

Р†РќРЎРЎР РЈРЉРІР†РЇ

$$\begin{array}{c} \text{PrP} \gg \text{CII} \text{ PjP}_{\mu} \text{PrP}^{\text{E}} \text{C} \pm \text{PSPsPiPs} \text{ P} \cdot \text{P}^{\circ} \text{C}^{\text{I}} \text{C}, \text{PsC}^{\text{I}} \text{C}^{\text{r}} \text{PIP}^{\circ} \text{PSPSCII} \text{ P} \gg \text{C} - \text{PeP}^{\circ} \text{C}^{\text{I}} \text{C}^{\text{H}} \text{PePsPiPs} \\ \text{P} \cdot \text{P}^{\circ} \text{C}^{\text{I}} \text{PsP} \pm \text{C}^{\text{r}} \end{array}$$

P P•PḥP“P†PḡPḥ

(REAGILA^{B®})

$$P\check{Y}P\epsilon P\gg P^{\circ}P\Gamma:$$
[illegible]

P''C-CHC≡P° CH₂PMuC≡PsPIPëPSP°: PeP°CH₂PePiCH₂P°P·PePS;

1 PeP°PiCǱCǱP»P° PjC-CǱC,PēC,CH PeP°CǱPePiCǱP°P·PēPSCǱ 1,5 PjPi (CǱ PIPēPiP»CǱPrC-PeP°CǱPePiCǱP°P·PēPSCǱ PiC-PrCǱPsC...P»PsCǱPePrCǱ 1,635 PjPi).

$$P''PsPiPsPjC-P\PSC-C\overline{H}P\mu C\#PsPIP\ddot{e}PSP\ddot{e}:PeC\overline{H}PsC...PjP^{\circ}P\gg CH\ PeC\acute{r}PeC\acute{r}C\overline{H}C\acute{r}PrP\cdot C\overline{I}PSP\ddot{e}PN_0$$

$$PiC\overline{H}P\mu P\P[P\mu P\gg P^{\circ}C,P\ddot{e}PSC-P\cdot PsPIP^{\circ}PSP\ddot{e}PN_0, PjP^{\circ}PiPSC-C\overline{H}\ C\acute{r}C,P\mu P^{\circ}C\overline{H}P^{\circ}C,.$$

P₉P^oPiCfCzP»Pë C,PIPμCTjPrC-: C,PëC,P^oPSCr PrC-PsPeCfPëPr, P• 171; P¶PμP»P^oC,PëPS; C†PsCtjPSPëP»Ps C†PsCtjPSPSPiPs PePsP»CHbPsCtjCr PrP»C¶ PrCtjCrPeCr: P•P^oP»C-P•P^o PsPeCfPëPr C†PsCtjPSPëPNe, P• 172; C€PμP»P^oPe; PμC,P^oPSPSP»; PIPsPrP^o; PiCtjPsPiC-P»PμPSPiP»C-PePsP»CHb; C-P•PsPiCtjPsPiP^oPSPSP»; P±CrC,P^oPSPSP»; P^oPjC-P^oPe PIPsPrPSPëPNe; PeP^oP»C-CT PiC-PrCtjPsPeCfPëPr.

P_LP°PĭCŦCŕP»Pë C,PİPµCŦPrC- PĭPs 3 PjPi

$$P''C-CHC\ddagger P^{\circ} CHP_{\mu}C\ddagger PsPIP\ddot{e}PSP^{\circ}: PeP^{\circ}CHP\ddot{e}P\ddot{i}CHP^{\circ}P\cdot P\ddot{e}PS;$$

1 PeP°PiCíCíP»P° PjC-CíC,PëC,CH PeP°CíPëPiCíP°P·PëPSCí 3 PjPi (Cí PIPëPiP»CíPrC-PeP°CíPëPiCíP°P·PëPSCí PiC-PrCíPSc...P»PsCíPëPrCí 3,270 PjPi).

$P''PsPiPsPjC-P\PSC-C\overline{H}P\mu C\#PsPIP\ddot{e}PSP\ddot{e}$: $PeC\overline{H}PsC...PjP^{\circ}P\gg CH$ $PeC\acute{r}PeC\acute{r}C\overline{H}C\acute{r}PrP\cdot C\overline{I}PSP\ddot{e}PN_0$
 $PiC\overline{H}P\mu P\P P\mu P\gg P^{\circ}C,P\ddot{e}PSC-P\cdot PsPIP^{\circ}PSP\ddot{e}PN_0$, $PjP^{\circ}PiPSC-C\overline{H}$ $C\acute{r}C$, $P\mu P^{\circ}C\overline{H}P^{\circ}C,..$

*P*_h*P*^o*PiCl'CzP*»*Pë C,PIPμCTjPrC-*: *C,PëC,P°PSCr PrC-PsPeCl'PëPr*, *P*• 171; *P¶PμP*»*P°C,PëPS*; *Cl'PiPμC†C-P°P*»*CHbPSPëPNë C‡PμCTjPIPsPSPëPNë PhPÿ*, *P*• 129; *PrC-P°PjP°PSC,PsPIPëPNë Cl'PëPSC-PNë FCF*, *P*• 133; *P·P°P*»*C-P·P° PsPeCl'PëPr P¶PsPIC,PëPNë*, *P*• 172; *C‡PsCTjPSPëP*»*Ps C‡PsCTjPSPsPiPs PePsP*»*CHbPsCTjCr PrP*»*C‡ PrCTjCrPeCr: P·P°P*»*C-P·P° PsPeCl'PëPr C‡PsCTjPSPëPNë*, *P*• 172; *C€PμP*»*P°Pe*; *PμC,P°PSPsP*»; *PIPsPrP°*; *PiCTjPsPiC-P*»*PμPSPiP*»*C-PePsP*»*CHb; C-P·PsPiCTjPsPiP°PSPsP*»; *P±Cr'C,P°PSPsP*»; *P°PjC-P°Pe PIPsPrPSPëPNë; PeP°P*»*C-CT PiC-PrCTjPsPeCl'PëPr*.

РљР°РјСђСђР»Рё С, РІРµСђРґ- РіРѕ 4,5 РјРі

$P''C-CHC\equiv P^{\circ}CH_2P\mu C\equiv PsPIP\ddot{e}PSP^{\circ}:PeP^{\circ}CHPePiCHP^{\circ}P\cdot PePS;$

1 PeP°PiCΓCíP»P° PjC-CΓC,PëC,CH PeP°CḡPëPiCḡP°P·PëPSCí 4,5 PjPi (Cí PIPëPiP»CΠPrC-PeP°CḡPëPiCḡP°P·PëPSCí PiC-PrCḡPsC...P»PsCḡPëPrCí 4,905 PjPi).

P''PsPiPsPjC-P\PSC- CḡPμC#PsPIPëPSPë: PeCḡPsC...PjP°P»CH PeCíPeCíCḡCíPrP·CḡPSPëPNë
PiCḡPμPḡPμP»P°C,PëPSC-P·PsPIP°PSPëPNë, PjP°PiPSC-Cḡ CíC,PμP°CḡP°C,.

PḡP°PiCíCáP»Pë C,PIPμCḡPrC-: C,PëC,P°PSCí PrC-PsPeCíPëPr, P• 171; PḡPμP»P°C,PëPS;
CíPiPμC†C-P°P»CHPSPëPNë C#PμCḡPIPSPSPëPNë PhPŸ, P• 129; PrC-P°PjP°PSC,PsPIPëPNë
CíPëPSC-PNë FCF, P• 133; P·P°P»C-P·P° PsPeCíPëPr PḡPsPIC,PëPNë, P• 172; C#PsCḡPSPëP»Ps
P±C-P»PsPiPs PePsP»CHPsCḡCí PrP»Cḡ PrCḡCíPeCí: PiP»P°P·CíCḡCH
C,,P°CḡPjP°C†PμPIC,PëC#PSP° (CëPμP»P°PeCí CḡPsP·C#PëPS PI PμC,P°PSPsP»C-); C,PëC,P°PSCí
PrC-PsPeCíPëPr, P• 171; C-P·PsPiCḡPsPiP°PSPsP»; P±CíC,P°PSPsP»; P°PjC-P°Pe PIPsPrPSPëPNë;
PiCḡPsPiC-P»PμPSPiP»C-PePsP»CH; CíPëPjPμC,PëPePsPS.

PḡP°PiCíCáP»Pë C,PIPμCḡPrC- PiPs 6 PjPi

P''C-CḡC#P° CḡPμC#PsPIPëPSP°: PeP°CḡPëPiCḡP°P·PëPS;

1 PeP°PiCíCáP»P° PjC-CíC,PëC,CH PeP°CḡPëPiCḡP°P·PëPSCí 6 PjPi (Cí PIPëPiP»CḡPrC-
PeP°CḡPëPiCḡP°P·PëPSCí PiC-PrCḡPsC...P»PsCḡPëPrCí 6,540 PjPi).

P''PsPiPsPjC-P\PSC- CḡPμC#PsPIPëPSPë: PeCḡPsC...PjP°P»CH PeCíPeCíCḡCíPrP·CḡPSPëPNë
PiCḡPμPḡPμP»P°C,PëPSC-P·PsPIP°PSPëPNë, PjP°PiPSC-Cḡ CíC,PμP°CḡP°C,.

PḡP°PiCíCáP»Pë C,PIPμCḡPrC-: C,PëC,P°PSCí PrC-PsPeCíPëPr, P• 171; PḡPμP»P°C,PëPS;
CíPiPμC†C-P°P»CHPSPëPNë C#PμCḡPIPSPSPëPNë PhPŸ, P• 129; PrC-P°PjP°PSC,PsPIPëPNë
CíPëPSC-PNë FCF, P• 133; C#PsCḡPSPëP»Ps C#PsCḡPSPsPiPs PePsP»CHPsCḡCí PrP»Cḡ
PrCḡCíPeCí: P·P°P»C-P·P° PsPeCíPëPr C#PsCḡPSPëPNë, P• 172; CëPμP»P°Pe; PμC,P°PSPsP»;
PIPsPrP°; PiCḡPsPiC-P»PμPSPiP»C-PePsP»CH; C-P·PsPiCḡPsPiP°PSPsP»; P±CíC,P°PSPsP»;
P°PjC-P°Pe PIPsPrPSPëPNë; PeP°P»C-Cḡ PiC-PrCḡPsPeCíPëPr.

P·C-PeP°CḡCíCHPeP° C,,PsCḡPjP°. *PḡP°PiCíCáP»Pë C,PIPμCḡPrC-.*

PhCíPSPsPIPSC- C,,C-P·PëPePs-C...C-PjC-C#PSC- PIP»P°CíC,PëPIPsCíC,C-:

PḡP°PiCíCáP»Pë PiPs 1,5 PjPi. *PŸPIPμCḡPrC- PḡPμP»P°C,PëPSPsPIC- PeP°PiCíCáP»Pë,*
CḡPsP·PjC-Cḡ B,, - 4. PḡCḡPëCëPμC#PeP° PeP°PiCíCáP»Pë Bḡ" P±C-P»P° PSPμPiCḡPsP·PsCḡP°,
PePsCḡPiCíCí PeP°PiCíCáP»Pë Bḡ" P±C-P»PëPNë PSPμPiCḡPsP·PsCḡPëPNë. PkP° PePsCḡPiCíCí
PeP°PiCíCáP»Pë PSP°PSPμCíPμPSPs PSP°PiPëCí B«GR 1.5B» C#PsCḡPSPëPj PePsP»CHPsCḡPsPj.
P'PjC-CíC, PeP°PiCíCáP» Bḡ" PiPsCḡPsCëPsPe P±C-P»PsPiPs P°P±Ps PḡPsPIC,CíPIP°C,Ps-
P±C-P»PsPiPs PePsP»CHPsCḡCí.

PḡP°PiCíCáP»Pë PiPs 3 PjPi. *PŸPIPμCḡPrC- PḡPμP»P°C,PëPSPsPIC- PeP°PiCíCáP»Pë,*
CḡPsP·PjC-Cḡ B,, - 4. PḡCḡPëCëPμC#PeP° PeP°PiCíCáP»Pë Bḡ" P·PμP»PμPSP°
PSPμPiCḡPsP·PsCḡP°, PePsCḡPiCíCí PeP°PiCíCáP»Pë Bḡ" P±C-P»PëPNë
PSPμPiCḡPsP·PsCḡPëPNë. PkP° PePsCḡPiCíCí PeP°PiCíCáP»Pë PSP°PSPμCíPμPSPs PSP°PiPëCí
B«GR 3B» C#PsCḡPSPëPj PePsP»CHPsCḡPsPj. P'PjC-CíC, PeP°PiCíCáP» Bḡ" PiPsCḡPsCëPsPe
P±C-P»PsPiPs P°P±Ps PḡPsPIC,CíPIP°C,Ps-P±C-P»PsPiPs PePsP»CHPsCḡCí.

PḡP°PiCíCáP»Pë PiPs 4,5 PjPi. *PŸPIPμCḡPrC- PḡPμP»P°C,PëPSPsPIC- PeP°PiCíCáP»Pë,*
CḡPsP·PjC-Cḡ B,, - 4. PḡCḡPëCëPμC#PeP° PeP°PiCíCáP»Pë Bḡ" P·PμP»PμPSP°
PSPμPiCḡPsP·PsCḡP°, PePsCḡPiCíCí PeP°PiCíCáP»Pë Bḡ" P·PμP»PμPSPëPNë
PSPμPiCḡPsP·PsCḡPëPNë. PkP° PePsCḡPiCíCí PeP°PiCíCáP»Pë PSP°PSPμCíPμPSPs PSP°PiPëCí
B«GR 4.5B» P±C-P»PëPj PePsP»CHPsCḡPsPj. P'PjC-CíC, PeP°PiCíCáP» Bḡ" PiPsCḡPsCëPsPe

$P \pm C - P \gg PsPiPs$ $P^\circ P \pm Ps$ $P \parallel PsPIC, CrPIP^\circ C, Ps - P \pm C - P \gg PsPiPs$ $PePsP \gg CHPsC\bar{H}C\bar{r}$.

$P_{\bar{b}}P^\circ PiC\bar{r}C\bar{z}P \gg P\bar{e} PiPs$ 6 $PjPi$. $P\bar{y}PIP_{\mu}C\bar{H}PrC - P \parallel P_{\mu}P \gg P^\circ C, P\bar{e}PSPsPIC - PeP^\circ PiC\bar{r}C\bar{r}P \gg P\bar{e}$, $C\bar{H}PsP \cdot PjC - C\bar{H}$ $\bar{b}_{,,}$ - 3. $P_{\bar{b}}C\bar{H}P\bar{e}C\bar{e}P_{\mu}C\bar{z}PeP^\circ$ $PeP^\circ PiC\bar{r}C\bar{r}P \gg P\bar{e} \bar{b}\bar{H}''$ $C_{,,}C - PsP \gg P_{\mu}C, PsPIP^\circ$ $PSP_{\mu}PiC\bar{H}PsP \cdot PsC\bar{H}P^\circ$, $PePsC\bar{H}PiC\bar{r}C\bar{r} PeP^\circ PiC\bar{r}C\bar{r}P \gg P\bar{e} \bar{b}\bar{H}''$ $P \pm C - P \gg P\bar{e}PN_{\bar{e}}$ $PSP_{\mu}PiC\bar{H}PsP \cdot PsC\bar{H}P\bar{e}PN_{\bar{e}}$. $P\bar{k}P^\circ$ $PePsC\bar{H}PiC\bar{r}C\bar{r} PeP^\circ PiC\bar{r}C\bar{r}P \gg P\bar{e} PSP^\circ PSP_{\mu}C\bar{r}P_{\mu}PSPs$ $PSP^\circ PiP\bar{e}C\bar{r}$ $B \ll GR \ 6B \gg$ $C\bar{z}PsC\bar{H}PSP\bar{e}Pj$ $PePsP \gg CHPsC\bar{H}PsPj$. $P'PjC - C\bar{r}C$, $PeP^\circ PiC\bar{r}C\bar{r}P \gg \bar{b}\bar{H}''$ $PiPsC\bar{H}PsC\bar{e}PsPe$ $P \pm C - P \gg PsPiPs$ $P^\circ P \pm Ps$ $P \parallel PsPIC, CrPIP^\circ C, Ps - P \pm C - P \gg PsPiPs$ $PePsP \gg CHPsC\bar{H}C\bar{r}$.

$P\bar{x}P^\circ C\bar{H}PjP^\circ PePsC, P_{\mu}C\bar{H}P^\circ PiP_{\mu}PIC, P\bar{e}C\bar{z}PSP^\circ PiC\bar{H}C\bar{r}PiP^\circ$. $P_{\bar{u}}C\bar{r}P\bar{e}C...PsP \gg P_{\mu}PiC, P\bar{e}C\bar{z}PSC - P \cdot P^\circ C\bar{r}PsP \pm P\bar{e}$, $C - PSC\bar{e}C - P^\circ PSC, P\bar{e}PiC\bar{r}P\bar{e}C...PsC, P\bar{e}C\bar{z}PSC - P \cdot P^\circ C\bar{r}PsP \pm P\bar{e}$.

$P_{\bar{b}}PsPr$ $P\bar{h}P\bar{y}PI^\Gamma$ N05A X15.

