₁PjC-C₁PSPsPìPs P·P°C₁C, PsC₁C₁PìP°PSPSCΠ PìC₇PμPìP°C₇P°C, C₁
PŸP°PNëPIPμC₇P± C-P· C₁PëP»C₇HPSPëPjPë C-PSPiC-P±C-C, PsC₇P°PjPë CYP3A4 (C, P°PePëPjPë
CΠPe C₇PëC, PsPSP°PIC-C₇, C₁P°PePIC-PSP°PIC-C₇, C, PμP»C-C, C₇PsPjC-C†PëPS,
PePμC, PsPePsPSP°P·PsP», C-C, C₇P°PePsPSP°P·PsP», PìPsC₇PëPePsPSP°P·PsP»,
PìPsP·P°PePsPSP°P·PsP», PSPμC,, P°P·PsPrPsPS). PμC₇Pë C₁C₁PjC-C₁PSPsPjC₁
P·P°C₁C, PsC₁C₁PìP°PSPSC- PìC₇PμPìP°C₇P°C, C₁ PŸP°PNëPIPμC₇P± P· PìPsPjC-C₇PSPëPjPë
C-PSPiC-P±C-C, PsC₇P°PjPë CYP3A4 C₁P»C-Pr PrPsC, C₇PëPjC₁PìP°C, PëC₁C₇
PsP±PμC₇PμP¶PSPsC₁C, C- C- C₇PμC, PμP»C₇HPSPs C₁PìPsC₁C, PμC₇C-PìP°C, Pë P·P°
PeP»C-PSC-C†PSPëPj C₁C, P°PSPsPj C... PìPsC₇PsPìPs C, P° PjPsP¶P»PëPìPëPjPë
PìPsP±C-C†PSPëPjPë C₇PμP°PeC†C-CΠPjPë.

PμC₇Pë C₁C₁PjC-C₁PSPsPjC₁ P·P°C₁C, PsC₁C₁PìP°PSPSC- P· C-PSPrC₁PeC, PsC₇PsPj CYP3A4
PeP°C₇P±P°PjP°P·PμPìC-PSPsPj (100 PjPì 2 C₇P°P·Pë PSP° PrPsP±C₁ PìC₇PsC, CΠPìPsPj
3 PrPSC-PI C, P° 200 PjPì 2 C₇P°P·Pë PSP° PrPsP±C₁ PìC₇PsC, CΠPìPsPj 17 PrPSC-PI) C₁
P·PrPsC₇PsPìPëC... PrPsP±C₇PsPìPsP»C₇C†C-PI C₁PëC₁C, PμPjPSP° PμPeC₁PìPsP·PëC†C-CΠ
P»P°PìP°C, PëPSC-P±C₁ P·PjPμPSC€C₁PìP°P»P°C₁C₇ PìC₇PëP±P»PëP·PSPs PSP° 72 %. PŸP»C-Pr
C₁PSPëPeP°C, Pë C₁C₁PjC-C₁PSPsPìPs P·P°C₁C, PsC₁C₁PìP°PSPSCΠ PìC₇PμPìP°C₇P°C, C₁
PŸP°PNëPIPμC₇P± P· PIC-PrPsPjPëPjPë C-PSPrC₁PeC, PsC₇P°PjPë CYP3A4 (PSP°PìC₇PëPeP»P°Pr
P· C₇PëC,, P°PjPìC-C†PëPSPsPj, C₇PëC,, P°P±C₁C, PëPSPsPj, PeP°C₇P±P°PjP°P·PμPìC-PSPsPj,
C,, PμPSC-C, PsC—PSPsPj P°P±Ps C, C₇P°PìPsC₇ P·PIC-C₇PsP±PsC₇).

P>P°PìP°C, PëPSC-P± C" C₁C₁P±C₁C, C₇P°C, PsPj PrP»CΠ C, C₇P°PSC₁PìPsC₇C, PSPëC...

$P \cdot P^{\circ} C \dot{I} C, P s C \dot{I} P s P I C \dot{I} P I P^{\circ} C, P \ddot{e} P \cdot P s P \pm P_{\mu} C \dot{H} P_{\mu} P \P P S C - C \dot{I} C, C \dot{H}.$

$P \ddot{Y} C \dot{I} P j C - C \dot{I} P S P_{\mu} P \cdot P^{\circ} C \dot{I} C, P s C \dot{I} C \dot{I} P I P^{\circ} P S P S C \dot{I} P \gg P^{\circ} P \dot{I} P^{\circ} C, P \ddot{e} P S C - P \pm C \dot{I} P \cdot$
 $P I P S C \dot{I} C, C \dot{H} C - C \ddot{e} P S C \dot{H} P s P I P_{\mu} P S P S P \ddot{e} P j P r P s C \dot{I} P_{\mu} C, P^{\circ} P e C \dot{I} P_{\mu} P \gg P s P j C \dot{I} C \dot{I} C, C, C'' P I P s P S P_{\mu}$
 $P I P \dot{I} P \gg P \ddot{e} P I P^{\circ} C'' P S P^{\circ} A U C P^{\circ} P \pm P s C_{\max} P \pm C \dot{I} P r C \dot{H} - C \dot{I} P e P s C - P \cdot C \dot{I} P \ddot{e} C \dots P^{\circ} P e C, P \ddot{e} P I P S P \ddot{e} C \dots$
 $C \dot{I} C \dot{I} P \pm C \dot{I} C, P^{\circ} P S C \dot{I} C - P N_{\circ}. P h P r P S P^{\circ} P e P \cdot P \pm C - P \gg C \dot{H} C \ddot{e} C \dot{I} C'' C, C \dot{H} C \dot{I} C \dot{I} C \dot{I} C \dot{I} P^{\circ} C \dot{I} C, P s C, P^{\circ}$
 $P S P_{\mu} P N_{\circ} C, C \dot{H} P s P \dot{I} P_{\mu} P S C - C -, C - P S P r C \dot{I} P e P s P I P^{\circ} P S P s C - P r P s C \dot{I} P_{\mu} C, P^{\circ} P e C \dot{I} P_{\mu} P \gg P s P j.$

$P \ddot{Y} C \dot{I} P j C - C \dot{I} P S P_{\mu} P \cdot P^{\circ} C \dot{I} C, P s C \dot{I} C \dot{I} P I P^{\circ} P S P S C \dot{I} P \dot{I} C \dot{H} P_{\mu} P \dot{I} P^{\circ} C \dot{H} P^{\circ} C, C \dot{I} P \ddot{Y} P^{\circ} P N_{\circ} P I P_{\mu} C \dot{H} P \pm P \cdot$
 $C - C \dot{H} P \ddot{e} P S P s C, P_{\mu} P e P^{\circ} P S P s P j (P \dot{I} C \dot{H} P \ddot{e} P \cdot P^{\circ} C \dot{I} C, P s C \dot{I} C \dot{I} P I P^{\circ} P S P S C - C \dot{I} P e C \dot{I} P e P \gg P^{\circ} P r P s P I P s C -$
 $C \dot{I} P^{\circ} C \dot{I} C, P \ddot{e} P S P \ddot{e} C \dot{H} P_{\mu} P \P P \ddot{e} P j C \dot{I} F O L F I R I) P \dot{I} C \dot{H} P \ddot{e} P \pm P \gg P \ddot{e} P \cdot P S P s P S P^{\circ} 40 \% P \cdot P \pm C - P \gg C \dot{H} C \ddot{e} C \dot{I} C''$
 $A U C S N - 38, P^{\circ} P e C, P \ddot{e} P I P S P s P \dot{I} P s P j P_{\mu} C, P^{\circ} P \pm P s P \gg C - C, C \dot{I} C - C \dot{H} P \ddot{e} P S P s C, P_{\mu} P e P^{\circ} P S C \dot{I}.$
 $P \ddot{Y} P s C \dot{I} P S P \ddot{e} P N_{\circ} P j P_{\mu} C \dots P^{\circ} P S C - P \cdot P j C, P^{\circ} P e P s C - P I P \cdot P^{\circ} C'' P j P s P r C - C - P S P_{\mu} P I C - P r P s P j P \ddot{e} P N_{\circ},$
 $P^{\circ} P \gg P_{\mu} P \dot{I} C \dot{H} P \ddot{e} P \dot{I} C \dot{I} P e P^{\circ} C'' C, C \dot{H} C \dot{I} C \dot{I} C, C \% P s P I C - P S P \dot{I} P s P I \dot{B} \dot{H}^{\text{TM}} C \dot{I} P \cdot P^{\circ} P S P \ddot{e} P N_{\circ} P \cdot$
 $C - P S P \dot{I} C - P \pm C \dot{I} P I P^{\circ} P S P S C \dot{I} P j P s P r P S P s P \dot{I} P s P^{\circ} P \pm P s P r P_{\mu} P e C - P \gg C \dot{H} P e P s C \dots$
 $C, C \dot{H} P^{\circ} P S C \dot{I} P \dot{I} P s C \dot{H} C, P S P \ddot{e} C \dots P \pm C - P \gg P e C - P \dot{I} P \dot{I} C - P r P I P \dot{I} P \gg P \ddot{e} P I P s P j P \gg P^{\circ} P \dot{I} P^{\circ} C, P \ddot{e} P S C - P \pm C \dot{I}.$
 $P \ddot{Y} P^{\circ} P N_{\circ} P I P_{\mu} C \dot{H} P \pm C \dot{I} P e P s P j P \pm C - P S P^{\circ} C \dot{I} C - C - P \cdot C - C \dot{H} P \ddot{e} P S P s C, P_{\mu} P e P^{\circ} P S P s P j C \dot{I} P \gg C - P r$
 $P \cdot P^{\circ} C \dot{I} C, P s C \dot{I} P s P I C \dot{I} P I P^{\circ} C, P \ddot{e} P \cdot P s P \pm P_{\mu} C \dot{H} P_{\mu} P \P P S C - C \dot{I} C, C \dot{H}, C \dot{H} P_{\mu} C, P_{\mu} P \gg C \dot{H} P S P s$
 $P e P s P S C, C \dot{H} P s P \gg C \dot{H} P I P^{\circ} C, P \ddot{e} P \dot{I} P s P \pm C - C \dot{I} P S C - C \dot{H} P_{\mu} P^{\circ} P e C \dot{I} C - C - C, P^{\circ} P \cdot P I P^{\circ} P \P P \ddot{e} C, P \ddot{e}$
 $P S P_{\mu} P s P \pm C \dots C - P r P S C - C \dot{I} C, C \dot{H} P \cdot P j P_{\mu} P S C \ddot{e} P_{\mu} P S P S C \dot{I} P r P s P \cdot P \ddot{e} C - C \dot{H} P \ddot{e} P S P s C, P_{\mu} P e P^{\circ} P S C \dot{I}.$

$P \gg P^{\circ} P \dot{I} P^{\circ} C, P \ddot{e} P S C - P \pm C - P S P \dot{I} C - P \pm C \dot{I} C'' C, C \dot{H} P^{\circ} P S C \dot{I} P \dot{I} P s C \dot{H} C, P S C - P \pm C - P \gg P e P \ddot{e} P g p \text{ in vitro } C \dot{I}$
 $P e P \gg C - P S C - C \dot{I} P S P s P \cdot P S P^{\circ} C \dot{I} C \% P \ddot{e} C \dots P e P s P S C \dot{I} P_{\mu} P S C, C \dot{H} P^{\circ} C \dot{I} C - C \dot{I} C \dots P \ddot{Y} C \dot{I} P j C - C \dot{I} P S P_{\mu}$
 $P \cdot P^{\circ} C \dot{I} C, P s C \dot{I} C \dot{I} P I P^{\circ} P S P S C \dot{I} P \gg P^{\circ} P \dot{I} P^{\circ} C, P \ddot{e} P S C - P \pm C \dot{I} P \cdot P \dot{I} P_{\mu} C \dot{H} P s C \dot{H} P^{\circ} P \gg C \dot{H} P S P \ddot{e} P j$
 $P r P \ddot{e} P \dot{I} P s P e C \dot{I} P \ddot{e} P S P s P j P \dot{I} C \dot{H} P \ddot{e} P \pm P \gg P \ddot{e} P \cdot P S P s P S P^{\circ} 80 \% P \cdot P \pm C - P \gg C \dot{H} C \ddot{e} C \dot{I} C'' P \dot{H} U C$
 $P r P \ddot{e} P \dot{I} P s P e C \dot{I} P \ddot{e} P S C \dot{I}. P \ddot{Y} P \gg C - P r P \cdot P s P \pm P_{\mu} C \dot{H} P_{\mu} P \P P S C - C \dot{I} C, C \dot{H} P \cdot P^{\circ} C \dot{I} C, P s C \dot{I} P s P I C \dot{I} P I P^{\circ} C, P \ddot{e}$
 $P \ddot{Y} P^{\circ} P N_{\circ} P I P_{\mu} C \dot{H} P \pm P \cdot P \dot{I} C \dot{H} P_{\mu} P \dot{I} P^{\circ} C \dot{H} P^{\circ} C, P^{\circ} P j P \ddot{e} P \cdot P I C \dot{I} P \cdot C \dot{H} P e P \ddot{e} P j C, P_{\mu} C \dot{H} P^{\circ} P \dot{I} P_{\mu} P I C, P \ddot{e} C \dot{I} P S P \ddot{e} P j$
 $C - P S P r P_{\mu} P e C \dot{I} P s P j, C \% P s C'' C \dot{I} C \dot{I} P \pm C \dot{I} C, C \dot{H} P^{\circ} C, P^{\circ} P j P \ddot{e} P r P \gg C \dot{I} C, C \dot{H} P^{\circ} P S C \dot{I} P \dot{I} P s C \dot{H} C, P S P \ddot{e} C \dots$
 $P \pm C - P \gg P e C - P \dot{I} P g p.$