$P\bar{x}P^\circ C\bar{H}PjP^\circ PePsP \gg PsPiC - C\bar{z}PSC - PIP \gg P^\circ C\bar{r}C, P\bar{e}PIPsC\bar{r}C, C -$

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

$P_{\bar{b}}P_{\mu}C...P^\circ PSC - P \cdot Pj$ $PrC - C -$

$P_{\bar{b}}P_{\mu}C...P^\circ PSC - P \cdot Pj$ $PrC - C -$ $PeP^\circ C\bar{H}P\bar{e}PiC\bar{H}P^\circ P \cdot P\bar{e}PSC\bar{r}$ $C\%_{\bar{o}}P_{\mu}$ PSP_{μ} $PiPsPIPSC - C\bar{r}C, C\bar{H}$ $PIC - PrPsPjP\bar{e}PN_{\bar{e}}$. $P_{\bar{u}}C\bar{H}PsC, P_{\mu}$ $C, P_{\mu}C\bar{H}P^\circ PiP_{\mu}PIC, P\bar{e}C\bar{z}PSP\bar{e}PN_{\bar{e}}$ $P_{\mu}C_{,,} P_{\mu}PeC$, $PeP^\circ C\bar{H}P\bar{e}PiC\bar{H}P^\circ P \cdot P\bar{e}PSC\bar{r}$ $PjPsP \parallel P_{\mu}$ $PsPiPsC\bar{r}P_{\mu}C\bar{H}P_{\mu}PrPePsPIC\bar{r}PIP^\circ C, P\bar{e}C\bar{r}C\bar{r} C\bar{z}P_{\mu}C\bar{H}P_{\mu}P \cdot$ $PePsPjP \pm C - PSP^\circ C\bar{z}C - C\bar{H}$ $PrC - C -$ $C\bar{z}P^\circ C\bar{r}C, PePsPIPsPiPs$ $P^\circ PiPsPSC - C\bar{r}C, P^\circ$ PSP° $D_3, D_2 -$ $PrPsC_{,,} P^\circ PjC - PSPsPIC - (P \cdot PSP^\circ C\bar{z}P_{\mu}PSPSC\bar{r}$ Ki $PIC - PrPiPsPIC - PrPSPs$ PI $PjP_{\mu}P \parallel P^\circ C...$ $0,085\bar{b}\bar{H}''0,3$ $PSP_{\bar{b}}$ $PiC\bar{H}PsC, P\bar{e}$ $0,49\bar{b}\bar{H}''0,71$ $PSP_{\bar{b}}$) C, P° $5-HT_{1A} - C\bar{r}P_{\mu}C\bar{H}PsC, PsPSC - PSPsPIC -$ $C\bar{H}P_{\mu}C\bar{z}P_{\mu}PiC, PsC\bar{H}P\bar{e}$ $(P \cdot PSP^\circ C\bar{z}P_{\mu}PSPSC\bar{r}$ Ki PI $PjP_{\mu}P \parallel P^\circ C...$ $1,4\bar{b}\bar{H}''2,6$ $PSP_{\bar{b}})$ $C - PrC - C -$ $P^\circ PSC, P^\circ PiPsPSC - C\bar{r}C, P^\circ$ PSP° $5-HT_{2B}, 5-HT_{2A} - C\bar{r}P_{\mu}C\bar{H}PsC, PsPSC - PSPsPIC - C, P^\circ$ $H_1 -$ $PiC - C\bar{r}C, P^\circ PjC - PSPsPIC - C\bar{H}P_{\mu}C\bar{z}P_{\mu}PiC, PsC\bar{H}P\bar{e}$ $(P \cdot PSP^\circ C\bar{z}P_{\mu}PSPSC\bar{r}$ Ki $PIC - PrPiPsPIC - PrPSPs$ PI $PjP_{\mu}P \parallel P^\circ C...$ $0,58\bar{b}\bar{H}''1,1$ $PSP_{\bar{b}}$, $18,8$ $PSP_{\bar{b}}$ C, P° $23,3$ $PSP_{\bar{b}})$. $P_{\bar{b}}P^\circ C\bar{H}P\bar{e}PiC\bar{H}P^\circ P \cdot P\bar{e}PS$ $PjP^\circ C''$ $PSP\bar{e}P \cdot CHPeC\bar{r}$ $P^\circ C_{,,} C - PSPSC - C\bar{r}C, CH$ $C\%_{\bar{o}}PsPrPs$ $5-HT_{2C} - C\bar{r}P_{\mu}C\bar{H}PsC, PsPSC - PSPsPIP\bar{e}C...$ C, P° $\alpha_1 - P^\circ PrC\bar{H}P_{\mu}PSPsC\bar{H}P_{\mu}C\bar{z}P_{\mu}PiC, PsC\bar{H}C - PI$ $(P \cdot PSP^\circ C\bar{z}P_{\mu}PSPSC\bar{r}$ Ki $PIC - PrPiPsPIC - PrPSPs$ 134 $PSP_{\bar{b}}$ C, P° 155 $PSP_{\bar{b}})$. $P_{\bar{b}}P^\circ C\bar{H}P\bar{e}PiC\bar{H}P^\circ P \cdot P\bar{e}PS$ PSP_{μ} $PjP^\circ C''$ $P \cdot PSP^\circ C\bar{z}PSPsC -$ $P^\circ C_{,,} C - PSPSPsC\bar{r}C, C - C\%_{\bar{o}}PsPrPs$ $C...PsP \gg C - PSP_{\mu}C\bar{H}PiC - C\bar{z}PSP\bar{e}C...$ $PjC\bar{r}C\bar{r}PeP^\circ C\bar{H}P\bar{e}PSPsPIP\bar{e}C...$ $C\bar{H}P_{\mu}C\bar{z}P_{\mu}PiC, PsC\bar{H}C - PI$ $(IC_{50} > 1000$ $PSP_{\bar{b}})$. $P''PIP^\circ$ $PsC\bar{r}PSPsPIPSP\bar{e}C...$ $P^\circ PeC, P\bar{e}PIPSP\bar{e}C...$ $PjP_{\mu}C, P^\circ P \pm PsP \gg C - C, P\bar{e} \bar{b}\bar{H}''$ $PrP_{\mu}P \cdot PjP_{\mu}C, P\bar{e}P \gg - PeP^\circ C\bar{H}P\bar{e}PiC\bar{H}P^\circ P \cdot P\bar{e}PS$ C, P° $PrP\bar{e}PrP_{\mu}P \cdot PjP_{\mu}C, P\bar{e}P \gg - PeP^\circ C\bar{H}P\bar{e}PiC\bar{H}P^\circ P \cdot P\bar{e}PS$ $\bar{b}\bar{H}''$ $P \cdot PI\bar{b}\bar{H}''^{\bar{m}}$ $C\bar{r}P \cdot C\bar{r}C\bar{H}C, CHC\bar{r}C\bar{r} P \cdot$ $C\bar{H}P_{\mu}C\bar{z}P_{\mu}PiC, PsC\bar{H}P^\circ PjP\bar{e}$ C, P° $PjP^\circ C\bar{H}C, CH$ $PiC\bar{H}PsC_{,,} C - P \gg CH$ $C_{,,} C\bar{r}PSPeC\bar{z}C - PsPSP^\circ P \gg CHPsPSC - P^\circ PeC, P\bar{e}PIPSPsC\bar{r}C, C - in vitro, P^\circ PSP^\circ P \gg PsPiC - C\bar{z}PSP\bar{e}PN_{\bar{e}}$ $PIP\bar{e}C...C - PrPSC - PN_{\bar{e}}$ $PrC - C\bar{H}C\bar{z}C - PN_{\bar{e}}$ $C\bar{H}P_{\mu}C\bar{z}PsPIP\bar{e}PSC -$.

$P\bar{x}P^\circ C\bar{H}PjP^\circ PePsPrP\bar{e}PSP^\circ PjC - C\bar{z}PSC - P_{\mu}C_{,,} P_{\mu}PeC, P\bar{e}$

$P''PsPeP \gg C - PSC - C\bar{z}PSC - PrPsC\bar{r}P \gg C - PrP \parallel P_{\mu}PSPSC\bar{r}$ $in vivo$ $PiPsPeP^\circ P \cdot C\bar{r}C\bar{H}C, CH$, $C\%_{\bar{o}}Ps$ $PeP^\circ C\bar{H}P\bar{e}PiC\bar{H}P^\circ P \cdot P\bar{e}PS$ $P \cdot PI\bar{b}\bar{H}''^{\bar{m}}$ $C\bar{r}P \cdot C\bar{r}C''C, CHC\bar{r}C\bar{r} P \cdot D_3 - C\bar{H}P_{\mu}C\bar{z}P_{\mu}PiC, PsC\bar{H}P^\circ PjP\bar{e}$ $C, P^\circ PePsC\bar{H}$ $P \parallel PjC - C\bar{H}PsC\bar{H}$, $C\%_{\bar{o}}Ps$ $PN_{\bar{e}}$ $C - P \cdot D_2 - C\bar{H}P_{\mu}C\bar{z}P_{\mu}PiC, PsC\bar{H}P^\circ PjP\bar{e}$ $C\bar{r}$ $C_{,,} P^\circ C\bar{H}PjP^\circ PePsP \gg PsPiC - C\bar{z}PSPs$ $P_{\mu}C_{,,} P_{\mu}PeC, P\bar{e}PIPSP\bar{e}C...$ $PrPsP \cdot P^\circ C....$ $P'P\bar{e}C\bar{r}PIP \gg C\bar{r}P \gg PsC\bar{r}C\bar{r}$ $P \cdot P^\circ P \gg P_{\mu}P \parallel PSP_{\mu}$ $PIC - Pr$ $PrPsP \cdot P\bar{e}$ $P \cdot PI\bar{b}\bar{H}''^{\bar{m}}$ $C\bar{r}P \cdot C\bar{r}PIP^\circ PSPSC\bar{r}$ $P \cdot D_3 - C, P^\circ$ $D_2 -$

PrPsC,,P°PjC-PSPsPIPëPjPë CḡPμC†PμPīC,PsCḡP°PjPë PiPsP»PsPIPSPsPiPs PjPsP·PeCṛ (P·
PīPμCḡPμPIP°P¶PSPëPj P·PIbḡ™CḷP·CṛPIP°PSPSCḷPj PI PrC-P»CḷPSPeP°C... P·
PīC-PrPIPëC%oPμPSPëPj CḡPëPSC,PμP·PsPj D₃) Cṛ PīP°C†C-C"°PSC,C-PI P·
CëPëP·PsC,,CḡPμPSC-C"°Cḡ, CḷPeC- PīCḡPëPμPjP°P»Pë C,PμCḡP°PīPμPIC,PëC†PSC- PrPsP·Pë
PeP°CḡPëPīCḡP°P·PëPSCṛ PīCḡPsC,CḷPiPsPj 15 PrPSC-PI.

P·PīP»PëPI PeP°CḡPëPīCḡP°P·PëPSCṛ PSP° C-PSC,PμCḡPIP°P» QT P±CṛPI PsC†C-PSPμPSPëPμ
Cṛ PīP°C†C-C"°PSC,C-PI C-P· CëPëP·PsC,,CḡPμPSC-C"°Cḡ P°P±Ps CëPëP·PsP°C,,PμPeC,PëPIPSPëPj
CḡPsP·P»P°PrPsPj. P PμP·CṛP»CHbC,P°C,Pë C...PsP»C,PμCḡC-PICḡCHbPePsPiPs
PjPsPSC-C,PsCḡCṛPIP°PSPSCḷ B P·PḡP" B P±CṛP»Pë B P·C-P±CḡP°PSC- B Cṛ B 129
PīP°C†C-C"°PSC,C-PI PīCḡPsC,CḷPiPsPj 12-PiPsPrPëPSPSPsPiPs PīPμCḡC-PsPrCṛ PSP°
PIPëC...C-PrPSPsPjCṛ CḡC-PIPSC- C,P° Cṛ CḡC-PIPSPsPIP°P¶PSPsPjCṛ CḡC,P°PSC-. PJ CḡP°P·C-
PIPëPePsCḡPëCḡC,P°PSPSCḷ CḡCṛP±C,PμCḡP°PīPμPIC,PëC†PSPëC... PrPsP· (9 PjPi/PrPsP±Cṛ
P°P±Ps 18 PjPi/PrPsP±Cṛ) PSPμ P±CṛP»Ps PIC-PrPjC-C†PμPSPs PīPsPrPsPIP¶PμPSPSCḷ
C-PSC,PμCḡPIP°P»Cṛ QT. PJ P¶PsPrPSPsPiPs P· PīP°C†C-C"°PSC,C-PI, CḷPeC-
P»C-PeCṛPIP°P»PëCḡCḷ PeP°CḡPëPīCḡP°P·PëPSPsPj, PSPμ PIC-PrPjC-C†P°P»PsCḡCḷ
PīPsPrPsPIP¶PμPSPSCḷ C-PSC,PμCḡPIP°P»Cṛ QT ≥ 60 PjCḡ PIC-Pr PIPëC...C-PrPSPsPiPs
CḡC-PIPSCḷ, C- P¶PsPrPμPS PīP°C†C-C"°PSC, PSPμ PjP°PI PīPsPrPsPIP¶PμPSPSCḷ
C-PSC,PμCḡPIP°P»Cṛ QT > 500 PjCḡ PīC-Pr C†P°Cḡ PrPsCḡP»C-PrP¶PμPSPSCḷ.

PḡP»C-PSC-C†PSP° PμC,,PμPeC,PëPIPSC-CḡC,CHb C,P° P±PμP·PīPμPeP°

*P·C,,PμPeC,PëPIPSC-CḡC,CHb PīCḡPë PePsCḡPsC,PePsC†P°CḡPSPsPjCḡ
P·P°CḡC,PsCḡCḡPIP°PSPSC-*

P·C,,PμPeC,PëPIPSC-CḡC,CHb PeP°CḡPëPīCḡP°P·PëPSCṛ PI P»C-PeCṛPIP°PSPSC-
PiPsCḡC,CḡPsC— CëPëP·PsC,,CḡPμPSC-C— P±CṛP»P° PIPëPIC†PμPSP° PI C,CḡCHbPsC...
P±P°PīP°C,PsC†PμPSC,CḡPsPIPëC...B B B B PjC-P¶PSP°CḡPsPrPSPëC...B B
B CḡP°PSPrPsPjC-P·PsPIP°PSPëC...B B B PīPsPrPIC-PμPSPsB B B CḡP»C-PīPëC...
B B B PīP»P°C†PμP±PsPePsPSC,CḡPsP»CHbPsPIP°PSPëC...B B B 6-C,PëP¶PSPμPIPëC...
PrPsCḡP»C-PrP¶PμPSPSCḷC..., PI CḷPePëC... P±CḡP°P»Pë CṛC†P°CḡC,CHb 1 754
PīP°C†C-C"°PSC,Pë PIC-PePsPj PIC-Pr 18 PrPs 60 CḡPsPeC-PI. PJ PICḡC-C...
PrPsCḡP»C-PrP¶PμPSPSCḷC... PiPsCḡC,CḡPsC— CëPëP·PsC,,CḡPμPSC-C—
PīPμCḡPIPëPSPSPsCḡ PeC-PSC†PμPIPsCḡ C,PsC†PePsCḡ P±CṛP»P° P·PjC-PSP° PIC-Pr
PIPëC...C-PrPSPsPiPs CḡC-PIPSCḷ PrPs 6 C,PëP¶PSCḷ P·P° P·P°PīP°P»CHbPSPëPjPë
PīPsPeP°P·PSPëPeP°PjPë CëPeP°P»Pë PsC†C-PSPePë PīPsP·PëC,PëPIPSPëC... C,P°
PSPμPīP°C,PëPIPSPëC... CḡPëPjPīC,PsPjC-PI (PANSS), P° PIC,PsCḡPëPSPSPsCḡ
PeC-PSC†PμPIPsCḡ C,PsC†PePsCḡ bḡ" P·PjC-PSP° PIC-Pr PIPëC...C-PrPSPsPiPs CḡC-PIPSCḷ
PrPs 6 C,PëP¶PSCḷ P·P° PīPsPeP°P·PSPëPeP°PjPë CëPeP°P»Pë P·P°PīP°P»CHbPSPsPiPs
PeP»C-PSC-C†PSPsPiPs PICḡP°P¶PμPSPSCḷ PīCḡPs C,CḷP¶PeC-CḡC,CHb
P·P°C...PIPsCḡCHPIP°PSPSCḷ (CGI-S). PJ PjC-P¶PSP°CḡPsPrPSPsPjCṛ
PīP»P°C†PμP±PsPePsPSC,CḡPsP»CHbPsPIP°PSPsPjCṛ PrPsCḡP»C-PrP¶PμPSPSC-, PI CḷPePsPjCṛ
PrP»Cḷ C†CṛC,P»PëPIPsCḡC,C- P°PSP°P»C-P·Cṛ PIPëPePsCḡPëCḡC,PsPICṛPIP°P»PëCḡCḷ
C,,C-PeCḡPsPIP°PSC- PrPsP·Pë 1,5 PjPi, 3,0 PjPi C,P° 4,5 PjPi PeP°CḡPëPīCḡP°P·PëPSCṛ C- 4,0
PjPi CḡPëCḡPīPμCḡPëPrPsPSCṛ, PICḡC- PrPsP·Pë PeP°CḡPëPīCḡP°P·PëPSCṛ C,P°
P°PeC,PëPIPSPëPμ PePsPSC,CḡPsP»CHb PīPsPeP°P·P°P»Pë CḡC,P°C,PëCḡC,PëC†PSPs
PrPsCḡC,PsPIC-CḡPSPμ PīPsPeCḡP°C%oPμPSPSCḷ CḷPe PīPμCḡPIPëPSPSPsC—, C,P°Pe C-
PIC,PsCḡPëPSPSPsC— PeC-PSC†PμPIPëC... C,PsC†PsPe Cṛ PīPsCḡC-PIPSCḷPSPSC- P·
PīP»P°C†PμP±Ps. PJ PjC-P¶PSP°CḡPsPrPSPsPjCṛ
PīP»P°C†PμP±PsPePsPSC,CḡPsP»CHbPsPIP°PSPsPjCṛ PrPsCḡP»C-PrP¶PμPSPSC-, PI CḷPePsPjCṛ
PrP»Cḷ C†CṛC,P»PëPIPsCḡC,C- P°PSP°P»C-P·Cṛ PIPëPePsCḡPëCḡC,PsPICṛPIP°P»PëCḡCḷ
C,,C-PeCḡPsPIP°PSC- PrPsP·Pë 3,0 PjPi C,P° 6,0 PjPi PeP°CḡPëPīCḡP°P·PëPSCṛ C- 10 PjPi

P°CTHPēPiC-PiCTHP°P·PsP»Cf, CŲPe PrPsP·Pē PeP°CTHPēPiCTHP°P·PēPSCf, C,P°Pe C-
P°PeC,PēPIPSPPēPNē PePsPSC,CTHPsP»CH PiPsPeP°P·P°P»Pē CfC,P°C,PēCfC,PēC±PSPs
PrPsCfC,PsPIC-CTHPSPμ PiPsPeCTHP°C%oPμPSPSCŲ PiPμCTHPiPēPSPSPSc— C-
PIC,PsCTHPēPSPSPSc— PeC-PSC†PμPIPēC... C,PsC±PsPe Cf PiPsCTHC-PIPSCLIPSPSC- P·
PiP»P°C†PμP±Ps. PJ C,CTHPμC,CHPsPjCf PjC-P¶PSP°CTHPsPrPSPsPjCf
PiP»P°C†PμP±PsPePsPSC,CTHPsP»CHPsPiP°PSPsPjCf PrPsCfP»C-PrP¶PμPSPSC-, PI CŲPePsPjCf
PrP»CŲ C±CfC,P»PēPIPsCfC,C- P°PSP°P»C-P·Cf PiPēPePsCTHPēCfC,PsPICfPiP°P»PēCfCŲ
C,,C-PeCfPsPiP°PSC-/P°PrP°PiC,PsPiP°PSC- PrPsP·Pē 3,0BĤ"6,0 PjPi C,P° 6,0BĤ"9,0 PjPi
PeP°CTHPēPiCTHP°P·PēPSCf, PsP±PēPrPIC- PiCTHCfPiPē PeP°CTHPēPiCTHP°P·PēPSCf
PiPsPeP°P·P°P»Pē CfC,P°C,PēCfC,PēC±PSPs PrPsCfC,PsPIC-CTHPSPμ PiPsPeCTHP°C%oPμPSPSCŲ
CŲPe PiPμCTHPiPēPSPSPSc—, C,P°Pe C- PIC,PsCTHPēPSPSPSc— PeC-PSC†PμPIPēC... C,PsC±PsPe
Cf PiPsCTHC-PIPSCLIPSPSC- P· PiP»P°C†PμP±Ps.

P PμP·CfP»CHC,P°C,Pē PiPēP·PSP°C†PμPSPSCŲ PiPμCTHPiPēPSPSPSc— PeC-PSC†PμPIPsC—
C,PsC±PePē PμC,,PμPeC,PēPIPSPsCfC,C- PSP°PiPμPrPμPSC- PI C,P°P±P»PēC†C- 1 PSPēP¶C±Pμ.
P PμP·CfP»CHC,P°C,Pē PiPēP·PSP°C†PμPSPSCŲ PIC,PsCTHPēPSPSPSc— PeC-PSC†PμPIPsC—
C,PsC±PePē PμC,,PμPeC,PēPIPSPsCfC,C- (CGI) C,P° PrPsPrP°C,PePsPiPēC... PeC-PSC†PμPIPēC...
C,PsC±PsPe PiC-PrC,PIPμCTHPPrP¶CfPiP°P»Pē PiPμCTHPiPēPSPSCf PeC-PSC†PμPICf C,PsC±PeCf.

PŷP°P±P»PēC†CŲ 1.B B B B P—PjC-PSPē PIC-Pr PiPēC...C-PrPSPsPiPs CTHC-PIPSCLIP PrPs 6
C,PēP¶PSCŲ P·P° P·P°PiP°P»CHPSPēPj PiPsPeP°P·PSPēPePsPj PANSS Cf
PrPsCfP»C-PrP¶PμPSPSCŲC... P·P°PiPsCfC,CTHPμPSPSCŲ C€PēP·PsC,,CTHPμPSC-C— BĤ"
PiCTHCfPiP° ITT.

<i>P'PēC...C-PrPSPēPNē</i>	<i>P—PjC-PSP°</i>	<i>P C-P·PSPēC†CŲ PI</i>	<i>P -</i>
<i>CTHC-PIPμPSCĤ</i>	<i>PŷPμCTHPμPrPSC"</i>	<i>P»C-PeC¿PiP°PSPSC-</i>	<i>P·PSP°C†PμPSPS</i>
<i>PŷPμCTHPμPrPSC"</i>	<i>P·PSP°C†PμPSPSCŲ</i>	<i>PI</i>	<i>CŲ</i>
<i>P·PSP°C†PμPSPSCŲ</i>	<i>LS (PŷPμ)</i>	<i>PiPsCTHC-PIPSCLIPSPS</i>	
<i>B± PŷP'</i>		<i>C- P· PiP»P°C†PμP±Ps</i>	
		<i>(95 % P"P†)</i>	

P—P°PiP°P»CHPSPēPNē PiPsPeP°P·PSPēPe PANSS (MMRM)

P"PsCfP»C-PrP¶PμPSPSCŲ RGH-MD-16 (n = 711)

PμP»P°C†PμP±Ps	97,3 B± 9,22	BĤ"13,29 (1,82)	BĤ"	BĤ"
PľP°CTHPēPiCTHP°P·Pē	97,1 B± 9,13	BĤ"21,27 (1,77)	BĤ"7,97 (BĤ"12,94, BĤ"3,01)	0,0017
PS 1,5 PjPi/PrPsP±Cf			BĤ"8,16 (BĤ"13,09, BĤ"3,22)	0,0013
PľP°CTHPēPiCTHP°P·Pē	97,2 B± 8,66	BĤ"21,45 (1,74)	BĤ"10,48 (BĤ"15,41, BĤ"5,55)	< 0,0001
PS 3 PjPi/PrPsP±Cf	96,7 B± 9,01	BĤ"23,77 (1,74)	BĤ"15,98 (BĤ"20,91, BĤ"11,04)	< 0,0001*
P PēCfPiPμCTHPēPrPsP98,1 B± 9,50		BĤ"29,27 (1,74)		
S 4 PjPi/PrPsP±Cf				

P"PsCfP»C-PrP¶PμPSPSCŲ RGH-MD-04 (n = 604)

PμP»P°C†PμP±Ps	96,5 B± 9,1	BĤ"14,3 (1,5)	BĤ"	BĤ"
PľP°CTHPēPiCTHP°P·Pē	96,1 B± 8,7	BĤ"20,2 (1,5)	BĤ"6,0 (BĤ"10,1, BĤ"1,9)	0,0044
PS 3 PjPi/PrPsP±Cf			BĤ"8,8 (BĤ"12,9, BĤ"4,7)	< 0,0001
PľP°CTHPēPiCTHP°P·Pē	95,7 B± 9,4	BĤ"23,0 (1,5)	BĤ"7,0 (BĤ"11,0, BĤ"2,9)	0,0008*
PS 6 PjPi/PrPsP±Cf	95,6 B± 9,0	BĤ"21,2 (1,4)		
PĤCTHPēPiC-PiCTHP°P·P	95,6 B± 9,0			
sP» 10 PjPi/PrPsP±Cf				

P"PsCfP»C-PrP¶PμPSPSCŲ RGH-MD-05 (n = 439)

PμP»P°C†PμP±Ps	96,6 B± 9,3	BĤ"16,0 (1,6)	BĤ"	BĤ"
PľP°CTHPēPiCTHP°P·Pē	96,3 B± 9,3	BĤ"22,8 (1,6)	BĤ"6,8 (BĤ"11,3, BĤ"2,4)	0,0029
PS				
3BĤ"6 PjPi/PrPsP±Cf				

$P \cdot C$, $P_{\mu}PeC$, $P\ddot{e}PIPSC-C\acute{r}C$, $CH_3PeP^{\circ}C\grave{H}P\ddot{e}P\acute{i}C\grave{H}P^{\circ}P \cdot P\ddot{e}PSC\acute{r}PIP \gg C-PeC\acute{r}PIP^{\circ}PSPSC-$
 $P\acute{i}P_{\mu}C\grave{H}P_{\mu}PIP^{\circ}P \P PSPsPSP_{\mu}PiP^{\circ}C$, $P\ddot{e}PIPSP\ddot{e}C \dots C\acute{r}P\ddot{e}PjPiC$, $PsPjC-PIC \notin P\ddot{e}P \cdot PsC$, $C\grave{H}P_{\mu}PSC-C-$
 $PrPsC\acute{r}P \gg C-PrP \P C\acute{r}PIP^{\circ}P \gg P^{\circ}C\acute{r}C\grave{U}PI26-C$, $P\ddot{e}P \P PSP_{\mu}PIPsPjC\acute{r}$
 $P \pm P^{\circ}PiP^{\circ}C$, $PsC \dagger P_{\mu}PSC$, $C\grave{H}PsPIPsPjC\acute{r}PiPsPrPIC-PM_{\circ}PSPsC\acute{r}P \gg C-P\acute{i}PsPjC\acute{r}PeP \gg C-PSC-C \dagger PSPsPjC\acute{r}$
 $PrPsC\acute{r}P \gg C-PrP \P P_{\mu}PSPSC- P \cdot P^{\circ}PeC$, $P\ddot{e}PIPSP\ddot{e}PjPePsPSC$, $C\grave{H}PsP \gg P_{\mu}Pj$. $P_{\circ}P^{\circ}C\grave{H}P\ddot{e}P\acute{i}C\grave{H}P^{\circ}P \cdot P\ddot{e}PS$
 $(PrC-P^{\circ}PiP^{\circ}P \cdot PsPSPrPsP \cdot 3B\grave{H}^{\circ}4PjPi, C \dagger C-P \gg CH_3PsPIP^{\circ}PrPsP \cdot P^{\circ}4,5PjPi)$
 $PrPsC\acute{r}P \gg C-PrP \P C\acute{r}PIP^{\circ}PIC\acute{r}C\grave{U}C\acute{r}PiPsC\grave{H}C-PIPSC\grave{U}PSPSC- P \cdot C\grave{H}P\ddot{e}C\acute{r}PiP_{\mu}C\grave{H}P\ddot{e}PrPsPSPsPj$
 $(PrC-P^{\circ}PiP^{\circ}P \cdot PsPSPrPsP \cdot 3B\grave{H}^{\circ}6PjPi, C \dagger C-P \gg CH_3PsPIP^{\circ}PrPsP \cdot P^{\circ}4PjPi)C\acute{r}PiP^{\circ}C \dagger C-C^{\circ}PSC, C-PI$
 $C-P \cdot PiP_{\mu}C\grave{H}C\acute{r}P\ddot{e}C\acute{r}C, C\acute{r}PIP^{\circ}P \gg CH_3PSP\ddot{e}PiP\ddot{e}PiP_{\mu}C\grave{H}P_{\mu}PIP^{\circ}P \P PSPsPSP_{\mu}PiP^{\circ}C$, $P\ddot{e}PIPSP\ddot{e}PiP\ddot{e}$

PyP°P±P»PëC†CЦ 2.B B B B PцC-PrCГCрPjPsPe CГPμP·CрP»CHC,P°C,C-PI
PrPsCГP»C-PrP¶PμPSPSCЦ RGH-188-005

$P_{\mu}C-C\Gamma P \gg C\Gamma P \pm P^{\circ}P_iP^{\circ}C, PsPeC\Gamma P^{\circ}C, PSP\ddot{e}C \dots PrPsP \cdot P_jP^{\circ}PeC\Gamma P\ddot{e}P_jP^{\circ}P \gg CH\dot{P}SP^{\circ}$
 $PePsPSC\dot{+}P_{\mu}PSC, C\Gamma P^{\circ}C\dot{+}C-C\Gamma P \quad PeP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PSC\dot{r} \quad C, P^{\circ} \quad P\ddot{N}ePsP_iPs \quad PsC\Gamma PSPsPIPSP\ddot{e}C \dots$
 $P^{\circ}PeC, P\ddot{e}PIPSP\ddot{e}C \dots P_jP_{\mu}C, P^{\circ}P \pm PsP \gg C-C, C-PI \quad C\dot{r} \quad B \quad P_iP \gg P^{\circ}P \cdot P_jC- \quad B \quad PeC\Gamma PsPIC-$
 $B \quad P \cdot P^{\circ}P \cdot PIP\ddot{e}C\dot{+}P^{\circ}P\ddot{N}e \quad B \quad PrPsC\Gamma C\Gamma P_iP^{\circ}C^{\prime\prime}C, CH\dot{C}\Gamma C\Gamma P \quad B \quad P_iC\Gamma P\ddot{e}P \pm P \gg P\ddot{e}P \cdot PSPs \quad B \quad C\dot{+}P_{\mu}C\Gamma P_{\mu}P \cdot$
 $B \quad 3B\dot{H}^{\circ}8 \quad P_iPsPrP\ddot{e}PS \quad P_iC-C\Gamma P \gg C\Gamma P \quad P \cdot P^{\circ}C\Gamma C, PsC\Gamma C\dot{r}PIP^{\circ}PSPSC\Gamma P.$

$P_{\mu}C\Gamma P\ddot{e}P\ddot{N}ePsP_j \quad PsPrPSC-C^{\prime\prime}C- \quad PrPsP \cdot P\ddot{e} \quad PeP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PSC\dot{r} \quad 1,5 \quad P_jP_i \quad C\Gamma P^{\circ}P \cdot PsP_j \quad P \cdot$
 $P_iC\Gamma PsPrC\dot{r}PeC, P^{\circ}P_jP\ddot{e} \quad P \cdot \quad PIP\ddot{e}C\Gamma PsPeP\ddot{e}P_j \quad PIP_jC-C\Gamma C, PsP_j \quad P\parallel P\ddot{e}C\dot{H}C\dot{r} \quad (PIC-Pr \quad 900 \quad PrPs \quad 1 \quad 000$
 $PeP^{\circ}P \gg PsC\dot{H}C-P\ddot{N}e) \quad P \cdot PSP^{\circ}C\dot{+}PSPs \quad PSP_{\mu} \quad PIP_iP \gg P\ddot{e}PIP^{\circ}PI \quad PSP^{\circ} \quad P_iPsPeP^{\circ}P \cdot PSP\ddot{e}Pe \quad C_{max} \quad P^{\circ}P \pm Ps \quad AUC$
 $PeP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PSC\dot{r} \quad (P \cdot PSP^{\circ}C\dot{+}P_{\mu}PSPSC\Gamma P \quad AUC_{0B\dot{H}^{\circ}\infty} \quad P_iC-PrPIP\ddot{e}C\%oC\dot{r}PIP^{\circ}P \gg PsC\Gamma C\Gamma P \quad PSP^{\circ}$
 $12 \%, \quad P \cdot PSP^{\circ}C\dot{+}P_{\mu}PSPSC\Gamma P \quad C_{max} \quad P \cdot PSP\ddot{e}P\parallel C\dot{r}PIP^{\circ}P \gg PsC\Gamma C\Gamma P \quad PSP^{\circ} \quad 5 \%, \quad P_iC\dot{H}P\ddot{e} \quad P_iC\dot{H}P\ddot{e}P\ddot{N}ePsP_jC-$
 $P \gg C-PeP^{\circ}C\Gamma C\dot{H}PePsP_iPs \quad P \cdot P^{\circ}C\Gamma PsP \pm C\dot{r} \quad P_iC-C\Gamma P \gg C\Gamma P \quad C-P\parallel C- \quad PI \quad P_iPsC\dot{H}C-PIPSC\Gamma PSC- \quad P \cdot$
 $P_iC\dot{H}P\ddot{e}P\ddot{N}ePsP_jPsP_j \quad PSP^{\circ}C, C\%oP_{\mu}). \quad P\dot{+}P\parallel P^{\circ} \quad C, P^{\circ}PePsP\parallel \quad P_jP^{\circ}P \gg P^{\circ} \quad P_jC-PSC-P_jP^{\circ}P \gg CH\dot{P}SP\ddot{e}P\ddot{N}e$
 $PIP_iP \gg P\ddot{e}PI \quad PSP^{\circ} \quad P_jP_{\mu}C, P^{\circ}P \pm PsP \gg C-C, P\ddot{e} \quad DCAR \quad C, P^{\circ} \quad DDCAR.$