$P \gg P^{\circ} P \dot{I} P^{\circ} C, P \ddot{e} P S C - P \pm C - P S P \dot{I} C - P \pm C \dot{I} C'' C, C \dot{H} P^{\circ} P S C \dot{I} P \dot{I} P s C \dot{H} C, P S C - P \pm C - P \gg P e P \ddot{e} B C R P C, P^{\circ}$
 $O A T P 1 B 1 \text{ in vitro. } P \dot{H} P \gg C - P S C - C \dot{I} P S P_{\mu} P \cdot P S P^{\circ} C \dot{I} P_{\mu} P S P S C \dot{I} C \dot{I} P \ddot{e} C \dots P_{\mu} C, P_{\mu} P e C, C - P \dot{I} P S P_{\mu}$
 $P I P \ddot{e} P I C \dot{I} P^{\circ} P \gg P s C \dot{I} C \dot{H}. P \acute{K} P_{\mu} P j P s P \P P S P^{\circ} P I P \ddot{e} P e P \gg C \dot{H} C \dot{I} P \ddot{e} C, P \ddot{e}, C \% P s P \gg P^{\circ} P \dot{I} P^{\circ} C, P \ddot{e} P S C - P \pm$
 $P j P s P \P P_{\mu} P I P \dot{I} P \gg P \ddot{e} P I P^{\circ} C, P \ddot{e} P S P^{\circ} C, P^{\circ} C \dot{H} P j P^{\circ} P e P s P e C - P S P_{\mu} C, P \ddot{e} P e C \dot{I} C \dot{I} C \dot{I} P \pm C \dot{I} C, C \dot{H} P^{\circ} C, C - P \dot{I}$
 $B C R P (P S P^{\circ} P \dot{I} C \dot{H} P \ddot{e} P e P \gg P^{\circ} P r C, P s P \dot{I} P s C, P_{\mu} P e P^{\circ} P S C \dot{I}) C, P^{\circ} O A T P 1 B 1 (P S P^{\circ} P \dot{I} C \dot{H} P \ddot{e} P e P \gg P^{\circ} P r$
 $C \dot{H} P s P \cdot C \dot{I} P I P^{\circ} C \dot{I} C, P \ddot{e} P S C \dot{I}) (P r P \ddot{e} P \dot{I}. C \dot{H} P s P \cdot P r C - P \gg B \ll P^{\circ} C \dot{H} P j P^{\circ} P e P s P e C - P S P_{\mu} C, P \ddot{e} P e P^{\circ} B \gg).$

$P \ddot{Y} C \dot{I} P j C - C \dot{I} P S P_{\mu} P \cdot P^{\circ} C \dot{I} C, P s C \dot{I} C \dot{I} P I P^{\circ} P S P S C \dot{I} P \dot{I} C \dot{H} P_{\mu} P \dot{I} P^{\circ} C \dot{H} P^{\circ} C, C \dot{I} P \ddot{Y} P^{\circ} P N_{\circ} P I P_{\mu} C \dot{H} P \pm P \cdot$
 $P e P^{\circ} P \dot{I} P_{\mu} C \dot{I} P \ddot{e} C, P^{\circ} P \pm C - P S P s P j, P \gg P_{\mu} C, C \dot{H} P s P \cdot P s P \gg P s P j P^{\circ} P \pm P s C, C \dot{H} P^{\circ} C \dot{I} C, C \dot{I} P \cdot C \dot{I} P j P^{\circ} P \pm P s P j$
 $C \dot{I} C \dot{I} C, C, C'' P I P s P S P_{\mu} P I P \dot{I} P \gg P \ddot{e} P I P^{\circ} C'' P S P^{\circ} C, P^{\circ} C \dot{H} P j P^{\circ} P e P s P e C - P S P_{\mu} C, P \ddot{e} C \dot{I} P S C -$
 $P \dot{I} P^{\circ} C \dot{H} P^{\circ} P j P_{\mu} C, C \dot{H} P \ddot{e} C \dot{I} P \ddot{e} C \dots P \dot{I} C \dot{H} P_{\mu} P \dot{I} P^{\circ} C \dot{H} P^{\circ} C, C - P \dot{I} (P^{\circ} P \pm P s P j P_{\mu} C, P^{\circ} P \pm P s P \gg C - C, C - P \dot{I}$
 $P e P^{\circ} P \dot{I} P_{\mu} C \dot{I} P \ddot{e} C, P^{\circ} P \pm C - P S C \dot{I}) C \dot{I} P \ddot{e} P \gg P^{\circ} P \dot{I} P^{\circ} C, P \ddot{e} P S C - P \pm C \dot{I}.$

$P' P \cdot P^{\circ} C'' P j P s P r C - C - P \cdot C - P \P P_{\mu} C \dot{H} C, P^{\circ} P S P^{\circ} P \dot{I} P s C \dot{I} P j P \ddot{e}$

$P' C - P s P r P s C \dot{I} C, C \dot{I} P \dot{I} P S C - C \dot{I} C, C \dot{H} P \gg P^{\circ} P \dot{I} P^{\circ} C, P \ddot{e} P S C - P \pm C \dot{I} P \cdot P \pm C - P \gg C \dot{H} C \ddot{e} C \dot{I} C'' C, C \dot{H} C \dot{I} C \dot{I} C P r P s$
 $4 C \dot{H} P^{\circ} P \cdot C - P \dot{I} P \dot{I} C \dot{H} P \ddot{e} C \dot{I} C \dot{I} P j C - C \dot{I} P S P s P j C \dot{I} P \cdot P^{\circ} C \dot{I} C, P s C \dot{I} C \dot{I} P I P^{\circ} P S P S C - P \cdot C - P \P P_{\mu} C \dot{H},$
 $P \cdot P^{\circ} P \gg P_{\mu} P \P P S P s P I C - P r P I P j C - C \dot{I} C, C \dot{I} P \dot{I} P S C - P N_{\circ} P \P P \ddot{e} C \dot{H} C - P \dot{I}. P' C - P \gg C \dot{H} C \ddot{e} P_{\mu} C, P s P \dot{I} P s,$
 $P \cdot P^{\circ} P \gg P_{\mu} P \P P S P s P I C - P r C, P \ddot{e} P \dot{I} C \dot{I} C - P \P C -, P \pm C - P s P r P s C \dot{I} C, C \dot{I} P \dot{I} P S C - C \dot{I} C, C \dot{H}$
 $P \gg P^{\circ} P \dot{I} P^{\circ} C, P \ddot{e} P S C - P \pm C \dot{I} P \dot{I} C \dot{H} P \ddot{e} P \pm P \gg P \ddot{e} P \cdot P S P s C \dot{I} 2 \dot{B} \dot{H} " 3 C \dot{H} P^{\circ} P \cdot P \ddot{e} P I P \ddot{e} C \% P^{\circ}, C \dot{I} P e C \% P s$
 $P \dot{I} C \dot{H} P_{\mu} P \dot{I} P^{\circ} C \dot{H} P^{\circ} C, P \dot{I} C \dot{H} P \ddot{e} P N_{\circ} P j P^{\circ} C'' C, C \dot{H} C \dot{I} C \dot{I} C \dot{I} C \dot{I} P \cdot 1 P \dot{I} P s P r P \ddot{e} P S C \dot{I} P \dot{I} C - C \dot{I} P \gg C \dot{I} C$
 $P \dot{I} C \dot{H} P \ddot{e} P N_{\circ} P s P j C \dot{I} C - P \P C -, P \dot{I} P s C \dot{H} C - P I P S C \dot{I} P S P s P \cdot C, P^{\circ} P e P s C \dot{H} P \dot{I} C \dot{H} P \ddot{e} P \dot{I} C \dot{H} P \ddot{e} P N_{\circ} P s P j C -$

$P^{\circ}C\bar{H}P_{\mu}PN_{\circ}P\bar{i}C_{\circ}, C\bar{H}C\bar{r}C, PsPIP\bar{e}PN_{\circ}C\bar{r}C-PePjPsP\bar{r}P_{\mu}C-PSPiC-P\pm C\bar{r}PIP^{\circ}C, P\bar{e}CYP3A4C\bar{r}C\bar{r}C, C-PSPeP^{\circ}C...PeP\bar{e}C\bar{e}P_{\mu}C\bar{r}PSP\bar{e}PeC\bar{r}C, P^{\circ}P\cdot P\pm C-P\gg CH\bar{C}C\bar{e}C\bar{r}PIP^{\circ}C, P\bar{e}P\pm C-PsPrPsC\bar{r}C, C\bar{r}PiPSC-C\bar{r}C, CH\bar{P}\gg P^{\circ}PiP^{\circ}C, P\bar{e}PSC-P\pm C\bar{r}C, C, PsPjC\bar{r}C\bar{r}P\gg C-PrC\bar{r}PSP\bar{e}PeP^{\circ}C, P\bar{e}PN_{\circ}PsPiPsP\cdot P\cdot C\bar{r}C, PsC\bar{r}C\bar{r}PIP^{\circ}PSPSC\bar{r}PiC-PrC\bar{r}P^{\circ}C\bar{r}P\gg C-PeC\bar{r}PIP^{\circ}PSPSC\bar{r}PiC\bar{H}P_{\mu}PiP^{\circ}C\bar{H}P^{\circ}C, PsPjP\bar{y}P^{\circ}PN_{\circ}PIP_{\mu}C\bar{H}P\pm.$

P''P°PSC- PIPeP°P·CřCřC,CH PSP° C,Pμ, C%oPs PePsPjP±C-PSP°C†C-Cl PıCřPμPıP°CřP°C,Cř PıP°PNıPIPμCřP± P· C...C-PjC-PsC,PμCřP°PıC-C''Cř C'' PjPμPSC€ PμC,,PμPeC,PëPIPSsCř, PSC-P¶ PePsPjP±C-PSP°C†C-Cl C,CřP°CřC,CřP·CřPjP°P±Cř P· C...C-PjC-PsC,PμCřP°PıC-C''Cř.

PᄡCᄡPᄡ P·P°CᄡC,PsCᄡCᄡPIP°PSPSC- P»P°PᄡP°C,PᄡPSC-P±Cᄡ PᄡPsPIC-PrPsPjP»CᄡP»PsCᄡCᄡ
 PᄡCᄡPs P·PjPᄡPSCᄡPᄡPSPSCᄡ C,,CᄡP°PeCᄡC-C— PIPᄡPePᄡPrCᄡ P»C-PIPsPiPs CᄡP»CᄡPSPsCᄡPeP°
 (PrPᄡPI. CᄡPsP·PrC-P» B«PᄡPsP±C-CᄡPSC- CᄡPᄡP°PeCᄡC-C-B»). P·P°PᄡP°C,PᄡPSC-P± PSPᄡ
 PsCᄡC-PSCᄡPIP°P»Pᄡ Cᄡ PᄡP°CᄡC-C”PSC,C-PI C-P· CᄡPᄡPjPᄡC,PsPjP°C,PᄡCᄡPSPsCᄡ
 CᄡPᄡCᄡCᄡPᄡPIPsCᄡ PSPᄡPrPsCᄡC,P°C,PSC-CᄡC,Cᄡ. P-P°CᄡC,PsCᄡPsPICᄡPIP°C,Pᄡ
 P»P°PᄡP°C,PᄡPSC-P± PrP»Cᄡ P»C-PeCᄡPIP°PSPSCᄡ C...PIPsCᄡPᄡC... P·
 PᄡPsCᄡCᄡCᄡPᄡPSPSCᄡPjPᄡ C,,CᄡPSPeCᄡC-C— P»C-PIPsPiPs CᄡP»CᄡPSPsCᄡPeP° CᄡP»C-Pr P·
 PsP±PᄡCᄡPᄡPᄡPSC-CᄡC,Cᄡ (PIPeP»CᄡCᄡP°CᄡCᄡPᄡ PsPrPSPsCᄡP°CᄡPSPᄡ
 P·P°CᄡC,PsCᄡCᄡPIP°PSPSCᄡ P· PᄡPsC,PᄡPSCᄡC-PNᄡPSPs PeP°CᄡPrC-PsC,PsPeCᄡPᄡCᄡPSPᄡPjPᄡ
 P»C-PeP°CᄡCᄡCᄡPePᄡPjPᄡ P·P°CᄡPsP±P°PjPᄡ). PᄡPᄡCᄡPᄡPr PᄡPsCᄡP°C,PePsPj
 P»C-PeCᄡPIP°PSPSCᄡ PᄡCᄡPᄡPᄡP°CᄡP°C,PsPj PᄡP°PNᄡPIPᄡCᄡP± CᄡP»C-Pr PIPᄡP·PSP°CᄡPᄡC,Pᄡ
 CᄡC-PIPᄡPSCᄡ C,,CᄡP°PeCᄡC-C— PIPᄡPePᄡPrCᄡ P»C-PIPsPiPs CᄡP»CᄡPSPsCᄡPeP° Cᄡ PICᄡC-C...
 C...PIPsCᄡPᄡC... PrP»Cᄡ C,PsPiPs, C%PsP± PᄡPᄡCᄡPᄡPePsPSP°C,PᄡCᄡCᄡ, C%Ps PNᄡPsPiPs
 PᄡPsCᄡP°C,PePsPIPᄡPNᄡ CᄡC-PIPᄡPSCᄡ Cᄡ PePsPᄡPSPsPiPs C...PIPsCᄡPsPiPs Cᄡ PjPᄡPᄡP°C...
 PICᄡC,P°PSPsPIP»PᄡPSPᄡC... PSPsCᄡPj. PᄡPsPSC,CᄡPsP»Cᄡ P·P° CᄡC-PIPSPᄡPj
 C,,CᄡP°PeCᄡC-C— PIPᄡPePᄡPrCᄡ CᄡP»C-Pr PᄡCᄡPsPrPsPIPᄡCᄡPIP°C,Pᄡ PiC-Pr CᄡP°Cᄡ
 P»C-PeCᄡPIP°PSPSCᄡ PᄡCᄡPᄡPᄡP°CᄡP°C,PsPj PᄡP°PNᄡPIPᄡCᄡP± PrP»Cᄡ C,PsPiPs, C%PsP±
 CᄡPSPᄡPePSCᄡC,Pᄡ PNᄡPsPiPs P·PjPᄡPSCᄡPᄡPSPSCᄡ PSPᄡPᄡCᄡPᄡ PrPsPiCᄡCᄡC,PᄡPjPᄡC...
 PSPsCᄡPj (PrPᄡPI. CᄡPsP·PrC-P» B«PᄡPiPsCᄡC-P± P·P°CᄡC,PsCᄡCᄡPIP°PSPSCᄡ C,P°
 PrPsP·PᄡB»). Pj PrPᄡCᄡPᄡPᄡC... PIPᄡPᄡPᄡPrPeP°C... P·PjPᄡPSCᄡPᄡPSPSCᄡ C,,CᄡP°PeCᄡC-C—
 PIPᄡPePᄡPrCᄡ P»C-PIPsPiPs CᄡP»CᄡPSPsCᄡPeP° PjPsPᄡPᄡ P±CᄡC,Pᄡ C,CᄡPᄡPᄡPᄡPj C,P°
 CᄡPiCᄡPᄡCᄡPᄡPSCᄡC,Pᄡ CᄡPᄡCᄡCᄡPᄡPICᄡ PSPᄡPrPsCᄡC,P°C,PSC-CᄡC,Cᄡ. P·CᄡP»Pᄡ
 PᄡPsPIC-PrPsPjP»PᄡPSPSCᄡ PᄡCᄡPs P»PᄡC,P°P»CᄡPSC- PIPᄡPᄡPᄡPrPePᄡ, C...PsCᄡP°
 PᄡCᄡPᄡCᄡPᄡPSP° C-C... PIPᄡPSPᄡPePSPᄡPSPSCᄡ P·P°P»PᄡCᄡP°C,CᄡCᄡCᄡ
 PSPᄡP·Bᄡ™ CᄡCᄡPsPIP°PSPsCᄡ. Pj PᄡCᄡPsPiCᄡP°PjC- PeP»C-PSC-CᄡPSPᄡC...
 PrPsCᄡP»C-PrPᄡPᄡPSCᄡ P»P°PᄡP°C,PᄡPSC-P±Cᄡ PᄡPsP±C-CᄡPSC- CᄡPᄡP°PeCᄡC-C— P·
 P±PsPeCᄡ CᄡPᄡCᄡCᄡCᄡ,PIPeP»CᄡCᄡP°CᄡCᄡPᄡ P·PjPᄡPSCᄡPᄡPSPSCᄡ C,,CᄡP°PeCᄡC-C—
 PIPᄡPePᄡPrCᄡ P»C-PIPsPiPs CᄡP»CᄡPSPsCᄡPeP°, CᄡPᄡPsCᄡC,PᄡCᄡC-PIP°P»PᄡCᄡCᄡ
 PᄡCᄡPᄡP±P»PᄡP·PSPs Cᄡ 1 % PᄡP°CᄡC-C”PSC,C-PI, CᄡPeC- PsC,CᄡPᄡPjCᄡPIP°P»Pᄡ
 P»P°PᄡP°C,PᄡPSC-P±. PᄡPᄡPjPᄡC,PsPjP°C,PᄡCᄡPSC- P·PjPᄡPSCᄡPᄡPSPSCᄡ C,,CᄡP°PeCᄡC-C—
 PIPᄡPePᄡPrCᄡ P»C-PIPsPiPs CᄡP»CᄡPSPsCᄡPeP° CᄡPiPsCᄡC,PᄡCᄡC-PIP°P»PᄡCᄡCᄡ
 PᄡCᄡPᄡP±P»PᄡP·PSPs Cᄡ 0,3 % PᄡP°CᄡC-C”PSC,C-PI, CᄡPeC- PsC,CᄡPᄡPjCᄡPIP°P»Pᄡ

$P-P^{\circ}CfC, PsCfCfPIP^{\circ}PSPSCf P \gg P^{\circ}PiP^{\circ}C, P\ddot{e}PSC-P \pm Cr P^{\circ}CfPsCfC-CfC''C, CHCfCf P \cdot$
 $CfPsP \cdot PIP\ddot{e}C, PePsPj P \gg P_{\mu}PiP_{\mu}PSP_{\mu}PIPsC- C, PsPeCfP\ddot{e}C \ddagger PSPsCfC, C-, PIPeP \gg CfC \ddagger P^{\circ}CfC \ddagger P\ddot{e}$
 $C-PSC, P_{\mu}CfCfC, P\ddot{e}CfC-P^{\circ}P \gg CHPSC- P \cdot P^{\circ}C...PIPsCfCfPIP^{\circ}PSPSCf P \gg P_{\mu}PiP_{\mu}PSC-PI C, P^{\circ}$
 $PiPSP_{\mu}PIPjPsPSC-C, P\ddot{e} (PrP\ddot{e}PI. CfPsP \cdot PrC-P \gg B \ll P_{\mu}PsP \pm C-C \ddagger PSC- CfP_{\mu}P^{\circ}PeCfC-C-B \gg).$
 $P\check{Y}C, P^{\circ}PS C...PIPsCfP\ddot{e}C... CfP \gg C-Pr PePsPSC, CfPsP \gg CfHIP^{\circ}C, P\ddot{e} PrP \gg Cf$
 $PIP\ddot{e}CfPIP \gg P_{\mu}PSPSCf CfP\ddot{e}PjPiC, PsPjC-PI P \gg P_{\mu}PiP_{\mu}PSP_{\mu}PIPsC- C, PsPeCfP\ddot{e}C \ddagger PSPsCfC, C-$
 $(PrP\ddot{e}CfPiPSPsP_{\mu}, PeP^{\circ}C\epsilon P_{\mu}P \gg CH, P \gg P\ddot{e}C...PsPjP^{\circ}PSPeP^{\circ}) C, P^{\circ} PiCfP\ddot{e}PiP\ddot{e}PSCfC, P\ddot{e}$
 $P \gg C-PeCfPIP^{\circ}PSPSCf PiP^{\circ}CfC-C''PSC, C-PI, Cr CfPeP\ddot{e}C... CfPsP \cdot PIP\ddot{e}PSCfP \gg P\ddot{e}CfCH$
 $CfP\ddot{e}PjPiC, PsPjP\ddot{e} 3-PiPs CfC, CrPiP_{\mu}PSCf C- P \pm C-P \gg CHC\epsilon P_{\mu} (P \cdot P^{\circ}$

PeP»P°CГPёC,,C-PeP°C†C-C"CH PiPsP±C-C‡PSPёC... CГPµP°PeC†C-PNё
PкP°C†C-PsPSP°P»CHBPSPsPiPs C-PSCГC,PeC,CrC,Cr CГP°PeCr). P>PµPiPµPSPµPIP°
C,PsPeCГPёC‡PSC-CГC,CH PjPsP¶Pµ CГCЦPiP°C,Pe C,CЦP¶PePsPiPs CГC-PIPSЦ C,P°
CГPiCГPёC‡PёPSCЦC,Pe PrPёC...P°P»CHBPSCr PSPµPrPsCГC,P°C,PSC-CГC,CH.
PµPsPIC-PrPsPjP»CЦP»PsCГCH PiCГPs P»PµC,P°P»CHBPSC- PIPёPiP°PrPePё, C...PsC‡P°
PiCГPёC‡PёPSPё C†PёC... PIPёPiP°PrPeC-PI P·P°P»PёCёPёP»PёCГCH
PSPµP·BГ™ CЦCГPsPIP°PSPёPjPё.

P" PµPiP°C,PsC,PsPeCГPёC‡PSC-CГC,CH

PµC-Pr C‡P°CГ P»C-PeCrPIP°PSPSCЦ PiCГPµPiP°CГP°C,PsPj PÿP°PNёPIPµCГP±
PiPsPIC-PrPsPjP»CЦP»PsCГCH PiCГPs CЦPiPёC%°P° PiPµPiP°C,PsC,PsPeCГPёC‡PSPsCГC,C-,
CЦPeC- PI CГC-PrPeC-CГPSPёC... PIPёPiP°PrPeP°C... PjPsP¶CrC,CH PiCГPёP·PIPµCГC,Pe PrPs
P»PµC,P°P»CHBPSPёC... PSP°CГP»C-PrPeC-PI. P'PёPSPёPeP°C,Pe
PiPµPiP°C,PsC,PsPeCГPёC‡PSC-CГC,CH PjPsP¶Pµ PiCГPsC,CЦPiPsPj PiPµCГC-PsPrCr PIC-Pr
PeC-P»CHPePsC... PrPSC-PI PiC-CГP»CЦ PiPsC‡P°C,PeCr P»C-PeCrPIP°PSPSCЦ
PiCГPµPiP°CГP°C,PsPj PrPs PeC-P»CHPePsC... PjC-CГCЦC†C-PI. PкP° PiPsC‡P°C,PeCr
C,PµCГP°PiC-C— PiP°C†C-C"PSC,C-PI CГP»C-Pr PiPsPIC-PrPsPjPёC,Pe PiCГPs
PiPsC,PµPSC†C-P°P» PiPµPiP°C,PsC,PsPeCГPёC‡PSPsCГC,C-. PαCrPSPeC†C-CH PiPµC‡C-PSPePё
(CГC-PIPµPSCH C,CГP°PSCГP°PjC-PSP°P·, P±C-P»C-CГCrP±C-PSCr C,P° P»CrP¶PSPsC—
C,,PsCГC,,P°C,P°P·Pё) CГP»C-Pr PiPµCГPµPIC-CГCЦC,Pe PiPµCГPµPr PiPsC‡P°C,PePsPj
P»C-PeCrPIP°PSPSCЦ, C%°PsPjC-CГCЦC‡PSPs PiC-Pr C‡P°CГ P»C-PeCrPIP°PSPSCЦ C,P°
PIC-PrPiPsPIC-PrPSPs PrPs PeP»C-PSC-C‡PSPsPiPs CГC,P°PSCr. PiPeC%°Ps P·PjC-PSPё
PiPµC‡C-PSPePsPIPsC— C,,CrPSPeC†C-C— PjP°CHC,CH C,CЦP¶PePёPNё C...P°CГP°PeC,PµCГ,
P»C-PeCrPIP°PSPSCЦ PiCГPµPiP°CГP°C,PsPj PÿP°PNёPIPµCГP± CГP»C-Pr PiCГPёPiPёPSPёC,Pe
C- PSPµ PiPsPSPsPIP»CHPIP°C,Pe. PµP°C†C-C"PSC,Pe, CЦPeC- C" PSPsCГC-CЦPjPё HLA-
P°P»PµP»CЦ DQA1*02:01 C,P° DRB1*07:01, PjP°CHC,CH PiC-PrPIPёC%°PµPSPёPNё CГPёP·PёPe
PiPµPiP°C,PsC,PsPeCГPёC‡PSPsCГC,C-, P°CГPsC†C-PNёPsPIP°PSPsC— C-P·
P·P°CГC,PsCГCrPIP°PSPSCЦ PiCГPµPiP°CГP°C,Cr PÿP°PNёPIPµCГP±. Pj PIPµP»PёPePsPjCr
CГP°PSPrPsPjC-P·PsPIP°PSPsPjCr PeP»C-PSC-C‡PSPsPjCr PrPsCГP»C-PrP¶PµPSPSC-
PjPsPSPsC,PµCГP°PiC-C— PiCГPµPiP°CГP°C,PsPj PÿP°PNёPIPµCГP± (1194 PiP°C†C-C"PSC,Pe)
P·P°PiP°P»CHBPSPёPNё CГPёP·PёPe C,CЦP¶PePsPiPs PiPµC‡C-PSPePsPIPsPiPs
CrCГP°P¶PµPSPSCЦ (PъP>Pÿ Cr 5 CГP°P·C-PI PIPёC%°Pµ PSPsCГPjPё, 3-C-PNё CГC,CrPiC-PSCH
C,CЦP¶PePsCГC,C- P·P° PeP»P°CГPёC,,C-PeP°C†C-C"CH PiPsP±C-C‡PSPёC... CГPµP°PeC†C-PNё
PкP°C†C-PsPSP°P»CHBPSPsPiPs C-PSCГC,PeC,CrC,Cr CГP°PeCr) P±CrPI 2,8 % C‡PµCГPµP· 1
CГC-Pe P»C-PeCrPIP°PSPSCЦ. P—P°PiP°P»CHBPSP° C‡P°CГC,PsC,P° Cr PSPsCГC-C—PI
P°P»PµP»C-PI DQA1*02:01 C,P° DRB1*07:01 CГC,P°PSPsPIPёP»P° 10,3 %, P° Cr
PiP°C†C-C"PSC,C-PI, CЦPeC- PSPµ PjP°P»Pё C†PёC... P°P»PµP»C-PI BГ™ 0,5 %.
PкPsCГC-PNёCГC,PIPs HLA-P°P»PµP»C-PI C" P·P°PiP°P»CHBPSPёPj CЦPiPёC%°PµPj (15BГ™25 %)
CГPµCГPµPr C"PiCГPsPiPµPNёC†C-PI, P°P·C-P°C,C-PI, P°C,,CГPsP°PjPµCГPёPeP°PSC†C-PI C,P°
P»P°C,PePSPsP°PjPµCГPёPeP°PSC†C-PI, P°P»Pµ C" PSPёP¶C‡PёPj (1 %) Cr CЦPiPsPSC†C-PI.

P— PsP±PµCГPµP¶PSC-CГC,CH CГP»C-Pr P·P°CГC,PsCГPsPICrPIP°C,Pe PiCГPµPiP°CГP°C,
PÿP°PNёPIPµCГP± PiP°C†C-C"PSC,P°Pj P· PiPsPjC-CГPSPsCH P°P±Ps C,CЦP¶PePsCH
PiPµC‡C-PSPePsPIPsCH PSPµPrPsCГC,P°C,PSC-CГC,CH C,P° PiP°C†C-C"PSC,P°Pj P·
C,CЦP¶PePsCH PSPёCГPePsPIPsCH PSPµPrPsCГC,P°C,PSC-CГC,CH (PrPёPI. CГPsP·PrC-P»Pё
B«PÿPiPsCГC-P± P·P°CГC,PsCГCrPIP°PSPSCЦ C,P° PrPsP·PёB» C,P°
B«PαP°CГPjP°PePsPeC-PSPµC,PёPeP°B»).