$P\ddot{N}eP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PS \quad P_jPsP\parallel PSP^{\circ} \quad P \cdot P^{\circ}C\dot{r}C, PsC\dot{r}PsPIC\dot{r}PIP^{\circ}C, P\ddot{e} \quad PSP_{\mu}P \cdot P^{\circ}P \gg P_{\mu}P\parallel PSPs \quad PIC-Pr$
 $P_iC\dot{H}P\ddot{e}P\ddot{N}ePsP_jC\dot{r} \quad C-P\parallel C-.$

P PsP · P_iPsPrC-P»

$P\acute{K}P^{\circ} \quad PsC\Gamma PSPsPIC- \quad P_iPsP_iC\dot{r}P \gg C\Gamma C\dot{+}C-P\ddot{N}ePSPsP_iPs \quad P^{\circ}PSP^{\circ}P \gg C-P \cdot C\dot{r}$
 $C,, P^{\circ}C\dot{H}P_jP^{\circ}PePsPeC-PSP_{\mu}C, P\ddot{e}PeP\ddot{e} \quad C\dot{r}C\Gamma PIPSP\ddot{e}P\ddot{N}e \quad PsP \pm B\dot{H}^{\circ}TM \quad C^{\prime\prime}P_j \quad C\dot{H}PsP \cdot P_iPsPrC-P \gg C\dot{r} \quad (P\dot{H}/P)$
 $C\dot{r}PeP \gg P^{\circ}PrP^{\circ}PI \quad 916 \quad P \gg \quad PrP \gg C\Gamma P \quad PeP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PSC\dot{r}, \quad 475 \quad P \gg \quad PrP \gg C\Gamma P \quad DCAR \quad C, P^{\circ} \quad 1 \quad 568 \quad P \gg$
 $PrP \gg C\Gamma P \quad DDCAR, \quad C\%oPs \quad PIPeP^{\circ}P \cdot C\dot{r}C^{\prime\prime} \quad PSP^{\circ} \quad P \cdot PSP^{\circ}C\dot{+}PSP\ddot{e}P\ddot{N}e \quad C\dot{H}PsP \cdot P_iPsPrC-P \gg$
 $PeP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PSC\dot{r} \quad C, P^{\circ} \quad P\ddot{N}ePsP_iPs \quad PsC\Gamma PSPsPIPSP\ddot{e}C \dots \quad P^{\circ}PeC, P\ddot{e}PIPSP\ddot{e}C \dots$
 $P_jP_{\mu}C, P^{\circ}P \pm PsP \gg C-C, C-PI. \quad P\ddot{N}eP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PS \quad C, P^{\circ} \quad P\ddot{N}ePsP_iPs \quad PsC\Gamma PSPsPIPSC-$
 $P^{\circ}PeC, P\ddot{e}PIPSC- \quad P_jP_{\mu}C, P^{\circ}P \pm PsP \gg C-C, P\ddot{e} \quad P^{\circ}PeC, P\ddot{e}PIPSPs \quad P \cdot P_iB\dot{H}^{\circ}TM \quad C\Gamma P \cdot C\dot{r}C\dot{H}C, CH\dot{C}\Gamma C\Gamma P$
 $(PeP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PS \quad B\dot{H}^{\circ} \quad PSP^{\circ} \quad 96B\dot{H}^{\circ} \quad "97 \%, \quad DCAR \quad B\dot{H}^{\circ} \quad PSP^{\circ} \quad 94B\dot{H}^{\circ} \quad "97 \%, \quad DDCAR \quad B\dot{H}^{\circ} \quad PSP^{\circ}$
 $92B\dot{H}^{\circ} \quad "97 \%) \quad P \cdot \quad P \pm C-P \gg PeP^{\circ}P_jP\ddot{e} \quad P_iP \gg P^{\circ}P \cdot P_jP\ddot{e}.$

P'C-PsC, C_HP^oPSCΓC,, PsC_HP_jP^oC₊C-C₊

$P\dot{H}P_{\mu}C, P^{\circ}P \pm PsP \gg C-P \cdot P_j \quad PeP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PSC\dot{r} \quad PIPeP \gg C\dot{H}C\dot{+}P^{\circ}C^{\prime\prime}$
 $PrP_{\mu}P_jP_{\mu}C, P\ddot{e}P \gg C\dot{H}PIP^{\circ}PSPSC\Gamma P \quad (DCAR \quad C, P^{\circ} \quad DDCAR), \quad P_iC-PrC\dot{H}PsPeC\dot{r}P\ddot{e}P \gg C\dot{H}PIP^{\circ}PSPSC\Gamma P$
 $(P_iC-PrC\dot{H}PsPeC\dot{r}P\ddot{e}Pr \quad PeP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PSC\dot{r}, \quad HCAR) \quad C, P^{\circ} \quad PePsP_jP \pm C-PSP^{\circ}C\dot{+}C-C\dot{H}$
 $PrP_{\mu}P_jP_{\mu}C, P\ddot{e}P \gg C\dot{H}PIP^{\circ}PSPSC\Gamma P \quad C, P^{\circ} \quad P_iC-PrC\dot{H}PsPeC\dot{r}P\ddot{e}P \gg C\dot{H}PIP^{\circ}PSPSC\Gamma P \quad (P_iC-PrC\dot{H}PsPeC\dot{r}P\ddot{e}-$
 $PrP_{\mu}P \cdot P_jP_{\mu}C, P\ddot{e}P \gg -PeP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PS, \quad HDCAR, \quad C, P^{\circ} \quad P_iC-PrC\dot{H}PsPeC\dot{r}P\ddot{e}-$
 $PrP\ddot{e}PrP_{\mu}P \cdot P_jP_{\mu}C, P\ddot{e}P \gg -PeP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PS, \quad HDDCAR). \quad P\acute{K}P^{\circ}PrP^{\circ}P \gg C- \quad P_jP_{\mu}C, P^{\circ}P \pm PsP \gg C-C, P\ddot{e}$
 $HCAR, \quad HDCAR \quad C, P^{\circ} \quad HDDCAR \quad P \pm C-PsC, C\dot{H}P^{\circ}PSC\dot{r}C,, PsC\dot{H}P_jC\dot{r}C\dot{H}C, CH\dot{C}\Gamma C\Gamma P \quad C\dot{r}$
 $PIC-PrP_iPsPIC-PrPSC- \quad PePsPSB\dot{H}^{\circ}TM \quad C\dot{H}P_iP^{\circ}C, P\ddot{e} \quad C\dot{r}C\dot{r}P \gg CH\dot{C}, P^{\circ}C, C\dot{r} \quad C, P^{\circ}$
 $P_iP \gg C\dot{H}PeC\dot{r}C\dot{H}PsPSC-PrC\dot{r}. \quad P^{\prime\prime}PsPrP^{\circ}C, PePsPIP\ddot{e}P\ddot{N}e \quad P_jP_{\mu}C, P^{\circ}P \pm PsP \gg C-C, \quad B\dot{H}^{\circ} \quad PeP\ddot{e}C\dot{r}P \gg PsC, P^{\circ}$
 $PrP_{\mu}C\dot{r}PrP\ddot{e}C \dots P \gg PsC\dot{H}PsC,, P_{\mu}PSC-P \gg C\dot{r}-P_iC-P_iP_{\mu}C\dot{H}P^{\circ}P \cdot P\ddot{e}PSC\dot{r}-PeP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PSC\dot{r}$
 $(DDCPPCAR) \quad B\dot{H}^{\circ} \quad C\dot{r}C, PIPsC\dot{H}C\dot{H}C^{\prime\prime}C, CH\dot{C}\Gamma C\Gamma P \quad PI \quad P_iC\dot{H}PsC\dot{+}P_{\mu}C\dot{r}C-$
 $PrP_{\mu}P \cdot P^{\circ}P \gg PeC-P \gg C\dot{r}PIP^{\circ}PSPSC\Gamma P \quad C, P^{\circ} \quad PSP^{\circ}C\dot{r}C, C\dot{r}PIPSPsP_iPs \quad PsPeP\ddot{e}C\dot{r}PSP_{\mu}PSPSC\Gamma P$
 $PeP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PSC\dot{r}.$

$P\ddot{N}eP^{\circ}C\Gamma P\ddot{e}P_iC\Gamma P^{\circ}P \cdot P\ddot{e}PS \quad P_jP_{\mu}C, P^{\circ}P \pm PsP \gg C-P \cdot C\dot{r}C^{\prime\prime}C, CH\dot{C}\Gamma C\Gamma P \quad CYP3A4 \quad C, P^{\circ} \quad P_jP_{\mu}PSC\epsilon PsC\dot{H}$
 $P_jC-C\dot{H}PsC\dot{H} \quad CYP2D6 \quad PrPs \quad DCAR \quad C, P^{\circ} \quad HCAR. \quad P\acute{K}P^{\circ}PrP^{\circ}P \gg C- \quad DCAR$
 $P_jP_{\mu}C, P^{\circ}P \pm PsP \gg C-P \cdot C\dot{r}C^{\prime\prime}C, CH\dot{C}\Gamma C\Gamma P \quad CYP3A4 \quad C, P^{\circ} \quad P_jP_{\mu}PSC\epsilon PsC\dot{H} \quad P_jC-C\dot{H}PsC\dot{H} \quad CYP2D6 \quad PrPs$
 $DDCAR \quad C, P^{\circ} \quad HDCAR. \quad P_{\mu}PsC, C-P_j \quad DDCAR \quad P_jP_{\mu}C, P^{\circ}P \pm PsP \gg C-P \cdot C\dot{r}C^{\prime\prime}C, CH\dot{C}\Gamma C\Gamma P \quad P \cdot P^{\circ}$
 $PrPsP_iPsP_jPsP_iPsC\dot{H} \quad CYP3A4 \quad PrPs \quad HDDCAR.$

[illegible]

PhPeC₇H₇P_μPjC- PiC₇H₇PiP_ē PiP°C†C-C''PSC,C-PI

PμPsC₇H₇CzC€PμPSPSC† C,,CzPSPeC†C-C— PSPēC₇H₇PsPe

PμPsPiC†P»C†C†C-PM_ēPSPμ C,,P°C₇H₇PjP°PePsPeC-PSPμC,PēC†PSPμ PjPsPrPμP»C₇H₇PIP°PSPSC† PIPēPePsPSC†PIP°P»PsC†C†C P· PIPēPePsC₇H₇PēC†C,P°PSPSC†Pj PrP°PSPēC... PIC-Pr PiP°C†C-C''PSC,C-PI, C†PeC- P±C†P»Pē P·P°P»C†C†PμPSC- PrPs PeP»C-PSC-C†PSPsPiPs PrPsC†P»C-PrP¶PμPSPSC† C†C,PSC†PsPIPS P»C-PeC†PIP°PSPSC† C€PēP·PsC,,C₇H₇PμPSC-C— PeP°C₇H₇PēPiC₇H₇P°P·PēPSPsPj, P· C₇H₇-P·PSPēPjPē PiPsPeP°P·PSPēPeP°PjPē C,,C†PSPeC†C-C— PSPēC₇H₇PsPe, PIPeP»C₇H₇C†PSPs P· PSPsC₇H₇PjP°P»C₇H₇PSPsC₇ C,,C†PSPeC†C-C₇ PSPēC₇H₇PsPe (PeP»C-C₇H₇PμPSC† PeC₇H₇PμP°C,PēPSC-PSC† (CrCl) ≥ 90 PjP»/C...PI) C- PiPsC₇H₇C€PμPSPSC†PjPē C,,C†PSPeC†C-C— PSPēC₇H₇PsPe P»PμPiPePsPiPs (CrCl 60B₇"89 PjP»/C...PI) C,P° C†PμC₇H₇PμPrPSC₇H₇PsPiPs C†C,C†PiPμPSC† C,C†P¶PePsC†C,C- (CrCl 30B₇"59 PjP»/C...PI). P₇H-C-P¶ PeP»C-C₇H₇PμPSC†PsPj PeP°C₇H₇PēPiC₇H₇P°P·PēPSC† PI PiP°P°P·PjC- C,P° PeP»C-C₇H₇PμPSC†PsPj PeC₇H₇PμP°C,PēPSC-PSC† PSPμ P±C†P»Ps P·PSP°PM_ēPrPμPSPs P¶PsPrPSPēC... C-C†C,PsC,PSPēC... P·PIB₇TM C†P·PeC-PI.

P''C-C† PeP°C₇H₇PēPiC₇H₇P°P·PēPSC† PSPμ PsC†C-PSC₇H₇PIP°P»P°C†C†C C† PiP°C†C-C''PSC,C-PI C-P· C,C†P¶PePēPjPē (CrCl < 30 PjP»/C...PI) PiPsC₇H₇C€PμPSPSC†PjPē C,,C†PSPeC†C-C— PSPēC₇H₇PsPe (PrPēPI. C₇H₇PsP·PrC-P» B«PŸPiPsC†C-P± P·P°C†C,PSC†C†PIP°PSPSC† C,P° PrPsP·PēB»).

PμPsC₇H₇CzC€PμPSPSC† C,,CzPSPeC†C-C— PiPμC†C-PSPePē

P''PsC†P»C-PrP¶PμPSPSC† PI PrPIPsC... C†P°C†C,PēPSP°C... (PsPrPSPsPeC₇H₇P°C,PSP° PrPsP·P° PeP°C₇H₇PēPiC₇H₇P°P·PēPSC† 1 PjPi [C†P°C†C,PēPSP° P₇] C,P° PeP°C₇H₇PēPiC₇H₇P°P·PēPS C† PrPsP±PsPIC-PM_ē PrPsP·C- 0,5 PjPi PiC₇H₇PsC,C†PiPsPj 14 PrPSC-PI [C†P°C†C,PēPSP° P']) PiC₇H₇PsIPsPrPēP»PsC†C†C P·P° C†C†P°C†C,C₇H₇ PiP°C†C-C''PSC,C-PI P· C₇H₇-P·PSPēPjPē C†C,C†PiPμPSC†PjPē PiPsC₇H₇C†C€PμPSC₇H₇ C,,C†PSPeC†C-C— PiPμC†C-PSPePē (PeP»P°C†Pē P₇ C,P° P' P·P° P₇SP°PM_ēP»PrPsPj B₇" PμB₇TM C₇H₇). PμC-C†P»C†C P·P°C†C,PSC†C†PIP°PSPSC† PsPrPSPsPeC₇H₇P°C,PSPsC— PrPsP·Pē PeP°C₇H₇PēPiC₇H₇P°P·PēPSC† 1 PjPi P°P±Ps PiC₇H₇PēPM_ēPsPjC† 0,5 PjPi PeP°C₇H₇PēPiC₇H₇P°P·PēPSC† PiC₇H₇PsC,C†PiPsPj 14 PrPSC-PI PiP°C†C-C''PSC,Pē P· PiPsC₇H₇C€PμPSPSC†PjPē C,,C†PSPeC†C-C— PiPμC†C-PSPePē P»PμPiPePsPiPs C†Pē C†PμC₇H₇PμPrPSC₇H₇PsPiPs C†C,C†PiPμPSC† C† PiPsC₇H₇-PIPSC†PSPSC- B P· PiP°C†C-C''PSC,P°PjPē P· PSPsC₇H₇PjP°P»C₇H₇PSPsC₇ C,,C†PSPeC†C-C''C₇H₇ PiPμC†C-PSPePē PjP°P»Pē PiC₇H₇PēP±P»PēP·PSPs PSP° 25 % PIPēC%₀C† PePsPSC†PμPSC,C₇H₇P°C†C-C₇H₇ PeP°C₇H₇PēPiC₇H₇P°P·PēPSC† (C_{max} C,P° AUC) C,P° PiC₇H₇PēP±P»PēP·PSPs PSP° 45 % PSPēP¶C†C† PePsPSC†PμPSC,C₇H₇P°C†C-C₇H₇ PsC†PSPsPIPS PēC... P°PeC,PēPIPS PēC... PjPμC,P°P±PsP»C-C,C-PI, PrPμP·PjPμC,PēP»-PeP°C₇H₇PēPiC₇H₇P°P·PēPSC† C,P° PrPēPrPμP·PjPμC,PēP»-PeP°C₇H₇PēPiC₇H₇P°P·PēPSC†.