P" C-P°CГPµCЦ

PµCГPё P·P°CГC,PsCГCrPIP°PSPSC- PiCГPµPiP°CГP°C,Cr PÿP°PNёPIPµCГP±

PİPsPIC-PrPsPjP»CİP»PsCİCİ PİCḡPs CḡPsP·PIPëC,PsPe PrC-P°CḡPµC—, PİPeP»CḡC‡P°CḡC‡Pë
 C,CİP¶PeC- PİPëPİP°PrPePë (PrPëPI. CḡPsP·PrC-P» B«PµPsP±C-C‡PSC- CḡPµP°PeC‡C-C—B»).
 P°C-P°CḡPµCİ PjPsP¶Pµ P±CḡC,Pë PİPsC,PµPSC‡C-PN°PSPs P¶PëC,C,C°PIP
 PSPµP±PµP·PİPµC‡PSPsCḡ, CİPeC%Ps CİCḡPİCḡPsPIPPrP¶CḡC°C,CḡCİCİ
 PrPµPiC-PrCḡP°C,P°C‡C-C°Cḡ, PSPëCḡPePsPIPSCḡ PSPµPrPsCİC,P°C,PSC-CİC,Cḡ,
 PSPµPN°C,CḡPsPİPµPSC-C°Cḡ C,P°/P°P±Ps PrPëCİP±P°P»P°PSCİPsPj
 PµP»PµPeC,CḡPsP»C-C,C-PI. PµPsPIC-PrPsPjP»CİP»PsCİCḡ PİCḡPs P»PµC,P°P»CḡPSC-
 PİPëPİP°PrPePë. P°C-P°CḡPµCİ P·P°P·PIPëC‡P°PN° PİPëPSPëPeP°C° CḡP°PSPs PİC-Pr C‡P°Cİ
 P»C-PeCḡPIP°PSPSCİ PİCḡPµPİP°CḡP°C,PsPj PÿP°PN°PIPµCḡP±, PjP°PN°P¶Pµ Cḡ
 PİPsP»PsPIPëPSPë C...PIPSCḡPëC... P· PrC-P°CḡPµC°Cḡ PIPsPSP° PİPëPSPëPeP°C°
 PİPİPµCḡC€Pµ PİCḡPsC,CİPİPsPj 6 PrPSC-PI. P—P°P·PIPëC‡P°PN° PrC-P°CḡPµCİ C,CḡPëPIP°C°
 4Bḡ“5 PrPSC-PI. P°C-P°CḡPµCİ, P°CİPsC‡C-PN°PsPIP°PSP° P· PİCḡPëPN°PsPjPsPj
 PİCḡPµPİP°CḡP°C,Cḡ PÿP°PN°PIPµCḡP±, P·P°P·PIPëC‡P°PN° C° PSPµPIPëCİPsPePsPİPs
 CİC,CḡPİPµPSCİ C,CİP¶PePsCİC,C-, P° C,CİP¶PeP° PrC-P°CḡPµCİ 3-PİPs C,P° 4-
 PİPs CİC,CḡPİPµPSCİ P·P° PeP»P°CİPëC,,C-PeP°C‡C-C°Cḡ PİPsP±C-C‡PSPëC...
 CḡPµP°PeC‡C-PN° PḡP°C‡C-PsPSP°P»CḡPSPsPİPs C-PSCİC,PëC,CḡC,Cḡ CḡP°PeCḡ
 PİPëPSPëPeP°P»P° Cḡ < 10 % C,P° < 1 % PİP°C‡C-C°PSC,C-PI PIC-PrPİPsPIC-PrPSPs. PḡP°
 PİPsC‡P°C,PeCḡ P»C-PeCḡPIP°PSPSCİ C...P°CḡP°PeC,PµCḡ PİPëPİPsCḡPsP¶PSPµPSCḡ
 PİP°C‡C-C°PSC,P° C,P° P±CḡPrCḡC-CİPeC- C-PSC€C- CİPëPjPİC,PsPjPë
 (P»PëC...PsPjP°PSPeP°, CİPİP°P·PjCḡCḡC‡PëPN° P±C-P»Cḡ, PSCḡPrPsC,P°,
 P±P»CḡPIP°PSPSCİ, P·P°PİP°PjPsCḡPsC‡PµPSPSCİ C,P° CİPİCḡP°PİP°)
 PİPsC,CḡC-P±PSPs PİPëCİPIPëC,Pë, C%PsP± PjP°C,Pë PjPsP¶P»PëPIC-CİC,Cḡ
 CİPİPsCİC,PµCḡC-PİP°C,Pë P·P° C—C... P·PjC-PSP°PjPë PİC-Pr C‡P°Cİ
 P»C-PeCḡPIP°PSPSCİ C,P° C-PrPµPSC,PëC,,C-PeCḡPIP°C,Pë PİP°C‡C-C°PSC,C-PI P·
 PİC-PrPIPëC%PµPSPëPj CḡPëP·PëPePsPj CḡPsP·PIPëC,PeCḡ PrC-P°CḡPµC—.
 PµP°C‡C-C°PSC,C-PI CİP»C-Pr PİPsPİPµCḡPµPrPëC,Pë, C%Ps PSPµPsP±C...C-PrPSPs
 PSPµPİP°PN°PSPs PrPsPİPsPIC-PrP°C,Pë PİCḡPs P±CḡPrCḡC-CİPeC- P·PjC-PSPë Cḡ
 C...P°CḡP°PeC,PµCḡC- PİPëPİPsCḡPsP¶PSPµPSCḡ PePëC€PµC‡PSPëPeCḡ. Pj
 PİPsC,PµPSC‡C-PN°PSPs C,CİP¶PePëC... PİPëPİP°PrPeP°C... PrC-P°CḡPµC— CİP»C-Pr
 PİPëP·PSP°C‡P°C,Pë PeC-P»CḡPeC-CİC,Cḡ PSPµPN°C,CḡPsC,,C-P»C-PI C,P°
 PİPëPjC-CḡCḡPIP°C,Pë C,PµPjPİPµCḡP°C,CḡCḡCḡ C,C-P»P°. B P°P°P¶P»PëPIPµ
 P·PSP°C‡PµPSPSCİ PjP°C° C€PIPëPrPePµ P»C-PeCḡPIP°PSPSCİ PrC-P°CḡPµC— C-P·
 PİPëPePsCḡPëCİC,P°PSPSCİPj PİCḡPsC,PëPrC-P°CḡPµPN°PSPëC...
 PİCḡPµPİP°CḡP°C,C-PI. PµCḡPë C,CİP¶PePsPjCḡ PİPµCḡPµP±C-PİCḡ
 P·P°C...PIPSCḡCḡPIP°PSPSCİ PjPsP¶Pµ P±CḡC,Pë PİPsC,CḡC-P±PSPµ
 PİPµCḡPsCḡP°P»CḡPSPµ P°P±Ps PIPSCḡC,CḡC-C€PSCḡPsPIPµPSPSPµ
 PİPİPµPrPµPSPSCİ PµP»PµPeC,CḡPsP»C-C,C-PI C,P° CḡC-PrPëPS,
 P·P°CİC,PsCİCḡPIP°PSPSCİ P°PSC,PëP±C-PsC,PëPeC-PI, C,P°PePëC... CİPe
 C,,C,PsCḡC...C-PSPsP»PsPSPë (PsCİPsP±P»PëPİPs CİPeC%Ps PrC-P°CḡPµCİ
 C,CḡPëPIP°C° P±C-P»CḡC€Pµ 24 PİPsPrPëPS, C° P»PëC...PsPjP°PSPeP° P°P±Ps
 PSPµPN°C,CḡPsPİPµPSC-Cİ 3-PİPs C,P° 4-PİPs CİC,CḡPİPµPSCİ),
 PİCḡPëPİPëPSPµPSPSCİ P°P±Ps PIC-PrPjC-PSP° P·P°CİC,PsCİCḡPIP°PSPSCİ
 PİCḡPµPİP°CḡP°C,Cḡ PÿP°PN°PIPµCḡP± (PrPëPI. CḡPsP·PrC-P» B«PÿPİPsCİC-P±
 P·P°CİC,PsCİCḡPIP°PSPSCİ C,P° PrPsP·PëB» Bḡ“ B«PµCḡPëPİPëPSPµPSPSCİ
 PİCḡPëPN°PsPjCḡ P°P±Ps P·PjPµPSC€PµPSPSCİ PrPsP·PëB» Bḡ“ B«P°C-P°CḡPµCİB»)).

PÿCİP¶PeC- C€PeC-CḡPSC- CḡPµP°PeC‡C-C—

P,, PİPsPIC-PrPsPjP»PµPSPSCİ PİCḡPs C,CİP¶PeC- C€PeC-CḡPSC- CḡPµP°PeC‡C-C— PİCḡPë

P·P°CÍ'C,PsCÍ'CrPIP°PSPSC- PíCĤPμPíP°CĤP°C,Cr PŷP°PNēPIPμCĤP±. Pj CĤP°P·C-
PíC-PrPsP·CĤPē PSP° PjCrP»CHC,PēC,,PsCĤPjPSCr PμCĤPēC,PμPjCr P°P±Ps CĤPμP°PeC†C-C—,
CĤPeC- C" P·P°PíCĤPsP·P»PēPIPēPjPē PrP»CĤ P¶PēC,C,CĤ, C,P°PeC- CĤPe CÍ'PēPSPPrCĤPsPj
PŷC,C-PIPμPSCÍ'P° BĤ" P"¶PsPSCÍ'PsPSP° P°P±Ps C,PsPeCÍ'PēC†PSPēPNē
PμPíC-PrPμCĤPjP°P»CHPSC-PNē PSPμPeCĤPsP»C-P· (PSP°PíCĤPēPeP»P°Pr
PíCĤPsPíCĤPμCÍ'CrCĤC†Pμ CēPeC-CĤPSPμ PIPēCÍ'PēPíP°PSPSCĤ C†P°CÍ'C,Ps P·
PíCrC...PēCĤC†CĤPjPē P°P±Ps PíPsCĤCrCēPμPSPSCĤPjPē CÍ'P»PēP·PsPIPsC—
PsP±PsP»PsPSPēPē), P»C-PeCÍ'PIP°PSPSCĤ PíCĤPμPíP°CĤP°C,PsPj PŷP°PNēPIPμCĤP± CÍ'P»C-Pr
PíCĤPēPíPēPSPēC,Pē.

*PŷC¿PíC¿C,PSC" P·P°CÍ'C,PsCÍ'CrPIP°PSPSCĤ P· C-PSPiC-P±C-C,PsCĤP°PjPē C,P°
C-PSPrC¿PeC,PsCĤP°PjPē CYP3A4*

PŷCrPíCrC,PSC" P·P°CÍ'C,PsCÍ'CrPIP°PSPSCĤ P»P°PíP°C,PēPSC-P±Cr P·
C-PSPiC-P±C-C,PsCĤP°PjPē C,P° C-PSPrCrPeC,PsCĤP°PjPē CYP3A4 CÍ'P»C-Pr
PíCĤPsPIPsPrPēC,Pē P· PsP±PμCĤPμP¶PSC-CÍ'C,CĤ C†PμCĤPμP· PIC-PrPíPsPIC-PrPSPs
P·P±C-P»CHCēPμPSPSCĤ P°P±Ps P·PjPμPSCēPμPSPSCĤ PePsPSC†PμPSC,CĤP°C†C-C—
P»P°PíP°C,PēPSC-P±Cr (PrPēPI. CĤPsP·PrC-P» B«P'P·P°C" PjPsPrC-CĤ P· C-PSCēPēPjPē
P»C-PeP°CĤCÍ'CHPePēPjPē P·P°CÍ'PsP±P°PjPē C,P° C-PSCēC- PIPēPrPē PIP·P°C" PjPsPrC-PNēB»).

PμC-Pr C†P°CÍ' P»C-PeCÍ'PIP°PSPSCĤ P»P°PíP°C,PēPSC-P±PsPj CÍ'P»C-Pr CrPSPēPeP°C,Pē
P·P°CÍ'C,PsCÍ'CrPIP°PSPSCĤ PíCĤPμPNēPíC,,CĤCrC,PsPIPsPíPs CÍ'PsPeCr (PrPēPI. CĤPsP·PrC-P»
B«P'P·P°C" PjPsPrC-CĤ P· C-PSCēPēPjPē P»C-PeP°CĤCÍ'CHPePēPjPē P·P°CÍ'PsP±P°PjPē C,P°
C-PSCēC- PIPēPrPē PIP·P°C" PjPsPrC-PNēB»).

PŷP»C-Pr CrPSPēPeP°C,Pē CÍ'CrPjC-CÍ'PSPsPíPs P·P°CÍ'C,PsCÍ'CrPIP°PSPSCĤ
PíCĤPμPíP°CĤP°C,Cr PŷP°PNēPIPμCĤP± P· C-PSCēPēPjPē P»C-PeP°CĤCÍ'CHPePēPjPē
P·P°CÍ'PsP±P°PjPē P· PíCrP·CHPePēPj C,PμCĤP°PíPμPIC,PēC†PSPēPj C-PSPrPμPeCÍ'PsPj, C%Ps
C" CÍ'CrP±CÍ'C,CĤP°C,P°PjPē PrP»CĤ CYP3A4 C,P°/P°P±Ps CYP2Pŷ8 (PrPēPI. CĤPsP·PrC-P»
B«P'P·P°C" PjPsPrC-CĤ P· C-PSCēPēPjPē P»C-PeP°CĤCÍ'CHPePēPjPē P·P°CÍ'PsP±P°PjPē C,P°
C-PSCēC- PIPēPrPē PIP·P°C" PjPsPrC-PNēB»).

PŷP»C-Pr CrPSPēPeP°C,Pē CÍ'CrPjC-CÍ'PSPsPíPs P·P°CÍ'C,PsCÍ'CrPIP°PSPSCĤ P·
CĤPμC†PsPIPēPSP°PjPē, C%Ps PíC-PrPIPēC%CrCĤC,CH CĤPκ CēP»CrPSPēP°,
PsCÍ'PeC-P»CHPePē CĤPsP·C†PēPSPSC-CÍ'C,CH C,P° P°P±CÍ'PsCĤP±C†C-CĤ
P»P°PíP°C,PēPSC-P±Cr PjPsP¶CÍ'C,CH P·PjPμPSCēCÍ'PIP°C,PēCÍ'CĤ (PrPēPI. CĤPsP·PrC-P»
B«P'P·P°C" PjPsPrC-CĤ P· C-PSCēPēPjPē P»C-PeP°CĤCÍ'CHPePēPjPē P·P°CÍ'PsP±P°PjPē C,P°
C-PSCēC- PIPēPrPē PIP·P°C" PjPsPrC-PNēB»).

P'PjC-CÍ'C, PSP°C,CĤC-CĤ

PíPμPNē PíCĤPμPíP°CĤP°C, PjC-CÍ'C,PēC,CH PjPμPSCēPμ 1 PjPjPsP»CH PSP°C,CĤC-CĤ (23 PjPi)
PSP° C,P°P±P»PμC,PeCr, C,PsP±C,Ps PíPíP°P¶P°C",CHCÍ'CĤ C,P°PePēPj, C%Ps PSPμ
PjC-CÍ'C,PēC,CH PSP°C,CĤC-CĤ.

*P—P°CÍ'C,PsCÍ'CrPIP°PSPSCĤ C¿ PíPμCĤC-PsPr PIP°PíC-C,PSPsCÍ'C,C- P°P±Ps
PíPsPrC¿PIP°PSPSCĤ PíCĤC¿PrPrCĤ.*

P-C-PSPePē CĤPμPíCĤPsPrCrPeC,PēPIPSPsPíPs PIC-PeCr

P-C-PSPsPe CḡPμPīCḡPsPrCfPeC,PēPIPSpSiPs PIC-PeCf CḡP»C-Pr PīPsPīPμCḡPμPrPēC,Pē PīCḡPs PSPμPsP±C...C-PrPSC-CḡC,CH PIPēPePsCḡPēCḡC,PsPICfPIP°C,Pē PIC-PrPīPsPIC-PrPSC-P·P°C...PsPrPē PePsPSC,CḡP°C†PμPīC†C-C— C,P° CḡPSPēPeP°C,Pē PIP°PiC-C,PSPsCḡC,C- PīC-Pr C†P°Cḡ P»C-PeCfPIP°PSPSCḡ PīCḡPμPīP°CḡP°C,PsPj PḡP°PNēPIPμCḡP± C,P° PīCḡPsC,CḡPīPsPj C%PsPSP°PNēPjPμPSC€Pμ 5 PrPSC-PI PīC-CḡP»Cḡ P·P°CḡC,PsCḡCfPIP°PSPSCḡ PsCḡC,P°PSPSCHPsC— PrPsP·Pē.

P'P°PiC-C,PSC-CḡC,CH

P''P°PSC- C%PsPrPs P·P°CḡC,PsCḡCfPIP°PSPSCḡ PīCḡPμPīP°CḡP°C,Cf PḡP°PNēPIPμCḡP± PIP°PiC-C,PSPēPj PḡC-PSPeP°Pj PIC-PrCḡCfC,PSC-. P' PrPsCḡP»C-PrPḡPμPSPSCḡC... PSP° C,PIP°CḡPēPSP°C... CḡPīPsCḡC,PμCḡC-PiP°P»P°CḡCH CḡPμPīCḡPsPrCfPeC,PēPIPSp° C,PsPeCḡPēC†PSC-CḡC,CH (PrPēPI. CḡPsP·PrC-P» B«PαP°CḡPjP°PePsP»PsPiC-C†PSC-PIP°P°CḡC,PēPIPsCḡC,C-B»). PμPsC,PμPSC†C-PNēPSPēPNē CḡPēP·PēPe PrP»Cḡ P»CḡPrPēPSPē PSPμPIC-PrPsPjPēPNē.

PḡP°PNēPIPμCḡP± PSPμ CḡP»C-Pr P·P°CḡC,PsCḡPsPICfPIP°C,Pē PīC-Pr C†P°Cḡ PIP°PiC-C,PSPsCḡC,C-, PsPeCḡC-Pj PIPēPīP°PrPeC-PI PeCḡP°PNēPSCḡPsC— PSPμPsP±C...C-PrPSPsCḡC,C-.

P"PsPrCfPIP°PSPSCḡ PīCḡCfPrPrCḡ

P'PμP·PīPμPeCf P·P°CḡC,PsCḡCfPIP°PSPSCḡ PīCḡPμPīP°CḡP°C,Cf PḡP°PNēPIPμCḡP± PīC-Pr C†P°Cḡ PīPsPrCfPIP°PSPSCḡ PīCḡCfPrPrCḡ PSPμ PICḡC,P°PSPsPIP»PμPSPs. PkPμPIC-PrPsPjPs, C†Pē PμPeCḡPeCḡPμC,CfC''C,CHCḡCḡ P»P°PīP°C,PēPSC-P± Cḡ PīCḡCfPrPSPμ PjPsP»PsPePs. Pj C%CrCḡC-PI CḡPīPsCḡC,PμCḡC-PiP°P»P°CḡCH P·P°C,CḡPēPjPeP° P·CḡPsCḡC,P°PSPSCḡ C%CrCḡCḡC,, PePsP»Pē PIPsPSPē PīC-PrPrP°PIP°P»PēCḡCḡ PIPiP»PēPICf P»P°PīP°C,PēPSC-P±Cḡ C†PμCḡPμP· PīCḡCfPrPSPμ PjPsP»PsPePs. P-C-PSPePē, CḡPeC-PsC,CḡPēPjCfCḡC,CH PḡP°PNēPIPμCḡP±, PjP°CḡC,CH PīCḡPēPīPēPSPēC,Pē PīPsPrCfPIP°PSPSCḡ PīCḡCfPrPrCḡ PSP° PīPμCḡC-PsPr P»C-PeCfPIP°PSPSCḡ C,P° C%PsPSP°PNēPjPμPSC€Pμ 5-C,Pē PrPSC-PI PīC-CḡP»Cḡ P·P°CḡC,PsCḡCfPIP°PSPSCḡ PsCḡC,P°PSPSCHPsC— PrPsP·Pē.

PαPμCḡC,PēP»CHPSC-CḡC,CH

P''P°PSC- C%PsPrPs P·P°CḡC,PsCḡCfPIP°PSPSCḡ PīCḡPμPīP°CḡP°C,Cf PḡP°PNēPIPμCḡP± PḡC-PSPeP°Pj CḡPμPīCḡPsPrCfPeC,PēPIPSpSiPs PIC-PeCf PIC-PrCḡCfC,PSC-.

P-PrP°C,PSC-CḡC,CH PIPiP»PēPIP°C,Pē PSP° C€PIPēPrPeC-CḡC,CH CḡPμP°PeC†C-C— PīCḡPē PePμCḡCḡPIP°PSPSC- P°PIC,PsC,CḡP°PSCḡPīPsCḡC,PsPj P°P±Ps C-PSC€PēPjPē PjPμC...P°PSC-P·PjP°PjPē.

PμCḡPμPīP°CḡP°C, PḡP°PNēPIPμCḡP± PSPμ PIPiP»PēPIP°C'' PSP° P·PrP°C,PSC-CḡC,CH PePμCḡCfPIP°C,Pē P°PIC,PsC,CḡP°PSCḡPīPsCḡC,PsPj P°P±Ps C-PSC€PēPjPē PjPμC...P°PSC-P·PjP°PjPē. P— PsPiP»CḡPrCf PSP° C,,P°CḡPjP°PePsP»PsPiC-C†PSC-PIP°P°CḡC,PēPIPsCḡC,C- P»P°PīP°C,PēPSC-P±Cḡ PNēPsPiPs PSPμCḡPīCḡPēCḡC,P»PēPIPēPNē PIPiP»PēPI PSP° C,P°PeC- PIPēPrPē PrC-CḡP»CHPSPsCḡC,C- PjP°P»PsPNēPjPsPIC-CḡPSPēPNē. PhPrPSP°Pe PīCḡPē PIPēCḡC-C€PμPSPSC- PīPēC,P°PSPSCḡ PīCḡPs P·PrP°C,PSC-CḡC,CH PīP°C†C-C''PSC,P° PIPēPePsPSCfPIP°C,Pē CḡPsP±PsC,Cf, C%Ps PīPsC,CḡPμP±CḡC'' PīC-PrPIPēC%PμPSPsC— PePsPSC†PμPSC,CḡP°C†C-C— CḡPIP°PiPē C,P° C€PIPēPrPePsCḡC,C-

PiCfPëC...PsPjPsC,PsCfPSPëC... CfPµP°PeC†C-PN, CfP»C-Pr P·PIPµCfPSCfC,Pë CfPIP°PiCf
PSP° PeP»C-PSC-C†PSPëPN Cfc,P°PS PiP°C†C-C”PSC,P° C,P° C...P°CfP°PeC,PµCf
PiPsP±C-C†PSPëC... CfPµP°PeC†C-PN.

PŸPiPsCfC-P± P·P°CfC,PsCfC¿PIP°PSPSCf C,P° PrPsP·Pë.

PµCfCfCf P»C-PeCfPIP°PSPSCf PiCfPµPiP°CfP°C,PsPj PŸP°PNPIPµCfP±
PiCfPëP·PSP°C†P°C” P»PëCfPµ P»C-PeP°Cf, CfiPePëPN PjP°C” PrPsCfPIC-Pr
P·P°CfC,PsCfCfPIP°PSPSCf PiCfPµCfPëPiCfC...P»PëPSPSPëC... PiCfPµPiP°CfP°C,C-PI.

PŸC,P°C,CfCf PiC-PiPµCfPµPeCfPiCfPµCfC-C— HER2 (ErbB2) PjP°C” P±CfC,Pë
PICfC,P°PSPsPIP»PµPSPëPN P·P° PSP°CfiPIPSC-CfC,Cf IHC3 C†Pë IHC2 P·
P°PjPiP»C-C,,C-PeP°C†C-C”Cf PiPµPSC-PI P°P±Ps P·P° P°PjPiP»C-C,,C-PeP°C†C-C”Cf
PiPµPSC-PI PsPeCfPµPjPs. PŸC,P°C,CfCf HER2 PjP°C” P±CfC,Pë
PIPëP·PSP°C†PµPSPëPN P·P° PrPsPiPsPjPsPiPsCf C,PsC†PSPëC... C-
PIP°P»C-PrPsPIP°PSPëC... PjPµC,PsPrC-PI.

P”PsP·Pë

PŸP°PNPIPµCfP± Cf PePsPjP±C-PSP°C†C-C— P· PeP°PiPµC†PëC,P°P±C-PSPsPj

P PµPePsPjPµPSPPrPsPIP°PSP° PrPsP·P° PiCfPµPiP°CfP°C,Cf PŸP°PNPIPµCfP±
CfC,P°PSPsPIPëC,Cf 1250 PjPi (5 C,P°P±P»PµC,PsPe) 1 CfP°P· PSP° PrPsP±Cf C%PsPrPSCf.

P PµPePsPjPµPSPPrPsPIP°PSP° PrPsP·P° PeP°PiPµC†PëC,P°P±C-PSCf Cf” 2000 PjPi/Pj²/PrPsP±Cf
P·P° 2 PiCfPëPNPsPjPë (PePsP¶PSC- 12 PiPsPrPëPS) PePsP¶PSPsPiPs PrPSCf P· 1-PiPs PiPs 14-
PN PrPµPSCf 21-PrPsP±PsPiPsPiPs C†PëPeP»Cf P»C-PeCfPIP°PSPSCf.
P PµPePsPjPµPSPPrCfC”,CfCfCf PiCfPëPNPjP°C,Pë PeP°PiPµC†PëC,P°P±C-PS P· C—P¶PµCf
P°P±Ps PiCfPµC,CfiPiPsPj 30 C...PI PiC-CfP»Cfi C—PrPë (PrPëPI. C-PSCfC,CfCfPeC†C-Cf
PrP»Cfi PjPµPrPëC†PSPsPiPs P·P°CfC,PsCfCfPIP°PSPSCf PeP°PiPµC†PëC,P°P±C-PSCf).

PŸP°PNPIPµCfP± Cf PePsPjP±C-PSP°C†C-C— P· C,CfP°CfC,CfP·CfPjP°P±PsPj

P PµPePsPjPµPSPPrPsPIP°PSP° PrPsP·P° PiCfPµPiP°CfP°C,Cf PŸP°PNPIPµCfP±
CfC,P°PSPsPIPëC,Cf 1000 PjPi (4 C,P°P±P»PµC,PePë) 1 CfP°P· PSP° PrPsP±Cf C%PsPrPSCf.

P PµPePsPjPµPSPPrPsPIP°PSP° PrPsP·P° C,CfP°CfC,CfP·CfPjP°P±Cf Cf” 4 PjPi/PePi PjP°CfPë
C,C-P»P° CfiPe PIPSCfC,CfC-CfPSCfPsPIPµPSPSP° PSP°PIP°PSC,P°P¶CfPIP°P»CfPSP°
PrPsP·P°, PiPsC,C-Pj 2 PjPi/PePi PjP°CfPë C,C-P»P° PIPSCfC,CfC-CfPSCfPsPIPµPSPSPs
1 CfP°P· PSP° C,PëP¶PrPµPSCf (PrPëPI. C-PSCfC,CfCfPeC†C-Cf PrP»Cfi PjPµPrPëC†PSPsPiPs
P·P°CfC,PsCfCfPIP°PSPSCf C,CfP°CfC,CfP·CfPjP°P±Cf).

PŸP°PNPIPµCfP± Cf PePsPjP±C-PSP°C†C-C— P· C-PSPiC-P±C-C,PsCfPµPj
P°CfPµPjP°C,P°P·Pë

P PµPePsPjPµPSPPrPsPIP°PSP° PrPsP·P° PiCfPµPiP°CfP°C,Cf PŸP°PNPIPµCfP±
CfC,P°PSPsPIPëC,Cf 1500 PjPi (6 C,P°P±P»PµC,PsPe) 1 CfP°P· PSP° PrPsP±Cf C%PsPrPSCf.