PμC-C†P»C†C P±P°PiP°C,PSC₇H₇P°P·PsPIPsPiPs PiC₇H₇PēPM_ēPsPjC† PeP°C₇H₇PēPiC₇H₇P°P·PēPSC† PePsPSC†PμPSC,C₇H₇P°C†C-C†C P·P°PiP°P»C₇H₇PSPsPiPs P°PeC,PēPIPS PiPs PePsPjPiPsPSPμPSC,P° (CAR DCAR DD CAR) (AUC C,P° C_{max}) C† PiPsC₇H₇-PIPSC†PSPSC- B P· PIC-PrPiPsPIC-PrPSPēPj PiPsPeP°P·PSPēPePsPj C†B PiP°C†C-C''PSC,C-PI P· PSPsC₇H₇PjP°P»C₇H₇PSPsC₇ C,,C†PSPeC†C-C''C₇H₇ PiPμC†C-PSPePē P·PSPēP·PēP»P°C†C†C PSP° 21B₇"22 % C,P° 13B₇"15 % PIC-PrPiPsPIC-PrPSPs C† B PiP°C†C-C''PSC,C-PI P· PiPsC₇H₇C€PμPSPSC†Pj C,,C†PSPeC†C-C— PiPμC†C-PSPePē (PμPαPμ) P»PμPiPePsPiPs C†Pē C†PμC₇H₇PμPrPSC₇H₇PsPiPs C†C,C†PiPμPSC† C,C†P¶PePsC†C,C-, C†PeC%₀Ps PIC₇H₇P°C...PsPIC†PIP°P»PēC†C†C PSPμP·PIB₇TM C†P·P°PSC- P·PIB₇TM C†P·P°PSC- PePsPSC†PμPSC,C₇H₇P°C†C-C—, B C,PSPrC- C†Pe PrP»C†C PSPμP·PIB₇TM C†P·P°PSPsPiPs P·P°PiP°P»C₇H₇PSPsPiPs PePsPjPiPsPSPμPSC,P° P±C†P»Ps C₇H₇PsP·C₇H₇P°C...PsPIP°PSPs P·PSPēP¶PμPSPSC† PSP° 12B₇"13 % C,P° PiC-PrPIPēC%₀PμPSPSC† PSP° 20B₇"25 %

PIC-PrPⁱPsPIC-PrPSPs B Cr PⁱP^oC†C-C''PSC,C-PI P· P_uP_αP_u P»P_uP_iPePsPiPs C,P^o
C†P_uC†P_uPrPSC_HPsPiPs C†C,CrP_iP_uPSC† C,C†P_uP_uPePsC†C,C-.

P''C-C† P_eP^oC†P_eP_iC†P^oP·P_ePSC† PSP_u PsC†C-PSC†P^oP»P^oC†C† Cr PⁱP^oC†C-C''PSC,C-PI C-P·
C,C†P_uP_uPeP_eP_jP_e (PeP»P^oC† P_uP^o P_uP^oPN_eP»PrPsP_j B† P_uB†TM C†) P_iPsC†C†C†P_uPSPSC†P_jP_e
C,,C†PSPeC†C-C— P_iP_uC†C-PSPeP_e (PrP_ePI. C†PsP·PrC-P» B«P_uP_iPsC†C-P±
P·P^oC†C,PsC†C†P^oPSPSC† C,P^o PrPsP·P_eB»).

P'C-Pe, C†C,P^oC,C† C,P^o C†P^oC†P^o

P_j P_iPsP_iC†P»C†C†C-PN_ePSPsP_jC† C,,P^oC†P_jP^oPePsPeC-PSP_uC,P_eC†PSPsP_jC† P^oPSP^oP»C-P·C-
PSP_u P±C†P»Ps PeP»C-PSC-C†PSPs P·PSP^oC†P_eP_jP_eC... PIC-PrP_jC-PSPSPsC†C,P_uPN_e Cr
PⁱP^oC†P^oP_jP_uC,C†P^oC... C,,P^oC†P_jP^oPePsPeC-PSP_uC,P_ePeP_e (AUC C,P^o C_{max}B
PeP^oC†P_eP_iC†P^oP·P_ePSC† C,P^o PN_ePsPiPs PsC†PSPsPIPSP_eC... P^oPeC,P_ePIPSP_eC...
P_jP_uC,P^oP±PsP»C-C,C-PI) P·P^oP»P_uP_uPSPs PIC-Pr PIC-PeC†, C†C,P^oC,C- C,P^o C†P^oC†P_e
PⁱP^oC†C-C''PSC,C-PI. P_uC-Pr C†P^oC† P^oPSP^oP»C-P·C† B B PIP_ePIC†P^oP»P_e B PrP^oPSC-
B C₀₀PsPrPs B 2 844 PⁱP^oC†C-C''PSC,C-PI C†C-P·PSP_eC... C†P^oC†, P· C†P_ePeC... 536
PⁱP^oC†C-C''PSC,C-PI P±C†P»P_e PIC-PePsP_j PIC-Pr 50 PrPs 65 C†PsPeC-PI, 933 PsC†PsP±P_e
P±C†P»P_e P_uC-PSPeP^oP_jP_e (PrP_ePI. C†PsP·PrC-P» B«P_uP_iPsC†C-P± P·P^oC†C,PsC†C†P^oPSPSC†
C,P^o PrPsP·P_eB»). P''P^oPSC- C₀₀PsPrPs PⁱP^oC†C-C''PSC,C-PI P»C-C,PSC_HPsPiPs PIC-PeC†
(P_iPsPSP^oPr 65 C†PsPeC-PI) PsP±P_jP_uP_uPSC-.

P_uP^oP»C-PSPSC†

P_uP_uC†P_uP· C,P_u, C₀₀Ps PeP^oC†P_eP_iC†P^oP·P_ePS PSP_u C'' C†C†P±C†C,C†P^oC,PsP_j PrP»C†
CYP1A2, PSP_u PsC†C-PeC†C''C,C†C†C† PIP_iP»P_ePIC† PⁱP^oP»C-PSPSC† PSP^o
C,,P^oC†P_jP^oPePsPeC-PSP_uC,P_ePeC† PeP^oC†P_eP_iC†P^oP·P_ePSC†.

P_uPsC,P_uPSC†C-PN_ePSP_ePN_e PIP_iP»P_ePI PeP^oC†P_eP_iC†P^oP·P_ePSC† PSP^o C-PSC†C-
P_iC†P_uPⁱP^oC†P^oC,P_e

P_uP^oC†P_eP_iC†P^oP·P_ePS C,P^o PN_ePsPiPs PsC†PSPsPIPSC- P^oPeC,P_ePIPSC- P_jP_uC,P^oP±PsP»C-C,P_e
PSP_u C-PSP_rC†PeC†P^oP»P_e P_uPSP·P_eP_jP_e CYP1A2, CYP2B6 C,P^o CYP3A4 C- PSP_u P±C†P»P_e
C-PSPiC-P±C-C,PsC†P^oP_jP_e CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP219, CYP2D6,
CYP2E1 C,P^o CYP3A4 *in vitro*. P_uP^oC†P_eP_iC†P^oP·P_ePS C,P^o PN_ePsPiPs PsC†PSPsPIPSC-
P^oPeC,P_ePIPSC- P_jP_uC,P^oP±PsP»C-C,P_e PSP_u C'' C-PSPiC-P±C-C,PsC†P^oP_jP_e
C,C†P^oPSC†P_iPsC†C,PSP_eC... P±C-P»PeC-PI OATP1B1, OATP1B3, BCRP,
PsC†P_iP^oPSC-C†PSPsPiPs PeP^oC,C-PsPSPSPsPiPs C,C†P^oPSC†P_iPsC†C,PSPsPiPs P±C-P»PeP^o 2
(OCT2) C,P^o PsC†P_iP^oPSC-C†PSP_eC... P^oPSC-PsPSPSP_eC... C,C†P^oPSC†P_iPsC†C,PSP_eC...
P±C-P»PeC-PI 1 C,P^o 3 (OAT1 C,P^o OAT3) *in vitro*. DCAR C,P^o DDCAR PSP_u P±C†P»P_e
C-PSPiC-P±C-C,PsC†P^oP_jP_e C,C†P^oPSC†P_iPsC†C,PSPsPiPs P±C-P»PeP^o P-gp, C...PsC†P^o
PeP^oC†P_eP_iC†P^oP·P_ePS P±C†PI C-PSPiC-P±C-C,PsC†PsP_j P-gp PI PeP_eC†P_uC†PSP_ePeC† (PrP_ePI.
C†PsP·PrC-P» B«P·P·P^oC''P_jPsPrC-C† P· C-PSC†P_eP_jP_e P»C-PeP^oC†C†C†PeP_eP_jP_e
P·P^oC†PsP±P^oP_jP_e C,P^o C-PSC†C- PIP_ePrP_e PIP·P^oC''P_jPsPrC-PN_eB»).

P''P^oPSC- PrPsPeP»C-PSC-C†PSP_eC... PrPsC†P»C-PrP_uP_uPSC_H P· P±P_uP·P_iP_uPeP_e

P_uP^oC†P_eP_iC†P^oP·P_ePS C†P_iC†P_eC†P_ePSC†PI PrPIP_sC†C,PsC†PsPSPSC† PeP^oC,P^oC†P^oPeC,C†
C,P^o PIC,PsC†P_ePSPSC- P·P_jC-PSP_e C†C-C,PeC-PIPeP_e (PIC-PrC†P^oC†P^oPSPSC† C,P^o
PeC-C†C,PsPiPsPrC-P±PSC† PrP_uP_iP_uPSP_uC†C-C† C†C-C,PeC-PIPeP_e) Cr C†PsP±P^oPe.
P—P^oP_iP^oP»C†PSP^o P_uPeC†P_iPsP·P_eC†C-C† (AUC) PeP^oC†P_eP_iC†P^oP·P_ePSC†,
B PrPsC†C†P_iPSC†C,P^o P_iC†P_e P·P^oC†C,PsC†C†P^oPSPSC- P_jP^oPeC†P_eP_jP^oP»C†PSPsC—

PrPsP·Pë, C%Ps PSPµ PīCḡPëP·PIPsPrPëC,CH PrPs CḡPsP·PIPëC,PeCí CĪPIPSPëC...
PSPµP±P°P¶P°PSPëC... PµC,,PµPeC,C-PI (NOAEL) P·P±PsPeCí PsCḡPiP°PSC-PI P·PsCḡCí, Cí 4,2
CḡP°P·P° PīPµCḡPµPIPëC%CrC” PeP»C-PSC-C±PSCí AUC PīCḡPë PjP°PeCíPëPjP°P»CHPSC-PNë
CḡPµPePsPjPµPSPPrPsPIP°PSC-PNë PrPsP·C- PrP»CĪ P»CḡPrPëPSPë (PḡP P”P) 6 PjPi PSP°
PrPsP±Cí. P—P±C-P»CHCëPµPSPSCĪ C±P°CíC,PsC,Pë
PrPµPiPµPSPµCḡP°C†C-C—/P°C,CḡPsC,,C-C— CíC-C,PeC-PIPePë
CíPiPsCíC,PµCḡC-PiP°P»PsCíCĪ Cí C%CrCḡC-PI-P°P»CHP±C-PSPsCíC-PI Cí 2-
CḡC-C±PSPsPjCí PrPsCíP»C-PrP¶PµPSPSC- PSP° C,P»C- PeP»C-PSC-C±PSPs
P·PSP°C±CíC%PsC— PµPeCíPiPsP·PëC†C-C— PīCḡPµPiP°CḡP°C,Cí.

PαPsCíC,,PsP»C-PīC-PrPsP· CíPiPsCíC,PµCḡC-PiP°PICíCĪ Cí P»PµPiPµPSCĪC... C%CrCḡC-PI,
CíPsP±P°Pe C,P° PjPëCëPµPNë (P·P·P°PiP°P»PµPSPSCĪPj P°P±Ps P±PµP· PSCḡPsPiPs) C,P° Cí
PePsCḡC- PSP°PrPSPëCḡPePsPIPëC... P·P°P»PsP· CíPsP±P°Pe PSP° C,,PsPSC-
PeP»C-PSC-C±PSPs P·PSP°C±CíC%PëC... PµPeCíPiPsP·PëC†C-PNë PīCḡPµPiP°CḡP°C,Cí.
PŸPiPsCíC,PµCḡC-PiP°P»PsCíCĪ P·P°PiP°P»PµPSPSCĪ P»PµPiPµPSCḡ Cí CíPsP±P°Pe, CĪPeC-
PsC,CḡPëPjCíPiP°P»Pë PeP°CḡPëPīCḡP°P·PëPS PīCḡPsC,CĪPiPsPj 1 CḡPsPeCí, PīCḡPë
C†CHPsPjCí NOAEL C,P° PIC-PrPiPsPIC-PrPSC- PiPsPeP°P·PSPëPePë AUC
PīPµCḡPµPIPëC%CrPiP°P»Pë B C,P°PeC- Cí CḡP°P·C- P·P°CíC,PsCíCíPiP°PSPSCĪB PḡP P”P>
Cí 2,7 (CíP°PjC†C-) C,P° 1,7 (CíP°PjPePë) CḡP°P·P°. KóP°PīCḡPëPeC-PSC†C- 2-
PjC-CíCĪC±PSPsPiPs PīPµCḡC-PsPrCí P±PµP· PīCḡPëPNëPsPjCí PīCḡPµPiP°CḡP°C,Cí PīCḡPë
PµPeCíPiPsP·PëC†C-C—, CĪPeP° PI 4,2 CḡP°P·P° B PīPµCḡPµPIPëC%CrC” PeP»C-PSC-C±PSCí
PµPeCíPiPsP·PëC†C-CḡB PīCḡPë PḡP P”P>, P·P°PiP°P»PµPSPSCĪ PSPµ
CíPiPsCíC,PµCḡC-PiP°P»PsCíCĪ; PīCḡPsC,Pµ P·P°PiP°P»PµPSPSCĪ P·P±PµCḡC-PiP°P»PsCíCĪ
PīCḡPë P±C-P»CHCë PIPëCíPsPePëC... PrPsP·P°C....

P”C-PīPµCḡC,CḡPsC,,C-CĪ PePsCḡPë PSP°PrPSPëCḡPePsPIPëC... P·P°P»PsP·
CíPiPsCíC,PµCḡC-PiP°P»P°CíCĪ PSP° C,P»C- PePsPSC†PµPSC,CḡP°C†C-C—
PīCḡPµPiP°CḡP°C,Cí, C%Ps PI 4,1 CḡP°P·P° PīPµCḡPµPIPëC%CrC” B C,P°PeCí PīCḡPë
P·P°CíC,PsCíCíPiP°PSPSC- PḡP P”P>, Cí C%CrCḡC-PI (C,C-P»CHPePë Cí CíP°PjPsPe) C,P°
PīCḡPë PeP»C-PSC-C±PSPs P·PSP°C±CíC%PëC... P·P°PiP°P»CHPSPëC...
PePsPSC†PµPSC,CḡP°C†C-CĪC... PeP°CḡPëPīCḡP°P·PëPSCí PI PīP»P°P·PjC- Cí PjPëCëPµPNë. Pj
CíPsP±P°Pe CíPiPsCíC,PµCḡC-PiP°P»P°CíCĪ PsP±PsCḡPsC,PSP°
PiC-PīPµCḡC,CḡPsC,,C-CĪ/PiC-PīPµCḡPiP°P°P·C-CĪ C,P°
PiP°PeCíPsP»C-P·P°C†C-CĪ/PIPµP·PëPeCíP»CĪC†C-CĪ PePsCḡPë PSP°PrPSPëCḡPePsPIPëC...
P·P°P»PsP·, NOAEL Cí 4,2 CḡP°P·P° PīPµCḡPµPIPëC%CrPiP°P»P° B C,P°PeCí PīCḡPë PḡP P”P>.

Pj CíP°PjPsPe C%CrCḡC-PI PIC-PrP·PSP°C±P°P»PsCíCĪ P·PSPëP¶PµPSPSCĪ
PīP»PsPrCḡC±PsCíC,C- C,P° C-PSPPrPµPeCíCí P·P°PiP»C-PrPSPµPSPSCĪ PīCḡPë
PeP»C-PSC-C±PSPs P·PSP°C±CíC%PëC... PµPeCíPiPsP·PëC†C-CĪC... Cí
PīPµCḡPµCḡP°C...CíPSPeCí PSP° PjPi/Pj² PīP»PsC%C- PīPsPiPµCḡC...PSC- C,C-P»P°.
P’PīP»PëPICí PSP° C,,PµCḡC,PëP»CHPSC-CíC,CH CíP°PjC†C-PI PīCḡPë
PµPeCíPiPsP·PëC†C-CĪC..., C%Ps PīPµCḡPµPIPëC%CrCḡC,CH PeP»C-PSC-C±PSCí
PµPeCíPiPsP·PëC†C-Cḡ PīCḡPë PḡP P”P> Cí 4,3 CḡP°P·P°, PSPµ
CíPiPsCíC,PµCḡC-PiP°P»PsCíCĪ.