PµCfPë P·P°CfC,PsCfCfPIP°PSPSC- PiCfPµPiP°CfP°C,Cf PŸP°PNPIPµCfP±B P·
P°P»CfC,PµCfPSP°C,PëIPSPëPj C-PSPiC-P±C-C,PsCfPµPj P°CfPµPjP°C,P°P·Pë

P·C–PeCfPIP°PSPSCl PÿP°PMPIPµCḡP±PsPj CÍP»C–Pr PíPµCḡPµCḡPIP°C,Pë Cr CḡP°P·C–
 PíPsCllPIPë PrC–P°CḡPµC— 3–PiPs CÍC,CfPíPµPSCl P°P±Ps PrC–P°CḡPµC— 1–PiPs P°P±Ps 2–
 PiPs CÍC,CfPíPµPSCl (P·P° PeP»P°CÍPëC,,C–PeP°C†C–C”Cḡ PíPsP±C–C‡PSPëC...
 CḡPµP°PeC†C–PNë PkP°C†C–PsPSP°P»CHbPSPsPiPs C–PSCÍC,PëC,CfC,Cf CḡP°PeCf) P·
 PsP·PSP°PeP°PjPë CrCÍPeP»P°PrPSPµPSPSCl (PIC–Pr PíPsPjC–CḡPSPëC... PrPs C,CllP¶PePëC...
 P°P±PrPsPjC–PSP°P»CHbPSPëC... CÍPíP°P·PjC–PI, PSCfPrPsC,Pë P°P±Ps P±P»CḡPIP°PSPSCl
 P±C–P»CHbCëPëC... P°P±Ps PIC–PrPíPsPIC–PrPSPëC... 2–PjCr CÍC,CfPíPµPSCḡ
 C,CllP¶PePsCÍC,C– (P·P° PeP»P°CÍPëC,,C–PeP°C†C–C”Cḡ PíPsP±C–C‡PSPëC... CḡPµP°PeC†C–PNë
 PkP°C†C–PsPSP°P»CHbPSPsPiPs C–PSCÍC,PëC,CfC,Cf CḡP°PeCf), P·PSPëP¶PµPSPSCl
 PíCḡP°C†PµP·PrP°C,PSPsCÍC,C–, PíCḡPsPíP°CÍPSPëC†Cll, CÍPµPíCÍPëCÍ,
 PSPµPNëC,CḡPsPíPµPSC–Cl, PIC–PrPeCḡPëC,P° PeCḡPsPIPsC,PµC‡P° P°P±Ps
 PrPµPiC–PrCḡP°C,P°C†C–Cl) (PrPëPI. CḡPsP·PrC–P»Pë B«PhCÍPsP±P»PëPIPsCÍC,C–
 P·P°CÍC,PsCÍCfPIP°PSPSClB» C,P° B«PµPsP±C–C‡PSC– CḡPµP°PeC†C–C–B»).

PIPIPsC7C- P»C-C,PSCHbPsPiPs PIC-PeCž

P"°PSC- P·P°CfC,PsCfCfPIP°PSPSClI PePsPjP±C-PSP°C†C-C— PŷP°PNēPIPμC7P± P·
PeP°PīPμC†PēC,P°P±C-PSPsPj C,P° PePsPjP±C-PSP°C†C-C— PŷP°PNēPIPμC7P± P·
C,C7P°CfC,CfP·CfPjP°P±PsPj PīP°C†C-C"PSC,P°Pj PIC-PePsPj PIC-Pr 65 C7PsPeC-PI
PsP±PjPμP¶PμPSC-.

P' PeP»C-PSC-C†PSPsPjCf PIPēPīC7PsP±CfPIP°PSPSC- C,,P°P·Pē III P·P°CfC,PsCfCfPIP°PSPSClI
PīC7PμPīP°C7P°C,Cf PŷP°PNēPIPμC7P± PI PePsPjP±C-PSP°C†C-C— P· P»PμC,C7PsP·PsP»PsPj
P·P° CfC†P°CfC,C7 PīP°C†C-C"PSC,C-PI P· PiPsC7PjPsPS-C7PμC†PμPīC,PsC7-
PīPsP·PēC,PēPIPSpēPj PjPμC,P°CfC,P°C,PēC†PSPēPj C7P°PePsPj PjPsP»PsC†PSPsC— P·P°P»PsP·Pē
(PīPsPīCfP»C†C†C-C† PICfC-C... C7P°PSPrPsPjC-P·PsPIP°PSPēC... PīP°C†C-C"PSC,C-PI P·P°
PīC7PēP·PSP°C†PμPSPēPj P»C-PeCfPIP°PSPSClIj, N 642) 44 % CfC†P°CfPSPēPeC-PI P±CfP»Pē
Cf PIC-C†C- PIC-Pr 65 C7PsPeC-PI. P7C-P¶ C†PēPjPē PīP°C†C-C"PSC,P°PjPē C,P°
PīP°C†C-C"PSC,P°PjPē PIC-PePsPj PrPs 65 C7PsPeC-PI P·P°PīP°P»PsPj PSPμ
CfPīPsCfC,PμC7C-PiP°P»PsCfC7 PIC-PrPjC-PSPSPsCfC,PμPNē C%°PsPrPs
PμC,,PμPeC,PēPIPSpCfC,C- C,P° P±PμP·PīPμPePē P·P°CfC,PsCfCfPIP°PSPSClI
PePsPjP±C-PSP°C†C-C— PīC7PμPīP°C7P°C,Cf PŷP°PNēPIPμC7P± P· P»PμC,C7PsP·PsP»PsPj.

PŷPīPsCfC-P± P·P°CfC,PsCfCžPIP°PSPSClI

PμC7PμPīP°C7P°C, PŷP°PNēPIPμC7P± PīC7PēP·PSP°C†PμPSPēPNē PrP»C†
PīPμC7PsC7P°P»CHbPSPsPiPs P·P°CfC,PsCfCfPIP°PSPSClI.

P"PsP±PsPICf PrPsP·Cf PīC7PμPīP°C7P°C,Cf PŷP°PNēPIPμC7P± PSPμ CfP»C-Pr PrC-P»PēC,Pē.
PŷP°PNēPIPμC7P± CfP»C-Pr PīC7PēPNēPjP°C,Pē C%°PsPSP°PNēPjPμPSC€Pμ P·P° PiPsPrPēPSCf
PrPs P°P±Ps C%°PsPSP°PNēPjPμPSC€Pμ C†PμC7PμP· PiPsPrPēPSCf PīC-CfP»C† C—PrPē. P"»C†
P·PjPμPSC€PμPSPSClI C-PSPrPēPIC-PrCfP°P»CHbPSPsC— PIP°C7C-P°P±PμP»CHbPSPsCfC,C-
PePsP¶PSPsPjCf PsPeC7PμPjPsPjCf PīP°C†C-C"PSC,Cf P·P°CfC,PsCfCfPIP°PSPSClI
PīC7PμPīP°C7P°C,Cf PŷP°PNēPIPμC7P± CfP»C-Pr CfC,P°PSPrP°C7C,PēP·CfPIP°C,Pē
PIC-PrPSPsCfPSPs CfPīPsP¶PēPIP°PSPSClI C—P¶C-, PSP°PīC7PēPeP»P°Pr, P·P°PIP¶PrPē
PīC7PēPNēPjP°C,Pē PīC7PμPīP°C7P°C, P·P° PsPrPSCf PiPsPrPēPSCf PrPs C—PrPē (PrPēPI.
C7PsP·PrC-P»Pē B«P'P·P°C"PjPsPrC-C† P· C-PSC€PēPjPē P»C-PeP°C7CfCHbPePēPjPē
P·P°CfPsP±P°PjPē C,P° C-PSC€C- PIPēPrPē PIP·P°C"PjPsPrC-PNēB»,
B«PαP°C7PjP°PePsPeC-PSPμC,PēPeP°B» PrP»C† PsC,C7PēPjP°PSPSClI C-PSC,,PsC7PjP°C†C-C—
C%°PsPrPs P°P±CfPsC7P±C†C-C—).

PμC7PsPīCfC%°PμPSC- PrPsP·Pē PīC7PμPīP°C7P°C,Cf PSPμ CfP»C-Pr PīC7PēPNēPjP°C,Pē
PrPsPrP°C,PePsPIPs, PSP°CfC,CfPīPSCf PrPsP·Cf CfP»C-Pr PīC7PēPNēPSClI,C,Pē P·PiC-PrPSPs P·
PīC7P°C,,C-PePsPj P·P°CfC,PsCfCfPIP°PSPSClI (PrPēPI. C7PsP·PrC-P»
B«PμPμC7PμPrPsP·CfPIP°PSPSClIb»).

PμC7Pē CfCfPjC-CfPSPsPjCf P·P°CfC,PsCfCfPIP°PSPSC- P· C-PSC€PēPjPē
PīC7PμPīP°C7P°C,P°PjPē PSPμPsP±C...C-PrPSPs PsP·PSP°PNēPsPjPēC,PēCfC† P·
C-PSCfC,C7CfPeC†C-C†PjPē PrP»C† PjPμPrPēC†PSPsPiPs P·P°CfC,PsCfCfPIP°PSPSClI C†PēC...
PīC7PμPīP°C7P°C,C-PI PrP»C† PsC,C7PēPjP°PSPSClI PIPeP°P·C-PIPsPe P· PrPsP·CfPIP°PSPSClI,
PIPeP»CHC†P°CHC†Pē P·PjPμPSC€PμPSPSClI PrPsP·Pē, PīC7PsC,PēPīPsPeP°P·P°PSPSClI C,P°
C-PSC,,PsC7PjP°C†C-C7 P· P±PμP·PīPμPePē.

P"°C-C,Pē.

P'PμP·PīPμPeP° P·P°CīC,PsCīCfPIP°PSPSCΠ PīCḡPμPīP°CḡP°C,Cr PŷP°PNēPIPμCḡP±
 PIPēPIC‡P°P»P°CīCḡ CΠPe PīCḡPē PjPsPSPsC,PμCḡP°PīC-C—, C,P°Pe C- PīCḡPē
 CīCfPīCfC,PSCHbPsPjCr P·P°CīC,PsCīCfPIP°PSPSC- P· C-PSCēPēPjPē
 C...C-PjC-PsC,PμCḡP°PīPμPIC,PēC‡PSPēPjPē PīCḡPμPīP°CḡP°C,P°PjPē PrP»CΠ
 P»C-PeCrPIP°PSPSCΠ CḡC-P·PSPēC... C,PēPīC-PI CḡP°PeCr P±C-P»CHCē PSC-P¶ Cr 20000
 PīP°C†C-C''PSC,C-PI, PIPeP»CḡC‡P°CḡC‡Pē 198 PīP°C†C-C''PSC,C-PI, CΠPeC-
 PsC,CḡPēPjCrPIP°P»Pē P»P°PīP°C,PēPSC-P± PI PePsPjP±C-PSP°C†C-C— P·
 PeP°PīPμC†PēC,P°P±C-PSPsPj, 149 PīP°C†C-C''PSC,C-PI, CΠPeC- PsC,CḡPēPjCrPIP°P»Pē
 P»P°PīP°C,PēPSC-P± PI PePsPjP±C-PSP°C†C-C— P· C,CḡP°CīC,CrP·CrPjP°P±PsPj, C,P° 654

PIP°C†C-C"PSC,Pë, CИPеC- PsC,CḡPëPjC†PIP°P»Pë P»P°PiP°C,PëPSC-P± PI
PePsPjP±C-PSP°C†C-C— P· P»PμC,CḡPsP·PsP»PsPj (PrPëPI. CḡPsP·PrC-P»
B«PαP°CḡPjP°PePsP»PsPiC-C†PSC- PIP»P°C†C,PëPIPsC†C,C-B»).

PkP°PNëPiPsCëPëCḡPμPSC-CëPëPjPë PSPμP±P°P¶P°PSPëPjPë CḡPμP°PeC†C-CИPjPë (> 25 %)
PiC-Pr C†P°C† P»C-PeC†PIP°PSPSCИ P»P°PiP°C,PëPSC-P±PsPj P±C†P»Pë CИPIPëC%P° P·
P±PsPeC† CëP»C†PSPePsPIPs-PePëCëPePsPIPsPiPs C,CḡP°PeC,C† (C,P°PeC- CИPe
PrC-P°CḡPμCИ, PSC†PrPsC,P° C,P° P±P»CḡPIP°PSPSCИ) C,P° PIPëC†PëPi. PμCḡPë
P·P°C†C,PsC†C†PIP°PSPSC- P»P°PiP°C,PëPSC-P±C† PI PePsPjP±C-PSP°C†C-C— P·
PeP°PiPμC†PëC,P°P±C-PSPsPj C,P°PePsP¶ C†P°C†C,Ps C†PiPsC†C,PμCḡC-PiP°P»P°C†Cḡ
PrPsP»PsPSPSPs-PiC-PrPsCëPsPIPsP° PμCḡPëC,CḡPsPrPëP·PμC†C,PμP·C-CИ [PμPμP·] (> 25 %).
P§P°C†C,PsC,P° PμPμP· P±C†P»P° PiPsPrC-P±PSPsCḡ PrPs C,P°PePsC— PI PiCḡC†PiP°C...
P·P°C†C,PsC†C†PIP°PSPSCИ P»P°PiP°C,PëPSC-P±C† P· PeP°PiPμC†PëC,P°P±C-PSPsPj C,P°
PeP°PiPμC†PëC,P°P±C-PSC† CИPe PjPsPSPsC,PμCḡP°PiC-C—. P"C-P°CḡPμCИ P±C†P»P°
PSP°PNëP±C-P»CḡCë PiPsCëPëCḡPμPSPsCḡ PSPμP±P°P¶P°PSPsCḡ CḡPμP°PeC†C-C"Cḡ,
CИPeP° PiCḡPëP·PIPsPrPëP»P° PrPs PiCḡPëPiPëPSPμPSPSCИ P»C-PeC†PIP°PSPSCИ, PiCḡPë
P·P°C†C,PsC†C†PIP°PSPSC- P»P°PiP°C,PëPSC-P±C† PI PePsPjP±C-PSP°C†C-C— P·
PeP°PiPμC†PëC,P°P±C-PSPsPj C†Pë P· P»PμC,CḡPsP·PsP»PsPj.

PμCḡPë P·P°C†C,PsC†C†PIP°PSPSC- P»P°PiP°C,PëPSC-P±C† PI PePsPjP±C-PSP°C†C-C— P·
C,CḡP°C†C,C†P·C†PjP°P±PsPj PSPμ P±C†P»Ps P·P°CḡPμC"C†C,CḡPsPIP°PSPs
PrPsPrP°C,PePsPIPëC... PSPμP±P°P¶P°PSPëC... CḡPμP°PeC†C-PNë. P'C†P»P°
PIC-PrP·PSP°C†PμPSP° PiC-PrPIPëC%PμPSP° C†P°C†C,PsC,P° C†PμCḡC†PμPIPsC—
C,PsPeC†PëC†PSPsC†C,C-, P°P»Pμ C†C- CИPIPëC%P° P·P° C...P°CḡP°PeC,PμCḡPsPj C,P°
C,CИP¶PeC-C†C,Cḡ P±C†P»Pë P°PSP°P»PsPiC-C†PSPëPjPë C,PëPj, C%Ps
C†PiPsC†C,PμCḡC-PiP°P»PëC†Cḡ C† PiCḡPsPiCḡP°PjC- PeP»C-PSC-C†PSPëC...
PrPsC†P»C-PrP¶PμPSCḡ P»P°PiP°C,PëPSC-P±C† (PrPëPI. CḡPsP·PrC-P»
B«PhC†PsP±P»PëPIPsC†C,C- P·P°C†C,PsC†C†PIP°PSPSCИB».
PлP°CḡPrC-PsC,PsPeC†PëC†PSC-C†C,Cḡ). P|C- PrP°PSC- P±P°P·C†CḡC,CḡC†CИ PSP°
PμPeC†PiPsP·PëC†C-C— C†C-C"C— PePsPjP±C-PSP°C†C-C— C† 149 PiP°C†C-C"PSC,C-PI PI
PsC†PSPsPIPsPjC† PIPëPiCḡPsP±C†PIP°PSPSC-.

PμPμCḡPμP»C-Pe PiPsP±C-C†PSPëC... CḡPμP°PeC†C-PNë Cž PIPëPiP»CИPrC-
C,P°P±P»PëC†C-

PμPsPIC-PrPsPjP»CИP»PsC†CИ PiCḡPs PSPëP¶C†PμP·P°P·PSP°C†PμPSC- PiPsP±C-C†PSC-
CḡPμP°PeC†C-C—, C%Ps PjP°CḡC,Cḡ PiCḡPëC†PëPSPSPs-PSP°C†P»C-PrPePsPIPëPNë
P·PiBḡ™ CИP·PsPe C-P· P·P°C†C,PsC†C†PIP°PSPSCИPj P»P°PiP°C,PëPSC-P±C† CИPe
PjPsPSPsC,PμCḡP°PiC-C— P°P±Ps P»P°PiP°C,PëPSC-P±C† PI PePsPjP±C-PSP°C†C-C— P·
PeP°PiPμC†PëC,P°P±C-PSPsPj, C,CḡP°C†C,C†P·C†PjP°P±PsPj P°P±Ps P»PμC,CḡPsP·PsP»PsPj.

P—P°C†C,PsC†PsPIC†C"C,CḡC†CИ C,P°PeP° PeP»P°C†PëC,,C-PeP°C†C-CИ C†P°C†C,PsC,Pë
PIPëPSPëPePSPμPSPSCИ PiPsP±C-C†PSPëC... PμC,,PμPeC,C-PI: PrC†P¶Pμ C†P°C†C,C- (³ 1/10);
C†P°C†C,C- (³ 1/100 вḡ" < 1/10); PSPμC†P°C†C,C- (³ 1/1000 вḡ" < 1/100);
PiPsPsPrPëPSPsPeC- (³ 1/10000 вḡ" < 1/1000); CḡC-PrPeC-C†PSC- (< 1/10000);
C†P°C†C,PsC,P° PSPμPIC-PrPsPjP° (C†P°C†C,PsC,P° PSPμ PjPsP¶Pμ P±C†C,Pë
PIC†C,P°PSPsPIP»PμPSP° PSP° PiC-PrC†C,P°PIC- PSP°CИPIPsPëC... PrP°PSPëC...).

PJ PjPμP¶P°C... PePsP¶PSPsC— PiCḡC†PiPë PSPμP±P°P¶P°PSC- CḡPμP°PeC†C-C—
PiCḡPμPrC†C,P°PIP»PμPSPs PI PiPsCḡCИPrPeC† P·PjPμPSCëPμPSPSCИ
C†PμCḡPNëPsP·PSPsC†C,C-.

P_μPsC₇CáC€P_μPSPSC₁₁ P· P±PsPeCá C-PjCáPSPSPsC— CÍPëCÍC,P_μPjPë
P_μPsPsPrPëPSPsPeC-P P_μP°PeC†C-C— PiC-PiP_μC₇C†C†C,P»PëPIPsCÍC,C-,
PIPeP»C₇C†P°C₇C†Pë P°PSP°C,,C-P»P°PeCÍC-C₇ (PrPëPI. C₇PsP·PrC-P»
B«P_μC₇PsC,PëPiPsPeP°P·P°PSPSC₁₁B»)
P_{7b}P_μC,P°P±PsP»C-C†PSC- PiPsC₇CáC€P_μPSPSC₁₁
P"CrP¶P_μ P_{7b}PSPsC₇P_μPeCÍC-C₁₁
C†P°CÍC,C-
P_μCÍPëC...C-C†PSC- PiPsC₇CáC€P_μPSPSC₁₁
*P"CrP¶P_μ P'P_μP·CÍPsPSPSC₁₁**
C†P°CÍC,C-
P_μPsC₇CáC€P_μPSPSC₁₁ P· P±PsPeCá PSP_μC₇PIPsPIPsC— CÍPëCÍC,P_μPjPë
P"CrP¶P_μ P"PsP»PsPIPsPëPN₀ P±C-P»CH^{Б₇}
C†P°CÍC,C-
*P_{7b}P°CÍC,C- P"PsP»PsPIPsPëPN₀ P±C-P»CH**
PŸP_μC₇C†P_μPIPs-CÍCáPrPëPSPSP° CÍPëCÍC,P_μPjP°
P_{7b}P°CÍC,C- P—PSPëP¶P_μPSPSC₁₁ C,,C₇P°PeC†C-C— PIPëPePëPrC† P»C-PIPsPiPs
C€P»C†PSPsC†PeP° (PrPëPI. C₇PsP·PrC-P» B«PŸPiPsCÍC-P±
P·P°CÍC,PsCÍC†PIP°PSPSC₁₁ C,P° PrPsP·PëB» Б₇"
B«P_μC₇PëPiPëPSP_μPSPSC₁₁ PiC₇PëPN₀PsPjC† P°P±Ps
P·PjP_μPSC€P_μPSPSC₁₁ PrPsP·PëB» Б₇" B«P_μPsC₇C†C€P_μPSPSC₁₁ P·
P±PsPeC† CÍP_μC₇C†P_μPIPs-CÍC†PrPëPSPSPsC— CÍPëCÍC,P_μPjPëB»
B C,P° C₇PsP·PrC-P» B«P_{7b}CÍPsP±P»PëPIPsCÍC,C-
P·P°CÍC,PsCÍC†PIP°PSPSC₁₁B»)
P_{7b}P°CÍC,PsC,P° PëP»C†PSPsC†PePsPIC- P°C₇PëC,PjC-C—/ torsades de pointes,
*PSP_μPIC-PrPsPjP° PiPsPrPsPIP¶P_μPSPSC₁₁ C-PSC,P_μC₇PIP°P»C† QT PSP° P·P_{7b}P****
PŸCáPrPëPSPSC- PiPsC₇CáC€P_μPSPSC₁₁
P"CrP¶P_μ P'C-PrC†C†C,C,C₁₁ PiC₇PëPiP»PëPIC-PI^{Б₇}
C†P°CÍC,C-
P"PëC...P°P»CH_{7b}PSP° CÍPëCÍC,P_μPjP°
P"CrP¶P_μ P_{7b}PsCÍPsPIP° PeC₇PsPIPsC,P_μC†P°^{Б₇}, PeP°C€P_μP»CH^{Б₇},
C†P°CÍC,C- P·P°PrPëC€PeP°^{Б₇}
P_{7b}P_μC†P°CÍC,C- P†PSC,P_μC₇CÍC,PëC†C-P°P»CH_{7b}PSC- P·P°C...PIPsC₇C₇PIP°PSPSC₁₁
P»P_μPiP_μPSC_{7b}/PiPSP_μPIPjPsPSC-C,
P_{7b}P°CÍC,PsC,P° P·P_μPiP_μPSP_μPIP° P°C₇C,P_μC₇C-P°P»CH_{7b}PSP°
*PSP_μPIC-PrPsPjP° PiC-PiP_μC₇C,P_μPSP·C-C₁₁***
PŸC_{7b}P°PIPsP° CÍPëCÍC,P_μPjP°
P"CrP¶P_μ P"C-P°C₇P_μC₁₁, C%₀Ps PjPsP¶P_μ CÍPiC₇PëC†PëPSC₁₁C,Pë
C†P°CÍC,C- PrP_μPiC-PrC₇P°C,P°C†C-C₇ (PrPëPI. C₇PsP·PrC-P» B«PŸPiPsCÍC-P±
P·P°CÍC,PsCÍC†PIP°PSPSC₁₁ C,P° PrPsP·PëB» Б₇"
B«P_μC₇PëPiPëPSP_μPSPSC₁₁ PiC₇PëPN₀PsPjC† P°P±Ps
P·PjP_μPSC€P_μPSPSC₁₁ PrPsP·PëB» Б₇" B«P†PSC€C- PiC₇PsC₁₁PIPë
C,PsPeCÍPëC†PSPsCÍC,C- PiC₇P_μPiP°C₇P°C,C†B» C,P° C₇PsP·PrC-P»
B«P_{7b}CÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PsCÍC†PIP°PSPSC₁₁B»),
PSC†PrPsC,P°, P±P»C_{7b}PIP°PSPSC₁₁, PrPëCÍPiP_μPiCÍC-C₁₁,*
CÍC,PsPjP°C,PëC,, P·P°PiPsC₇*, P±C-P»CH PI C€P»C†PSPeC†**
P_{7b}P°CÍC,C- P—P°PiPsC₇^{Б₇}
P"P_μPiP°C,PsP±C-P»C-P°C_{7b}PSP° CÍPëCÍC,P_μPjP°
P_{7b}P°CÍC,C- P"C-PiP_μC₇P±C-P»C-C₇C†P±C-PSP_μPjC-C₁₁,
PiP_μPiP°C,PsC,PsPeCÍPëC†PSC-CÍC,CH (PrPëPI. C₇PsP·PrC-P»
B«P_{7b}CÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PsCÍC†PIP°PSPSC₁₁B»)
PëPeC-C_{7b}P° C,P° PiC-PrC€PeC-C_{7b}PSC- C,PëP°PSPëPSPë

P"CrP¶Pµ C‡P°CÍC,C- P'PëCÍPëPí (PIPeP»CĤC‡P°CĤC‡Pë P°PePSPµC,,PsCĤPjPSPëPNë PrPµCĤPjP°C,PëC,) (PrPëPI. CĤPsP·PrC-P» B«PŸPíPsCÍC-P± P·P°CÍC,PsCÍCíPíP°PSPSCĬ C,P° PrPsP·PëB» BĤ" B«PµCĤPëPíPëPSPµPSPSCĬ PíCĤPëPNëPsPjCí P°P±Ps P·PjPµPSCëPµPSPSCĬ PrPsP·PëB» BĤ" B«P†PSCëC- PíCĤPsCĬPIPë C,PsPeCÍPëC‡PSPsCÍC,C- PíCĤPµPíP°CĤP°C,CíB»), CÍCíC...C-CÍC,CĤ CëPeC-CĤPë*^{БĤ}, PrPsP»PsPSPSPs-PíC-PrPsCëPsPIPSP° PµCĤPëC,CĤPsPrPëP·PµCÍC,PµP·C-CĬ*, P°P»PsPíPµC†C-CĬ^{БĤ}, CÍPIPµCĤP±C-P¶^{БĤ}

PŞP°CÍC,C- PjCĤP°P¶PµPSPSCĬ PSC-PíC,C-PI, PIPeP»CĤC‡P°CĤC‡Pë PíP°CĤP°PSC-C...C-C—; C,CĤC-C%PëPSPë CëPeC-CĤPë PŸPµCĤPNëPsP·PSC- CëPeC-CĤPSC- CĤPµP°PeC†C-C—, PIPeP»CĤC‡P°CĤC‡Pë CÍPëPSPrCĤPsPj PŸC,C-PIPµPSCÍP° BĤ" P"¶PsPSCÍPsPSP° (PŸPŸP") C,P° C,PsPeCÍPëC‡PSPëPNë PµPíC-PrPµCĤPjP°P»CĤPSPëPNë PSPµPeCĤPsP»C-P· (PŸP·PĤ)**

PµC-CÍC,PePsPIPs-PjëĤ™ CĬP·PsPIP° CÍPëCÍC,PµPjP° C,P° CÍPíPsP»C¿C‡PSP° C,PeP°PSPëPSP°

P"CrP¶Pµ C‡P°CÍC,C- P'C-P»CĤ PI PeC-PSC†C-PIPeP°C...^{*БĤ}, P±C-P»CĤ Cí CÍPíPëPSC-*^{БĤ}, P°CĤC,CĤP°P»PíC-CĬ^{БĤ}

P—P°PiP°P»CĤPSC- PíPsCĤC¿CëPµPSPSCĬ

P"CrP¶Pµ C‡P°CÍC,C- PŸP»P°P±PeC-CÍC,CĤ, P·P°PíP°P»PµPSPSCĬ CÍP»PëP·PsPIPsC— PsP±PsP»PsPSPëPë (PjCíPePsP·PëC,)*, P°CÍC,PµPSC-CĬ^{БĤ}

* P|C- PSPµP±P°P¶P°PSC- CĤPµP°PeC†C-C— CÍPíPsCÍC,PµCĤC-PíP°P»PëCÍCĤ PíCĤPë P·P°CÍC,PsCÍCíPíP°PSPSC- P»P°PíP°C,PëPSC-P±Cí PI PePsPjP±C-PSP°C†C-C— P· PeP°PíPµC†PëC,P°P±C-PSPsPj.