P’PiPµPrPµPSPSCĪ PeP°CḡPëPīCḡP°P·PëPSCí C%CrCḡP°Pj Cí PīPµCḡC-PsPr
PsCḡPiP°PSPsPiPµPSPµP·Cí B CíPīCḡPëC±PëPSCĪP»Ps PiP°PrPë CḡPsP·PIPëC,PeCí,
P·PSPëP¶PµPSPSCĪ PIPëP¶PëPiP°PSPSCĪ PīPsC,PsPjCíC,PIP° C,P° P·P°C,CḡPëPjPeCí
CḡPsP·PIPëC,PeCí PīCḡPë PµPeCíPiPsP·PëC†C-CĪC... PīCḡPµPiP°CḡP°C,Cí, PjPµPSCëPëC...,
PSC-P¶B PµPeCíPiPsP·PëC†C-CĪ Cí P»CḡPrPëPSPë PīCḡPë PḡP P”P> 6 PjPi PSP° PrPsP±Cí. Pj
PeCḡPsP»C-PI PeP°CḡPëPīCḡP°P·PëPS B C±PëPSPëPI C,PsPeCíPëC±PSCí PrC-Cḡ PSP°
PjP°C,PµCḡPëPSCíCHPePëPNë PsCḡPiP°PSC-P·Pj, P°P»Pµ PSPµ CíC,P°PSPsPiPëPi

PSPµP±PµP·PīPµPePē PrP»CĬ PīP»PsPrP° PīCĤPē PµPeCĬPīPsP·PēC†C-CĬC..., Cr 5,8 CĤP°P·P° PIPēC%oPēC... P·P° PeP»C-PSC-C†PSCr PµPeCĬPīPsP·PēC†C-CĤ PīCĤPē PĥP P'P».

PĤP»C-PSC-C†PSPs P·PSP°C†CfC%oC- PµPeCĬPīPsP·PēC†C-C— PeP°CĤPēPīCĤP°P·PēPSCr, CĬPePēPNē PIPiPsPrPēP»Pē PIP°PiC-C,PSPēPj CĬP°PjPeP°Pj C%oCrCĤC-PI Cr PīPµCĤC-PsPr PsCĤPīP°PSPsPiPµPSPµP·Cr, PīCĤPsC,CĬPiPsPj CrCĬC-C" C— PIP°PiC-C,PSPsCĬC,C- C,P° PīPµCĤC-PsPrCr PīCĤCfPrPSPsPiPs PIPēPiPsPrPsPICrPIP°PSPSCĬ,B P·PSPēP¶CfPIP°P»Pē PīPsCĬC,PSP°C,P°P»CHPSPµ PIPēP¶PēPIP°PSPSCĬ, PjP°CĬCr C,C-P»P° PīCĤPē PSP°CĤPsPrP¶PµPSPSC- C,P° PjP°CĬCr C,C-P»P° PīC-CĬP»CĬ PIC-PrP»CrC†PµPSPSCĬ PIC-Pr PīCĤCfPrPµPNē PīPsC,PsPjCĬC,PIP°B PīPµCĤCēPsPiPs PīPsPePsP»C-PSPSCĬ. PĤCĤC-Pj C,PsPiPs, P·P° PIC-PrCĬCrC,PSPsCĬC,C- C,PsPeCĬPēC†PSPsC— PrC-C— PSP° PjP°C,PµCĤPēPSCĬCHPePēPNē PsCĤPīP°PSC-P·Pj CĬPīPsCĬC,PµCĤC-PiP°P»P°CĬCĬ P±P»C-PrC-CĬC,CH,B P·PSPēP¶PµPSPSCĬ C,PµPjPīPµCĤP°C,CfCĤPē C,C-P»P° C,P° P·P°C,CĤPēPjPeP° CĤPsP·PIPēC,PeCr Cr PīP»PsPrP° (PSPµPrPsCĤPsP·PIPēC,PsPe PSPēCĤPePsPIPēC... CĬPsCĬPsC†PeC-PI C,P° P·PSPēP¶PµPSPSCĬ CĬP»CrC...PsPiPsPiPs CĤPµC,,P»PµPeCĬCr Cr CĬP°PjC†C-PI). PαPµCĤC,PēP»CHPSC-CĬC,CH B PīPsC,PsPjCĬC,PIP° B PīPµCĤCēPsPiPs PīPsPePsP»C-PSPSCĬ B PSPµ P·P°P·PSP°P»P° P·PjC-PS, PsPrPSP°Pe Cr C%oCrCĤC-PI PrCĤCfPiPsPiPs PīPsPePsP»C-PSPSCĬ PIC-PrP·PSP°C†P°P»PēCĬCĬ P°PSP°P»PsPiC-C†PSC- PeP»C-PSC-C†PSC- PsP·PSP°PePē C,P° P·PSPēP¶PµPSPSCĬ PjP°CĬPē C,C-P»P°.

PĤP°CĤPēPīCĤP°P·PēPS C,P° PNēPsPiPs PjPµC,P°P±PsP»C-C,Pē PīCĤPsPSPēPeP°P»Pē PI PjPsP»PsPePs C%oCrCĤC-PI Cr PīPµCĤC-PsPr PīCĤCfPrPSPsPiPs PIPēPiPsPrPsPICrPIP°PSPSCĬ.

PĤP»C-PSC-C†PSC- C...P°CĤP°PeC,PµCĤPēCĬC,PēPePē.

PµPsPeP°P·P°PSPSCĬ.

P"»CĬ P»C-PeCrPIP°PSPSCĬ CēPēP·PsC,,CĤPµPSC-C— Cr PrPsCĤPsCĬP»PēC... PīP°C†C-C" PSC,C-PI.

PµCĤPsC,PēPīPsPeP°P·P°PSPSCĬ.

PµC-PrPIPēC%oPµPSP° C†CfC,P»PēPIC-CĬC,CH PrPs PrC-CĤC†PsC— CĤPµC†PsPIPēPSPē P°P±Ps PrPs P±CfPrCH-CĬPePsC— P· PrPsPīPsPjC-P¶PSPēC... CĤPµC†PsPIPēPS.

PŸCfPīCfC,PSC" P·P°CĬC,PsCĬCrPIP°PSPSCĬ PīPsC,CfP¶PSPsPiPs C-PSPiC-P±C-C,PsCĤP° CYP3A4 (PrPēPI. CĤPsP·PrC-P» B«P'P·P°C"PjPsPrC-CĬ P· C-PSCēPēPjPē P»C-PeP°CĤCĬCHPePēPjPē P·P°CĬPsP±P°PjPē C,P° C-PSCēC- PIPēPrPē PIP·P°C"PjPsPrC-PNēB»).

PŸCfPīCfC,PSC" P·P°CĬC,PsCĬCrPIP°PSPSCĬ PīPsC,CfP¶PSPsPiPs P°P±Ps PīPsPjC-CĤPSPsPiPs C-PSPrCfPeC,PsCĤP° CYP3A4 (PrPēPI. CĤPsP·PrC-P» B«P'P·P°C"PjPsPrC-CĬ P· C-PSCēPēPjPē P»C-PeP°CĤCĬCHPePēPjPē P·P°CĬPsP±P°PjPē C,P° C-PSCēC- PIPēPrPē PIP·P°C"PjPsPrC-PNēB»).

P'P·P°C"PjPsPrC-CĬ P· C-PSCēPēPjPē P»C-PeP°CĤCĬCHPePēPjPē P·P°CĬPsP±P°PjPē C,P° C-PSCēC- PIPēPrPē PIP·P°C"PjPsPrC-PNē.

PuPsC,PuPSC†C-PN₂PSPëPN₂ PIPiP»PëPI C-PSC€PëC... PïC₃PuPiP°C₃P°C,C-PI PSP°
PeP°C₃PëPïC₃P°P·PëPS

$\text{P}\mu\text{C}, \text{P}^\circ\text{P}\pm\text{PsP}\gg\text{C}-\text{P}\cdot\text{Pj}$ $\text{PeP}^\circ\text{C}\mathfrak{H}\text{P}\ddot{\text{P}}\text{P}\text{C}\mathfrak{H}\text{P}^\circ\text{P}\cdot\text{P}\ddot{\text{P}}\text{PSCr}$ $\text{C}, \text{P}^\circ\text{P}\mu\text{PsPiPs}$ $\text{PsC}\mathfrak{I}\text{PSPsPIPSP}\ddot{\text{C}}\dots$
 $\text{P}^\circ\text{PeC}, \text{P}\ddot{\text{P}}\text{PIPSP}\ddot{\text{C}}\dots$ $\text{PjP}\mu\text{C}, \text{P}^\circ\text{P}\pm\text{PsP}\gg\text{C}-\text{C}, \text{C}-\text{PI}, \text{PrP}\mu\text{P}\cdot\text{PjP}\mu\text{C}, \text{P}\ddot{\text{P}}\text{P}\gg\text{Cr}-\text{PeP}^\circ\text{C}\mathfrak{H}\text{P}\ddot{\text{P}}\text{P}\text{C}\mathfrak{H}\text{P}^\circ\text{P}\cdot\text{P}\ddot{\text{P}}\text{PSCr}$
 (DCAR) $\text{C}, \text{P}^\circ\text{PrP}\ddot{\text{P}}\text{PrP}\mu\text{P}\cdot\text{PjP}\mu\text{C}, \text{P}\ddot{\text{P}}\text{P}\gg\text{Cr}-\text{PeP}^\circ\text{C}\mathfrak{H}\text{P}\ddot{\text{P}}\text{P}\text{C}\mathfrak{H}\text{P}^\circ\text{P}\cdot\text{P}\ddot{\text{P}}\text{PSCr}$ $(\text{DDCAR}), \text{P}\ddot{\text{P}}\mu\text{C}\mathfrak{H}\text{P}\mu\text{PIP}^\circ\text{P}\mathfrak{I}\text{PSPs}$
 $\text{PsPiPsC}\mathfrak{I}\text{P}\mu\text{C}\mathfrak{H}\text{P}\mu\text{PrPePsPICrC}''\text{C}, \text{C}\mathfrak{H}\text{C}\mathfrak{I}\text{C}\mathfrak{I}$ $\text{CYP3A4 P}\cdot\text{PjC}-\text{PSC}-\text{PjP}^\circ\text{P}\gg\text{C}\mathfrak{H}\text{PSP}\ddot{\text{P}}\text{Pj}$ $\text{PIP}\ddot{\text{P}}\gg\text{P}\ddot{\text{P}}\text{IPsPj}$
 $\text{CYP2D6}.$

P†PSPiC-P±C-C,PsCḤPë CYP3A4

[illegible]

PSpμCḡPμP· PrPsPIPiPēPNē PiPμCḡC-PsPr PSp°PiC-PIPIPēPIPμPrPμPSPSCḡ P°PeC,PēPIPSPēC...
 PePsPjPiPsPSPμPSC,C-PI PeP°CḡPēPiCḡP°P·PēPSCr PiPsPrP°P»CHC€Pμ
 PiC-PrPIPēC%oPμPSPSCḡ PIPjC-ClC,Cr P·P°PiP°P»CHPSPsPiPs PeP°CḡPēPiCḡP°P·PēPSCr PI
 PiP»P°P·PjC- PjPsPḡPμ PsC±C-PeCrPIP°C,PēClCḡ PiC-Pr C±P°Cl P±C-P»CHC€
 C,CḡPēPIP°P»PsPiPs PePsPjP±C-PSPsPIP°PSPsPiPs PiCḡPēPNēPsPjCr. PŷPsPjCr
 PePsPjP±C-PSPsPIP°PSPēPNē PiCḡPēPNēPsPj PeP°CḡPēPiCḡP°P·PēPSCr P· PiPsC,CrPḡPSPēPjPē
 C-PSPiC-P±C-C,PsCḡP°PjPē CYP3A4 (PSP°PiCḡPēPeP»P°Pr, P±PsC±PμPiCḡPμPIC-Cḡ,
 PeP»P°CḡPēC,CḡPsPjC-C†PēPS, PePsP±C-C†PēClC,P°C,, C-PSPrPēPSP°PIC-Cḡ,
 C-C,CḡP°PePsPSP°P·PsP», PePμC,PsPePsPSP°P·PsP», PSPμC,,P°P·PsPrPsPs,
 PSPμP»C,,C-PSP°PIC-Cḡ, PiPsP·P°PePsPSP°P·PsP», CḡPēC,PsPSP°PIC-Cḡ,
 ClP°PePIC-PSP°PIC-Cḡ, C,PμP»P°PiCḡPμPIC-Cḡ, C,PμP»C-C,CḡPsPjC-C†PēPS,
 PIPsCḡPēPePsPSP°P·PsP») PiCḡPsC,PēPiPsPeP°P·P°PSPēPNē (PrPēPI. CḡPsP·PrC-P»
 B«PμCḡPsC,PēPiPsPeP°P·P°PSPSCḡB»).

P·CḥPëC,CḥPSPjC-C†PëPS (500 PjPi PrPIC-C†C- PSP° PrPsP±C†), PîPsPjC-CḥPSPëPñ
C-PSPiC-P±C-C,PScḥ CYP3A4, PIPëPeP»PëPeP°PI C† C†PµCḥPµPrPSCḥPsPjC† 1,4-
PeCḥP°C,PSPµ (PrC-P°PîP°P·PsPS 1,03Bḥ“2,32 CḥP°P·P°) P·P±C-P»CḥC€PµPSPSCµ
PµPeC†PîPsP·PëC†C-C— P·P°PîP°P»CḥPSPsPiPs PeP°CḥPëPîCḥP°P·PëPSC† PI PîP»P°P·PjC-
PeCḥPSPiC- PîC-C†P»Cµ 3 C,PëP¶PSC-PI PsPrPSPsC†P°C†PSPsPiPs P·P°C†C,PSc†C†PIP°PSPSCµ.
PŷP°PePëPj C†PëPSPsPj, PîCḥPsC,CµPiPsPj PîPµCḥC-PsPrC† PsPrPSPsC†P°C†PSPsPiPs
P·P°C†C,PSc†C†PIP°PSPSCµ PeP°CḥPëPîCḥP°P·PëPSC† P· PîPsPjC-CḥPSPëPj
C-PSPiC-P±C-C,PScḥPsPj CYP3A4 (PSP°PîCḥPëPeP»P°Pr, PµCḥPëC,CḥPsPjC-C†PëPSPsPj,
C„P»C†PePsPSP°P·PsP»PsPj, PrPëP»C,C-P°P·PµPjPsPj, PIPµCḥP°PîP°PjC-P»PsPj)
CḥPµPePsPjPµPSP†C†C”C,CḥC†Cµ PePsPSC,CḥPsP»CḥPIP°C,Pë C-PSPrPëPIC-PrC†P°P»CḥPSC†
CḥPµP°PeC†C-Cḥ C,P° PîPµCḥPµPSPsC†PëPjC-C†C,Cḥ C-, CµPeC‰Ps PSPµPsP±C...C-PrPSPs,
PrPsP·C† PeP°CḥPëPîCḥP°P·PëPSC† C†P»C-Pr (C,PëPjC†P°C†PsPIPs) P·PjPµPSC€PëC,Pë,
PICḥP°C...PsPIC†CḥC†Pë PîPsC,PµPSC†C-PñPSPsPiPµ P·P±C-P»CḥC€PµPSPSCµ
PµPeC†PîPsP·PëC†C-C—. P’PSP°C†P»C-PrPsPe C,CḥPëPIP°P»PsPiPs PîPµCḥC-PsPrC†
PSP°PîC-PIPIPëPIPµPrPµPSPSCµ PeP°CḥPëPîCḥP°P·PëPSC† C,P° PñPsPiPs P°PeC,PëPIPSPëC...
PjPµC,P°P±PsP»C-C,C-PI PîPsC†P°C,PSPe, PîCḥPëPîPëPSPµPSPSCµ P»C-PeC†PIP°PSPSCµ
PîPsPjC-CḥPSPëPj C-PSPiC-P±C-C,PScḥPsPj CYP3A4 P°P±Ps P·PjC-PSP° PrPsP·Pë
PîPsPIPSC-C†C,Cḥ PSPµ PIC-PrPsP±CḥP°P·PëC,CḥC†Cµ PSP° CḥC-PIPSCµC...

Pj PrPsCfP»C-PrP¶PµPSPSC- PIP·P°C”PjPsPrC— P»C-PeP°CĤCfCHbPePëC... P·P°CfPs±C-PI
28-PrPµPSPSPµ P»C-PeCfPIP°PSPSC¶ PeP°CĤPëPîCĤP°P·PëPSPsPj Cr PrPsP·C- 6 PjPi PSP°
PrPsP±Cf PSPµ PjP°P»Ps PeP»C-PSC-C†PSPs P·PSP°C†CrC%oPsPiPs PIPiP»PëPICf PSP°
C,,P°CĤPjP°PePsPeC-PSPµC,PëPeCf PîPµCĤPsCĤP°P»CHbPSPëC... PePsPSC,CĤP°C†PµPîC,PëPIC-PI
(PµC,PëPSC-P»PµCfC,CĤP°PrC-PsP»Cr C,P° P»PµPIPsPSPsCĤPiPµCfC,CĤPµP»Cr).