^{БĤ} P|C- PSPµP±P°P¶P°PSC- CĤPµP°PeC†C-C— CÍPíPsCÍC,PµCĤC-PíP°P»PëCÍCĤ PíCĤPë P·P°CÍC,PsCÍCíPíP°PSPSC- P»P°PíP°C,PëPSC-P±Cí PI PePsPjP±C-PSP°C†C-C— P· P»PµC,CĤPsP·PsP»PsPj.

** PĤPµP±P°P¶P°PSC- CĤPµP°PeC†C-C—, CĬPeC- P±CíP»Pë PsC,CĤPëPjP°PSC- P·C- CÍPíPsPSC,P°PSPSPëC... PíPsPIC-PrPsPjP»PµPSCĤ C,P° PíCíP±P»C-PeP°C†C-PNë.

PĤPíPëCÍ PsPeCĤPµPjPëC... PSPµP±P°P¶P°PSPëC... CĤPµP°PeC†C-PNë

P—PjPµPSCëPµPSPSCĬ C,,CĤP°PeC†C-C— PIPëPePëPrC¿ P»C-PIPsPíPs CëP»C¿PSPsC‡PeP° C,P° PíPsPrPsPIP¶PµPSPSCĬ C-PSC,PµCĤPIP°P»C¿ QT

P—PSPëP¶PµPSPSCĬ C,,CĤP°PeC†C-C— PIPëPePëPrCí P»C-PIPsPíPs CëP»CíPSPsC‡PeP° (PαP'P>Pë) CÍPíPsCÍC,PµCĤC-PíP°P»PsCÍCĤ PíCĤPëP±P»PëP·PSPs Cí 1 % C...PIPsCĤPëC..., CĬPeC- PsC,CĤPëPjCíPíP°P»Pë P»P°PíP°C,PëPSC-P±, PíCĤPë C†CĤPsPjCí P±C-P»CĤCë PSC-P¶ Cí 70 % PíPµCĤPµP±C-Pí P±CíPI P±PµP·CÍPëPjPíC,PsPjPSPëPj. PŸC,P°PS PíPsP»C-PíCëPëPICÍCĬ P°P±Ps PIC-PrPSPsPIPëPICÍCĬ P±C-P»CĤCë PSC-P¶ PI 70 % PIPëPíP°PrPeC-PI, CÍPµCĤPµPr CĬPePëC... PjP°PNëP¶Pµ Cí 60 % PIPëPíP°PrPeC-PI P·P°CÍC,PsCÍPsPICíPíP°P»Pë P»P°PíP°C,PëPSC-P±, P° PíCĤPëP±P»PëP·PSPs PI 40 % PIPëPíP°PrPeC-PI P·P°CÍC,PsCÍCíPíP°PSPSCĬ P»P°PíP°C,PëPSC-P±Cí P±CíP»Ps PíCĤPsPrPsPIP¶PµPSPµ. PŸPëPjPíC,PsPjP°C,PëC‡PSPµ P·PjPµPSCëPµPSPSCĬ PαP'P>Pë CÍPíPsCÍC,PµCĤC-PíP°P»PsCÍCĬ PI 0,3 % PíP°C†C-C" PSC,C-PI, CĬPeC- PsC,CĤPëPjCíPíP°P»Pë P»P°PíP°C,PëPSC-P± CĬPe PjPsPSPsC,PµCĤP°PíC-CĤ P°P±Ps PI PePsPjP±C-PSP°C†C-C— P· C-PSCëPëPjPë PíCĤPsC,PëCĤP°PePsPIPëPjPë P»C-PeP°CĤCÍCĤPePëPjPë P·P°CÍPsP±P°PjPë. PŸPëPjPíC,PsPjPë PIPeP»CĤC‡P°P»Pë P·P°PrPëCëPeCí, CÍPµCĤC†PµPICí PSPµPrPsCÍC,P°C,PSC-CÍC,CĤ C,P° PíC-PrCÍPëP»PµPSPµ CÍPµCĤC†PµP±PëC,C,CĬ.

P—P°PiP°P»PsPj 58 % P· C†PëC... PïP°C†C—C"°PSC,C—PI, PI C‡PëPëC... PSPµ PIPëPSPëPeP»Ps P¶PsPrPSPëC... C†PëPjPïC,PSPjC—PI, PsPrC†P¶P°P»Pë. P—PjPµPSC€PµPSPSC‡ PαP'P>Pë C†PïPsC†C,PµC‡C—PiP°P»PsC†C‡ C† 2,5 % PïP°C†C—C"°PSC,C—PI, C‡PëC— PsC,C‡PëPjC†PIP°P»Pë P»P°PïP°C,PëPSC—P± PI PePsPjP±C—PSP°C†C—C— P· PeP°PïPµC†PëC,P°P±C—PSPsPj, PïPsC‡C—PIPSC‡PSPs P· 1,0 % PïP°C†C—C"°PSC,C—PI, C‡PëC— PsC,C‡PëPjC†PIP°P»Pë PeP°PïPµC†PëC,P°P±C—PS C‡Pë PjPsPSPsC,PµC‡P°PïC—C‡. P—PjPµPSC€PµPSPSC‡ PαP'P>Pë C†PïPsC†C,PµC‡C—PiP°P»PsC†C‡ C† 3,1 % PïP°C†C—C"°PSC,C—PI, C‡PëC— PsC,C‡PëPjC†PIP°P»Pë P»P°PïP°C,PëPSC—P± PI PePsPjP±C—PSP°C†C—C— P· P»PµC,C‡PSP·PsP»PsPj, PïPsC‡C—PIPSC‡PSPs P· 1,3 % PïP°C†C—C"°PSC,C—PI, C‡PëC— PsC,C‡PëPjC†PIP°P»Pë P»PµC,C‡PSP·PsP» PïP»C‡C† PïP»P°C†PµP±Ps. P—PjPµPSC€PµPSPSC‡ PαP'P>Pë C†PïPsC†C,PµC‡C—PiP°P»PsC†C‡ C† 6,7 % PïP°C†C—C"°PSC,C—PI, C‡PëC— PsC,C‡PëPjC†PIP°P»Pë P»P°PïP°C,PëPSC—P± PI PePsPjP±C—PSP°C†C—C— P· C,C‡P°C†C,C†P·C†PjP°P±PsPj, PïPsC‡C—PIPSC‡PSPs P· 2,1 % PïP°C†C—C"°PSC,C—PI, C‡PëC— PsC,C‡PëPjC†PIP°P»Pë P»P°PïP°C,PëPSC—P± C‡Pë PjPsPSPsC,PµC‡P°PïC—C‡.

PµPsPrPsPIP¶PµPSPSC‡ C—PSC,PµC‡PIP°P»C† QT (PjP°PeC†PëPjP°P»C‡PSPµ C†PµC‡PµPrPSC" ΔΔQTcF 8,75 C†; 90 % P"Pt 4,08, 13,42), P·P°P»PµP¶PSPµ PIC—Pr PePsPSC†PµPSC,C‡P°C†C— PïC‡PµPïP°C‡P°C,C†, P±C†P»Ps PIC—PrP·PSP°C†PµPSPs PI C†PïPµC†C—P°P»C‡PSPsPjC† PrPsC†P»C—PrP¶PµPSPSC— C† PïP°C†C—C"°PSC,C—PI P· PïPsC€PëC‡PµPSPëPjPë C†PsP»C—PrPSPëPjPë PïC†C...P»PëPSP°PjPë (PrPëPI. C‡PSP·PrC—P» B«PhC†PsP±P»PëPIPsC†C,C— P·P°C†C,PSC†C†PIP°PSPSC‡B»).

P"°C—P°C‡PµC‡

P"°C—P°C‡PµC‡ C†PïPsC†C,PµC‡C—PiP°P»P°C†C‡ PïC‡PëP±P»PëP·PSPs C† 65 % PïP°C†C—C"°PSC,C—PI, C‡PëC— PsC,C‡PëPjC†PIP°P»Pë P»P°PïP°C,PëPSC—P± PI PePsPjP±C—PSP°C†C—C— P· PeP°PïPµC†PëC,P°P±C—PSPsPj, C† 64 % PïP°C†C—C"°PSC,C—PI, C‡PëC— PsC,C‡PëPjC†PIP°P»Pë P»P°PïP°C,PëPSC—P± PI PePsPjP±C—PSP°C†C—C— P· P»PµC,C‡PSP·PsP»PsPj, C,P° C† 62 % PïP°C†C—C"°PSC,C—PI, C‡PëC— PsC,C‡PëPjC†PIP°P»Pë P»P°PïP°C,PëPSC—P± PI PePsPjP±C—PSP°C†C—C— P· C,C‡P°C†C,C†P·C†PjP°P±PsPj. P'°C—P»C‡C€C—C†C,C‡ PIPëPïP°PrPeC—PI PrC—P°C‡PµC— PSP°P»PµP¶P°P»Pë PrPs 1—PiPs C†Pë 2—PiPs C†C,C†PïPµPSC‡ C,C‡P¶PePsC†C,C— C,P° PSPµ PïC‡PëP·PIPµP»Pë PrPs PïC‡PëPïPëPSPµPSPSC‡ P»C—PeC†PIP°PSPSC‡ P»P°PïP°C,PëPSC—P±PsPj. P"°C—P°C‡PµC‡ PrPsP±C‡Pµ C‡PµP°PïC†PIP°P»P° PSP° PïC‡PSC,,C—P»P°PeC,PëC†PSPµ P»C—PeC†PIP°PSPSC‡ (PrPëPI. C‡PSP·PrC—P» B«PhC†PsP±P»PëPIPsC†C,C— P·P°C†C,PSC†C†PIP°PSPSC‡B»).

PhPrPSP°Pe PïPsPIC—PrPsPjP»C‡P»PsC†C‡ PïC‡Ps PeC—P»C‡PeP° PIPëPïP°PrPeC—PI PïPsC†C,C‡PSC— PSPëC‡PePsPIPsC— PSPµPrPsC†C,P°C,PSPsC†C,C— PSP° C,,PsPSC— C,C‡P¶PePsC— PrPµPiC—PrC‡P°C,P°C†C—C— PIPSP°C†P»C—PrPsPe PrC—P°C‡PµC—.

P'PëC†PëPï

P'PëC†PëPï C†PïPsC†C,PµC‡C—PiP°PIC†C‡ PïC‡PëP±P»PëP·PSPs C† 28 % PïP°C†C—C"°PSC,C—PI, C‡PëC— PsC,C‡PëPjC†PIP°P»Pë P»P°PïP°C,PëPSC—P± PI PePsPjP±C—PSP°C†C—C— P· PeP°PïPµC†PëC,P°P±C—PSPsPj, C† 45 % PïP°C†C—C"°PSC,C—PI, C‡PëC— PsC,C‡PëPjC†PIP°P»Pë P»P°PïP°C,PëPSC—P± PI PePsPjP±C—PSP°C†C—C— P· P»PµC,C‡PSP·PsP»PsPj, C,P° C† 23 % PïP°C†C—C"°PSC,C—PI, C‡PëC— PsC,C‡PëPjC†PIP°P»Pë P»P°PïP°C,PëPSC—P± PI PePsPjP±C—PSP°C†C—C— P· C,C‡P°C†C,C†P·C†PjP°P±PsPj. P'PëC†PëPï P·P°P·PIPëC†P°Pµ P±C†PI PSPëP·C‡PePsPiPs C†C,C†PïPµPSC‡ C,C‡P¶PePsC†C,C— C— PSPµ PïC‡PëP·PIPsPrPëPI PrPs PïC‡PëPïPëPSPµPSPSC‡ P»C—PeC†PIP°PSPSC‡ P»P°PïP°C,PëPSC—P±PsPj. P·C—PeP°C‡C‡Pj, C‡PëC— PïC‡PëP·PSP°C†P°C‡C,C‡ PïC‡PµPïP°C‡P°C,Pë, C‡PµPePsPjPµPSPPrPsPIP°PSPs PIPëPePsPSC†PIP°C,Pë PsPiP»C‡Pr C€PeC—C‡Pë PïP°C†C—C"°PSC,P° PrPs P»C—PeC†PIP°PSPSC‡ C,P° C‡PµPiC†P»C‡C‡PSPs PïC—Pr C†P°C† P»C—PeC†PIP°PSPSC‡. PµP°C†C—C"°PSC,P°Pj, C†

PIPIP°PεPsPIPεP°.

PμPs 10 P°P±Ps PīPs 12 C,P°P±P»PμC,PsPe Cr P±P»C-CÍC,PμCḡC-; PīPs 7 P±P»C-CÍC,PμCḡC-PI Cr PeP°CḡC,PsPSPSC-PNē PePsCḡPsP±C†C-.

PμPs 70 P°P±Ps 84 C,P°P±P»PμC,PePē Cr C„P»P°PePsPSC-; PīPs 1 C„P»P°PePsPSCr PI PeP°CḡC,PsPSPSC-PNē PePsCḡPsP±C†C-.

PњP°C,PμPiPsCḡC-CЦ PIC-PrPīCrCÍPeCr. P—P° CḡPμC†PμPīC,PsPj.

P’PēCḡPsP±PSPēPe.

PŸP°PSPPrPsP· PŸ.P .P>.

PњC-CÍC†PμP·PSP°C...PsPrP¶PμPSPSCЦ PIPēCḡPsP±PSPēPeP° C,P° P°PrCḡPμCÍP° PjC-CÍC†CЦ PīCḡPsPIP°PrP¶PμPSPSCЦ PNēPsPiPs PrC-CЦP»CHΨSPsCÍC,C-.

P’CrP». P>C-PIPμP·PμPSC-, 7Pђ, 540472, PŸPēCḡPiCr PњCrCḡPμC€, PsPeCḡCrPi PњCrCḡPμC€, P CrPjCrPSC-CЦ.