РѹС-Р·PSCЇ РrРёСГРёС-PSРµР·С-СЇ вѢ” С†Рµ СГРёPSPPrСѢPsPj, C%Ps
PіСѢPsСЇPIР»СЇС”C,СѢСГСЇ СѢРёС,PjC-С†PSPёPjPё PjPёPjPsPIC-P»СѢPSPёPjPё
СѢСГС...P°PjPё PіРµСѢРµPIР°P¶PSPs СЇР·РёРёР° С,P°/P°P±Ps PsP±P»РёС†С†СЇ С- PjPsP¶Рµ
СѢPsP·PIРёPIР°C,РёСГСЇ СГ РіР°С†С-С”PSC,C-PI, СЇРёС- P»C-РёСГСѢC,СѢСГСЇ
P°PSC,РёPіСГРёС...PsC,РёРёР°PjPё. PіРёC%Ps СГРёPjPіC,PsPjPё PіC-Р·PSCѢPsC—
РrРёСГРёС-PSРµР·С-С— Р·вѢ™ СЇPIР»СЇСѢC,СѢСГСЇ СГ РіР°С†С-С”PSC,P°, СЇРёРёPNё
P»C-РёСГС”C,СѢСГСЇ РёР°СѢРёPіСѢР°P·РёPSPsPj, PіPsC,СѢC-Р±PSPs СѢPsP·PіP»СЇPSCГС,Рё
PSРµPsP±C...C-PrPSC-СГС,СѢ PіСѢРёPіРёPSPµPSPSCЇ B P·P°СГС,PsСГСГPIР°PSPSCЇ
С†СѢPsPіPs PіСѢРµPіР°СѢР°C,СГ.

РГPIPsСѢPsP±P° РµР°СѢРёС-PSCГPsPSP°

PіРёC%Ps P°PSC,РёPіСГРёС...PsC,РёС†PSC- P·P°СГPsP±Pё PіСѢРёP·PSP°С†Р°СѢC,СѢСГСЇ
PіР°С†С-С”PSC,P°Pj C-Р· C...PIPsСѢPsP±PsСѢ РµР°СѢРёС-PSCГPsPSP°, C,Ps PjPsP¶P»РёPIРµ
P·P°PіPsСГС,СѢРµPSPSCЇ C„PsPSPsPіPsPіPs P·P°C...PIPsСѢСѢPIР°PSPSCЇ C,P°
PіPsPіC-СѢСРµPµPSPSCЇ PіРµСѢРµP±C-PіСГ C...PIPsСѢPsP±Pё РµР°СѢРёС-PSCГPsPSP°.
PŷPsPjСГ, PіСѢРёP·PSP°С†Р°СѢРё РёР°СѢРёPіСѢР°P·РёPS PіР°С†С-С”PSC,P°Pj C-Р·
C...PIPsСѢPsP±PsСѢ РµР°СѢРёС-PSCГPsPSP°, P»C-РёР°СѢC- PjP°СѢC,СѢ P·PIР°P¶СГPIР°C,Рё
СГРіC-PIPIC-PrPSPsСРµPµPSPSCЇ РёPsСѢРёСГС,СѢ/СѢРёP·РёРё.

РŷРёPjPіC,PsPjPё P· P±PsРёСГ PsC†PµPNё/ РёР°C,P°СѢР°РёC,P°

Pj PrPsРёP»C-PSC-С†PSPёC... PrPsСГР»C-PrP¶PµPSPSCЇC... РёР°СѢРёPіСѢР°P·РёPSCГ PI
СГPsP±P°Рё P±СГР»Ps PіPsPjC-С†PµPSPs PіPsPjСГC,PSC-PSPSCЇ РёСѢРёСРёC,P°P»РёРёР°/
РёР°C,P°СѢР°РёC,P° (PrРёPI. СѢPsP·PrC-P»Pё B«PµPsP±C-С†PSC- СѢРµP°РёС†С-С—B» C,P°
B«P”P°PSC- PrPsРёP»C-PSC-С†PSPёC... PrPsСГР»C-PrP¶PµPSCѢ P· P±PµP·PіРµРёPёB»).

РµСѢРёС†PёPSPSPs-PSP°СГР»C-PrРёPsPIРёPNё P·PівѢ™ СЇР·PsРё PjC-P¶ P·PjC-PSP°PjPё PI
РёСѢРёСРёC,P°P»РёРёСГ/ РёР°C,P°СѢР°РёC,PsСѢ, C%Ps СГРіPіPsСГС,РµСѢC-PіР°P»РёСГСЇ
PіC-Pr С†Р°СГ PrPsСГР»C-PrP¶PµPSCѢ СГ P»СѢPrPµPNё, C- P·P°СГС,PsСГСГPIР°PSPSCЇPj
РёР°СѢРёPіСѢР°P·РёPSCГ PSPµ P±СГPI СГСГС,P°PSPsPIР»PµPSPёPNё. РµСѢPsC,Рµ
PіР°С†С-С”PSC,P°Pj, СГ СЇРёРёС... PjPsP¶СГC,СѢ СѢPsP·PIРёPSCГC,РёСГСЇ СГРёPjPіC,PsPjPё,
C%Ps PіPsC,РµPSC†C-PNёPSPs PjP°СѢC,СѢ PIC-PrPSPsСРµPµPSPSCЇ PrPs РёР°C,P°СѢР°РёC,Рё,
PіPsC,СѢC-Р±PSPs PіPsСѢР°PrРёC,Рё PіСѢPsPNёC,Рё PsC„C,P°P»СѢPjPsP»PsPіC-С†PSPµ
PsP±СГС,РµP¶PµPSPSCЇ, P° PіPsC,C-Pj СГР»C-Pr PіPsPIC,PsСѢPSPs B СѢPsP·PіP»СЇPSCГC,Рё
PіРёC,P°PSPSCЇ PіСѢPs PіСѢPsPrPsPIР¶PµPSPSCЇ P»C-РёСГPIР°PSPSCЇ.

P—P»PsСЇРёС-СГPSPёPNё PSPµPNёСѢPsP»PµPіC,РёС†PSPёPNё СГРёPSPPrСѢPsPj
РµPsC,РµPSC†C-PNёPSPs P»PµC,P°P»СѢPSPёPNё РёPsPjPіP»PµРёСГ СГРёPjPіC,PsPjC-PI, C%Ps
PjP°C” PSP°P·PICГ P·P»PsСЇРёС-СГPSPёPNё PSPµPNёСѢPsP»PµPіC,РёС†PSPёPNё СГРёPSPPrСѢPsPj
(P—PќPŷ), PIC-PrP·PSP°С†Р°С”C,СѢСГСЇ PіСѢРё P»C-РёСГPIР°PSPSC-
P°PSC,РёPіСГРёС...PsC,РёРёР°PjPё. PљP»C-PSC-С†PSPёPjPё PіСѢPsСЇPIР°PjPё P—PќPŷ C”
PіC-PіРµСѢPіC-СѢРµРёСГС-СЇ, PjвѢ™ СЇР·PsPIР° СѢРёPіC-PrPSC-СГС,СѢ,
PіC-PrPIРёC%PµPSPёPNё СѢC-PIРµPSCѢ РёСѢРµP°C,РёPSC-PSC„PsСГС„PsРёC-PSP°P·Рё PI
СГРёСѢPsPIР°C,С†C-, P·PjC-PSPµPSPёPNё PіСГРёC...C-С†PSPёPNё СГС,P°PS C,P° PsP·PSP°РёРё
СѢPsP·P»P°PrСГ PIРµPіРµC,P°C,РёPIРSPsC— PSPµСѢPIPsPIPsC— СГРёСГС,РµPjPё
(PSPµСѢРµPіСГP»СЇСѢPSPёPNё PіСГP»СѢСГ P°P±Ps P°СѢC,РµСѢC-P°P»СѢPSPёPNё C,РёСГРё,
C,P°C...C-РёР°СѢPrC-СЇ, PrC-P°C„PsСѢРµP· C,P° СГРµСѢС†PµPIР° P°СѢРёC,PjC-СЇ).
P”PsPrP°C,РёPsPIC- PsP·PSP°РёРё PjPsP¶СГC,СѢ PIРёP»СѢС†P°C,Рё
PjC-PsPіP»PsP±C-PSCГСѢC-СѢ (СѢР°P±PrPsPjC-PsP»C-P·) C,P° PіPsСГС,СѢСГ PSPёСѢРёPsPICГ
PSPµPrPsСГС,P°C,PSC-СГС,СѢ. PіРёC%Ps СГ РіР°С†С-С”PSC,P° СѢPsP·PIРёPIР°СѢC,СѢСГСЇ
СГРёPjPіC,PsPjPё, C%Ps PIРёР°P·СГСѢC,СѢ PSP° P—PќPŷ, P°P±Ps СГ PSCѢPsPіPs
P·вѢ™ СЇPIР»СЇС”C,СѢСГСЇ PIРёСГPsРёР° C,РµPjPіРµСѢР°C,СГСѢР° P· PSPµPIC-PrPsPjPёC...

PiCḡPēC†PēPS P±PμP· PrPsPrP°C,PePsPIPēC... PeP»C-PSC-C†PSPēC... PiCḡPsCḡPIC-PI P—PḡPŸ,
P·P°C†C-,PsC†C†PIP°PSPSCḡ PeP°CḡPēPiCḡP°P·PēPSC† PjP°C” P±C†C,Pē PSPμPiP°PNḡPSPs
PiCḡPēPiPēPSPμPSPμ.

PŸC†PrPsPjPē C,P° PePsPSPIC†P»CHC†C-C—

PḡP°CḡPēPiCḡP°P·PēPS PiPsC,CḡC-P±PSPs PsP±PμCḡPμP¶PSPs PiCḡPēP·PSP°C†P°C,Pē
PiP°C†C-C”PSC,P°Pj, C† CḡPePēC... PI P°PSP°PjPSPμP·C- C” C†C†PrPsPjPē P°P±Ps
PiP°C-,PsP»PsPiC-C†PSC- C†C,P°PSPē, C°Ps PiPsC,PμPSC†C-PNḡPSPs P·PSPēP¶C†CḡC,CH
C†C†PrPsPjPSPēPNḡ PiPsCḡC-Pi.

PμP°C†C-C”PSC,Pē P»C-C,PSCHPsPiPs PIC-PeC† P· PrPμPjPμPSC†C-C”Cḡ

P”C-Cḡ PeP°CḡPēPiCḡP°P·PēPSC† C† PiP°C†C-C”PSC,C-PI P»C-C,PSCHPsPiPs PIC-PeC† P·
PrPμPjPμPSC†C-C”Cḡ PSPμ P±C†P»P° PIPēPIC†PμPSP°, C,PjC† P»C-PeP°CḡC†CHPePēPNḡ
P·P°C†C-P± PSPμ CḡPμPePsPjPμPSP†C”C,CHC†Cḡ PrPs P·P°C†C-,PsC†C†PIP°PSPSCḡ
C,P°PePēPj PiP°C†C-C”PSC,P°Pj C†PμCḡPμP· PiC-PrPIPēC°PμPSPēPNḡ CḡPēP·PēPe
P·P°PiP°P»CHPSPsC— P»PμC,P°P»CHPSPsC†C,C-.

P PēP·PēPe PIPēPSPēPePSPμPSPSCḡ PiPsCḡC†C€PμPSCH PjPsP·PePsPIPsPiPs
PeCḡPsPIPsPsP±C-PiC† (PμPḡPḡ)

Pj CḡP°PSP†PsPjC-P·PsPIP°PSPēC... PiP»P°C†PμP±PsPePsPSC,CḡPsP»CHPsPIP°PSPēC...
PeP»C-PSC-C†PSPēC... PrPsC†P»C-PrP¶PμPSPSCḡC... C† PiCḡC†PiC- PiP°C†C-C”PSC,C-PI C-P·
PrPμPjPμPSC†C-C”Cḡ, CḡPeC- P»C-PeC†PIP°P»PēC†Cḡ PrPμCḡPePēPjPē P°C,PēPiPsPIPēPjPē
P°PSC,PēPiC†PēC...PsC,PēPeP°PjPē, P±C†P»Ps PiPsPjC-C†PμPSPs, C°Ps CḡPēP·PēPe
PIPēPSPēPePSPμPSPSCḡ PμPḡPḡ P·P±C-P»CHC€PμPSPēPNḡ PiCḡPēP±P»PēP·PSPs PI C,CḡPē
CḡP°P·Pē. PḡPμC...P°PSC-P·Pj PiC-PrPIPēC°PμPSPSCḡ CḡPēP·PēPeC† PSPμPIC-PrPsPjPēPNḡ.
PμC-PrPIPēC°PμPSPēPNḡ CḡPēP·PēPe PμPḡPḡ PSPμ PjPsP¶PSP° PIPēPeP»CḡC†P°C,Pē PiCḡPē
PiCḡPēPNḡPsPjC- C-PSC€PēC... P°PSC,PēPiC†PēC...PsC,PēPeC-PI P°P±Ps PrP»Cḡ C-PSC€PēC...
PiCḡC†Pi PiP°C†C-C”PSC,C-PI. PḡP°CḡPēPiCḡP°P·PēPS PiPsC,CḡC-P±PSPs PsP±PμCḡPμP¶PSPs
PiCḡPēP·PSP°C†P°C,Pē PiP°C†C-C”PSC,P°Pj P· C†PēPSPSPēPeP°PjPē CḡPēP·PēPeC†
PIPēPSPēPePSPμPSPSCḡ C-PSC†C†P»CHC,C†.

P—P°C...PIPsCḡCHPIP°PSPSCḡ C†PμCḡC†PμPIPs-C†C†PrPēPSPSPsC— C†PēC†C,PμPjPē

P—PjC-PSPē P°CḡC,PμCḡC-P°P»CHPSPsPiPs C,PēC†PeCž

PḡP°CḡPēPiCḡP°P·PēPS PjPsP¶Pμ C†PiCḡPēC†PēPSCḡC,Pē CḡPe PsCḡC-,PsC†C,P°C,PēC†PSC†
PiC-PiPsC,PμPSP·C-Cḡ, C,P°Pe C- PiC-PiPμCḡC,PμPSP·C-Cḡ (PrPēPI. CḡPsP·PrC-P»
B«PμPsP±C-C†PSC- CḡPμP°PeC†C-C—B»). PḡP°CḡPēPiCḡP°P·PēPS PiPsC,CḡC-P±PSPs
PsP±PμCḡPμP¶PSPs P·P°C†C-,PsC†PsPIC†PIP°C,Pē PiP°C†C-C”PSC,P°Pj, C† CḡPePēC... PI
P°PSP°PjPSPμP·C- C” P·P°C...PIPsCḡCHPIP°PSPSCḡ C†PμCḡC†PμPIPs-C†C†PrPēPSPSPsC—
C†PēC†C,PμPjPē C- CḡPeC- C†C...PēP»CHPSC- PrPs P·PjC-PS P°CḡC,PμCḡC-P°P»CHPSPsPiPs
C,PēC†PeC†. PμPsC,CḡC-P±PSPs B PePsPSC,CḡPsP»CHPIP°C,Pē P°CḡC,PμCḡC-P°P»CHPSPēPNḡ
C,PēC†Pe.

P—PjC-PSPē PSP° PμP»PμPeC,CḡPsPeP°CḡPrC-PsPiCḡP°PjC- (P·PḡP”)

Pj PiP°C†C-C”PSC,C-PI, CḡPeC- PiCḡPēPNḡPjP°CḡC,CH P°PSC,PēPiC†PēC...PsC,PēPePē, PjPsP¶Pμ
CḡPsP·PIPēPIP°C,PēC†Cḡ PiPsPrPsPIP¶PμPSPSCḡ C-PSC,PμCḡPIP°P»C† QPŸ.

Pj PeP»C-PSC-C†PSPsPjC† PrPsC†P»C-PrP¶PμPSPSC-, CḡPePμ PiCḡPsPIPsPrPēP»Pē PrP»Cḡ

PsC†C-PSPePë PîPsPrPsPIP¶PµPSPSC‡ C-PSC,PµC‡PIP°P»C† QT, PîC‡Pë PîC‡PëPNëPsPjC-
PeP°C‡PëPîC‡P°P·PëPSC† PSPµ P±C†P»Ps PîPsPjC-C†PµPSPs P¶PsPrPSPsPiPs
PîPsPrPsPIP¶PµPSPSC‡ C-PSC,PµC‡PIP°P»C† QT C† PîPsC‡C-PIPSC‡PSPSC- P· PîP»P°C†PµP±Ps
(PrPëPI. C‡PsP·PrC-P» B«PαP°C‡PjP°PePsPrPëPSP°PjC-PeP°B»). Pj PeP»C-PSC-C†PSPëC...
PrPsC†P»C-PrP¶PµPSPSC‡C... PîPsPIC-PrPsPjP»C‡P»PsC†C‡ P»PëCëPµ PîC‡Ps
PrPµPeC-P»C‡PeP° PIPëPîP°PrPeC-PI PSPµP·PSP°C†PSPsPiPs PîPsPrPsPIP¶PµPSPSC‡
C-PSC,PµC‡PIP°P»C† QT PîC‡Pë PîC‡PëPNëPsPjC- PeP°C‡PëPîC‡P°P·PëPSC† (PrPëPI.
C‡PsP·PrC-P» B«PµPsP±C-C†PSC- C‡PµP°PeC†C-C—B»). PÿPsPjC† PeP°C‡PëPîC‡P°P·PëPS
C,C‡PµP±P° PsP±PµC‡PµP¶PSPs P·P°C†C,PsC†PsPIC†PIP°C,Pë PîP°C†C-C”PSC,P°Pj, C†
C‡PePëC... PI P°PSP°PjPSPµP·C- C” C†PµC‡C†PµPIPs-C†C†PrPëPSPSPµ
P·P°C...PIPsC‡C‡PIP°PSPSC‡ P°P±Ps PîPsPrPsPIP¶PµPSPSC‡ C-PSC,PµC‡PIP°P»C† QT PI
C†C-PjPµPNëPSPsPjC† P°PSP°PjPSPµP·C-, P° C,P°PePsP¶ PîP°C†C-C”PSC,P°Pj, C‡PeC-
P»C-PeC†PIP°P»PëC†C‡ PîC‡PµPîP°C‡P°C,P°PjPë, C%oPs PjPsP¶C†C,C‡ PîPsPrPsPIP¶PëC,Pë
C-PSC,PµC‡PIP°P» QT (PrPëPI. C‡PsP·PrC-P» B«PαP°C‡PjP°PePsPrPëPSP°PjC-PeP°B»).

P’PµPSPsP·PSP° C,C‡PsPjP±PsPµPjP±PsP»C-C‡ (P’PÿP·)

PµPsPIC-PrPsPjP»C‡P»PsC†C‡ PîC‡Ps PIPëPîP°PrPePë PIPëPSPëPePSPµPSPSC‡ P’PÿP· PîC‡Pë
P·P°C†C,PsC†C†PIP°PSPSC- P°PSC,PëPîC†PëC...PsC,PëC†PSPëC... P·P°C†PsP±C-PI.
P‡C†PeC-P»C‡PePë C† PîP°C†C-C”PSC,C-PI, C‡PeC- PîC‡PëPNëPjP°C‡C,C‡
P°PSC,PëPîC†PëC...PsC,PëPePë, C†P°C†C,Ps PIPëPSPëPeP°C‡C,C‡ PSP°P±C†C,C-
C†PëPSPSPëPePë C‡PëP·PëPeC† C‡PsP·PIPëC,PeC† P’PÿP·, PIC†C- PjPsP¶P»PëPIC-
C†PëPSPSPëPePë PIPëPSPëPePSPµPSPSC‡ P’PÿP· C†P»C-Pr PIPëC‡PIPëC,Pë PîPµC‡PµPr C,P°
PîC-Pr C†P°C† P»C-PeC†PIP°PSPSC‡ PeP°C‡PëPîC‡P°P·PëPSPsPj, P° C,P°PePsP¶ C,C‡PµP±P°
PîC‡PsPIPsPrPëC,Pë C—C...PSC‡ PîC‡PsC,,C-P»P°PeC,PëPeC†.

P”C-PîPµC‡PiP»C-PePµPjC-C‡ C,P° C†C†PeC‡PsPIPëPNë PrC-P°P±PµC,

Pj PîP°C†C-C”PSC,C-PI C-P· C†C†PeC‡PsPIPëPj PrC-P°P±PµC,PsPj P°P±Ps C†
PîP°C†C-C”PSC,C-PI C-P· C†PëPSPSPëPeP°PjPë C‡PëP·PëPeC† C‡PsP·PIPëC,PeC†
C†C†PeC‡PsPIPsPiPs PrC-P°P±PµC,C† (PSP°PîC‡PëPeP»P°Pr, PsP¶PëC‡C-PSPSC‡,
PSP°C‡PIIPSC-C†C,C‡ PrC-P°P±PµC,C† PI C†C-PjPµPNëPSPsPjC† P°PSP°PjPSPµP·C-), C‡PeC-
PîPsC†PëPSP°C‡C,C‡ P»C-PeC†PIP°PSPSC‡ P°C,PëPîPsPIPëPjPë
P°PSC,PëPîC†PëC...PsC,PëPeP°PjPë, C†P»C-Pr PePsPSC,C‡PsP»C‡PIP°C,Pë C‡C-PIPSC-
PiP»C‡PePsP·Pë PI C†PëC‡PsPIP°C,C†C-. PµC-Pr C†P°C† PeP»C-PSC-C†PSPëC...
PrPsC†P»C-PrP¶PµPSC‡ PeP°C‡PëPîC‡P°P·PëPSC† PîPsPIC-PrPsPjP»C‡P»PsC†C‡ PîC‡Ps
PîPsP±C-C†PSC- C‡PµP°PeC†C-C— C†C,PsC†PsPIPSs C‡C-PIPSC-PI PiP»C‡PePsP·Pë (PrPëPI.
C‡PsP·PrC-P» B«PαP°C‡PjP°PePsPrPëPSP°PjC-PeP°B»).

P—PjC-PSPë PjP°C†Pë C,C-P»P°

PµC‡Pë PîC‡PëPNëPsPjC- PeP°C‡PëPîC‡P°P·PëPSC† C†PîPsC†C,PµC‡C-PiP°P»PsC†C‡
P·PSP°C†PSPµ P·P±C-P»C‡CëPµPSPSC‡ PjP°C†Pë C,C-P»P°. PµP°C†C-C”PSC,P°Pj C†P»C-Pr
C‡PµPiC†P»C‡C‡PSPs PePsPSC,C‡PsP»C‡PIP°C,Pë PjP°C†C† C,C-P»P° (PrPëPI. C‡PsP·PrC-P»
B«PµPsP±C-C†PSC- C‡PµP°PeC†C-C—B»).

P‡PrPSPsC†P°C†PSPµ P»C-PeC†PIP°PSPSC‡ PîPsPjC-C‡PSPëPjPë C-PSPiC-P±C-C,PsC‡P°PjPë
CYP3A4

P‡PrPSPsC†P°C†PSPµ P·P°C†C,PsC†C†PIP°PSPSC‡ PeP°C‡PëPîC‡P°P·PëPSC† P·
PîPsPjC-C‡PSPëPjPë C-PSPiC-P±C-C,PsC‡P°PjPë CYP3A4 PjPsP¶Pµ PîC‡PëP·PIPµC†C,Pë PrPs
P·P±C-P»C‡CëPµPSPSC‡ P·P°PiP°P»C‡PSPsC— PµPeC†PîPsP·PëC†C-C—

PeP°CḡPēPīCḡP°P·PēPSCṛ. P PμPePsPjPμPSPṛCṛC" C,CHCṛCḷ PjPsPSC-C,PsCḡPēPSPi
C-PSPrPēPIC-PrCṛP°P»CHBPSPsC— CḡPμP°PeC†C-C— C,P° PīPμCḡPμPSPsCṛPēPjPsCṛC,C- C,P°,
CḷPeC%Ps PSPμPsP±C...C-PrPSPs, PrPsP·Cṛ PeP°CḡPēPīCḡP°P·PēPSCṛ CṛP»C-Pr
(C,PēPjC†P°CṛPsPIPs) P·PjPμPSCēPēC,Pē P· CṛCḡP°C...CṛPIP°PSPSCḷPj
PīPsC,PμPSC†C-PMsPSPsPiPs P·P±C-P»CHCēPμPSPSCḷ PμPeCṛPīPsP·PēC†C-C— (PrPēPI.
CḡPsP·PrC-P» B«P'P·P°C" PjPsPrC-Cḷ P· C-PSCēPēPjPē P»C-PeP°CḡCṛCHPePēPjPē
P·P°CṛPsP±P°PjPē C,P° C-PSCēC- PIPēPrPē PIP·P°C" PjPsPrC-PMsB»).

P"PsPīPsPjC-PḡPSC- CḡPμC†PsPIPēPSPē

P PμP°PiC-P»P°, PeP°PīCṛCṛP»Pē C,PIPμCḡPrC- PīPs 3 PjPi, 4,5 PjPi C,P° 6 PjPi, PjC-CṛC,CḷC,CH
P±P°CḡPIPSPēPe CṛPīPμC†C-P°P»CHBPSPēPMs C†PμCḡPIPsPSPēPMs PḡPṽ (P• 129), C%Ps
PjPsPḡPμ CṛPīCḡPēC†PēPSCḷC,Pē P°P»PμCḡPiC-C†PSC- CḡPμP°PeC†C-C—.

*P—P°CṛC,PsCṛCṛPIP°PSPSCḷ Cṛ PīPμCḡC-PsPr PIP°PiC-C,PSPsCṛC,C- P°P±Ps
PiPsPrCṛPIP°PSPSCḷ PiCḡCṛPrCḡ.*

P-C-PSPePē CḡPμPīCḡPsPrCṛPeC,PēPIPSPsPiPs PIC-PeCṛ/ PḡC-PSPePē, CḷPeC-
PIPēPePsCḡPēCṛC,PsPICṛCḡC,CH PePsPSC,CḡP°C†PμPīC†C-Cḡ

P-C-PSPeP°Pj CḡPμPīCḡPsPrCṛPeC,PēPIPSPsPiPs PIC-PeCṛ PīPsC,CḡC-P±PSPs CṛPSPēPeP°C,Pē
PIP°PiC-C,PSPsCṛC,C- PiC-Pr C†P°Cṛ PīCḡPēPMsPsPjCṛ P»C-PeP°CḡCṛCHPePsPiPs
P·P°CṛPsP±Cṛ P PμP°PiC-P»P°. PμP°C†C-C" PSC,PePē CḡPμPīCḡPsPrCṛPeC,PēPIPSPsPiPs
PIC-PeCṛ PjP°CḡC,CH PIPēPePsCḡPēCṛC,PsPICṛPIP°C,Pē PIPēCṛPsPePsPμC,,PμPeC,PēPIPSC-
PjPμC,PsPrPē PePsPSC,CḡP°C†PμPīC†C-C— PiC-Pr C†P°Cṛ P»C-PeCṛPIP°PSPSCḷ C,P°
C%PsPSP°PMsPjPμPSCēPμ PīCḡPsC,CḷPiPsPj 10 C,PēPḡPSC-PI PiC-CṛP»Cḷ PīCḡPēPMsPsPjCṛ
PsCṛC,P°PSPSCHPsC— PrPsP·Pē PīCḡPμPīP°CḡP°C,Cṛ P PμP°PiC-P»P°.

P'P°PiC-C,PSC-CṛC,CH

P"°PSC- C%PsPrPs P·P°CṛC,PsCṛCṛPIP°PSPSCḷ PeP°CḡPēPīCḡP°P·PēPSCṛ PIP°PiC-C,PSPePj
PḡC-PSPeP°Pj PIC-PrCṛCṛC,PSC- P°P±Ps PsP±PjPμPḡPμPSC-.

P"PsCṛP»C-PrPḡPμPSPSCḷ PSP° C,PIP°CḡPēPSP°C... PīPsPeP°P·P°P»Pē
CḡPμPīCḡPsPrCṛPeC,PēPIPSṛ C,PsPeCṛPēC†PSC-CṛC,CH, PIPeP»CḡC†PSPs P· PIP°PrP°PjPē
CḡPsP·PIPēC,PeCṛ Cṛ C%CṛCḡC-PI (PrPēPI. CḡPsP·PrC-P» B«P"°PSC-
PrPsPeP»C-PSC-C†PSPēC... PrPsCṛP»C-PrPḡPμPSCḡ P· P±PμP·PīPμPePēB»).

P—P°CṛC,PsCṛCṛPIP°PSPSCḷ PīCḡPμPīP°CḡP°C,Cṛ P PμP°PiC-P»P° PSPμ
CḡPμPePsPjPμPSPṛCṛC" C,CHCṛCḷ PīCḡPsC,CḷPiPsPj PIP°PiC-C,PSPsCṛC,C-, P° C,P°PePsPḡ
PḡC-PSPeP°Pj CḡPμPīCḡPsPrCṛPeC,PēPIPSPsPiPs PIC-PeCṛ, CḷPeC- PSPμ
PIPēPePsCḡPēCṛC,PsPICṛCḡC,CH PμC,,PμPeC,PēPIPSCṛ PePsPSC,CḡP°C†PμPīC†C-Cḡ.
PμC-CṛP»Cḷ PīCḡPēPīPēPSPμPSPSCḷ P»C-PeCṛPIP°PSPSCḷ PeP°CḡPēPīCḡP°P·PēPSPsPj
C†PμCḡPμP· PīPsPIC-P»CHBPSPμ PIPēPIPμPrPμPSPSCḷ P°PeC,PēPIPSPēC...
PePsPjPīPsPSPμPSC,C-PI PjPμC,PsPrPē PePsPSC,CḡP°C†PμPīC†C-C— PīPsC,CḡC-P±PSPs
P·P°CṛC,PsCṛPsPICṛPIP°C,Pē C%PsPSP°PMsPjPμPSCēPμ PīCḡPsC,CḷPiPsPj 10 C,PēPḡPSC-PI.

PkPsPIPsPSP°CḡPsPrPḡPμPSC-, PSP° CḷPePēC... PIPiP»PēPIP°P»Pē
P°PSC,PēPīCṛPēC...PsC,PēPePē (PIPeP»CḡC†PSPs P· PeP°CḡPēPīCḡP°P·PēPSPsPj) PīC-Pr C†P°Cṛ
C,CḡPμC,CHPsPiPs C,CḡPēPjPμCṛC,CḡCṛ PIP°PiC-C,PSPsCṛC,C-, P·PSP°C...PsPrCḷC,CHCṛCḷ
PI PiCḡCṛPīC- CḡPēP·PēPeCṛ CḡPsP·PIPēC,PeCṛ C,P°PePēC... PīPsP±C-C†PSPēC...

CḡPμP°PeC†C-PM₆, CḡPe PμPeC†C, CḡP°PīC-CḡP°PjC-PrPSC- CḡPēPjPīC, PsPjPē C, P°/P°P±Ps
 CḡPēPjPīC, PsPjPē PIC-PrPjC-PSPē, CḡPeC- PjPsP¶C†C, CH P±C†C, Pē CḡC-P·PSPsC—
 C, CḡP¶PePsC†C, C- C, P° C, CḡPēPIP°P»PsC†C, C-. PμPsPIC-PrPsPjP»CḡP»PsC†Cḡ PīCḡPs
 P·P±C†PrP¶PμPSPSCḡ, PiC-PīPμCḡC, PsPSC-Cḡ, PiC-PīPsC, PsPSC-Cḡ, C, CḡPμPjPsCḡ,
 CḡPsPSP»PēPIC-C†C, CH, CḡPμCḡPīC-CḡP°C, PsCḡPSPēPN₆ PrPēC†C, CḡPμCḡ-CḡPēPSPḡCḡPsPj
 C, P° PīPsCḡC†C¶PμPSPSCḡ PIP¶PēPIP°PSPSCḡ C—P¶C-. PḡC- C†CḡPeP»P°PrPSPμPSPSCḡ
 CḡC-P·PSPēP»PēC†Cḡ P·P° C, CḡP¶PeC-C†C, CH; CḡPeC%Ps C† PrPμCḡPePēC...
 PIPēPīP°PrPeP°C... CḡPēPjPīC, PsPjPē P·PSPēPeP°P»Pē CḡP°PjC- CḡPsP±PsCḡ, C, Ps PI
 C-PSCēPēC... PIPēPīP°PrPeP°C... PSPsPIPsPSP°CḡPsPrP¶PμPSC- PīPsC, CḡPμP±C†PIP°P»Pē
 P»C-PeC†PIP°PSPSCḡ C† PIC-PrPrC-P»PμPSPSC- C-PSC, PμPSCḡPēPIPSPsC— C, PμCḡP°PīC-C—
 C, P° C, CḡPēPIP°P»PsC— PīPsCḡPīC-C, P°P»C-P·P°C†C-C—. PḡPsPjC† P·P° C†C, P°PSPsPj
 PSPsPIPsPSP°CḡPsPrP¶PμPSPēC... PīPsC, CḡC-P±PSPs CḡPμC, PμP»CHPSPs
 CḡPīPsC†C, PμCḡC-PiP°C, Pē.

P°PsPrC†PIP°PSPSCḡ PīCḡC†PrPrCḡ

P°PsC†C- PSPμPIC-PrPsPjPs, C†Pē PIPēPrC-P»CḡCḡC, CHC†Cḡ PeP°CḡPēPīCḡP°P·PēPS C, P°
 PM₆PsPiPs PsCḡPSPsPIpsc- PjPμC, P°P±PsP»C-C, Pē P· PjPsP»PsPePsPj P»CḡPrPēPSPē.
 PḡP°CḡPēPīCḡP°P·PēPS C, P° PM₆PsPiPs PjPμC, P°P±PsP»C-C, Pē PIPēPrC-P»CḡCḡC, CHC†Cḡ P·
 PjPsP»PsPePsPj C%C†CḡC-PI PīC-Pr C†P°Cḡ P»P°PeC, P°C†C-C— (PrPēPI. CḡPsP·PrC-P»
 B«P°P°PSC- PrPsPeP»C-PSC-C†PSPēC... PrPsCḡP»C-PrP¶PμPSCḡ P· P±PμP·PīPμPePēB»). PḡPμ
 PjPsP¶PSP° PIPēPeP»CḡC†P°C, Pē PIPīP»PēPIC† PSP°
 PSPsPIPsPSP°CḡPsPrP¶PμPSPēC.../PSPμPjPsPIP»CḡC,. PμC-Pr C†P°Cḡ P»C-PeC†PIP°PSPSCḡ
 PeP°CḡPēPīCḡP°P·PēPSPsPj PīPsC, CḡC-P±PSPs PīPμCḡPμCḡPIP°C, Pē PīPsPrC†PIP°PSPSCḡ
 PīCḡC†PrPrCḡ.

PμPμCḡC, PēP»CHPSC-C†C, CH

P·PīP»PēPI PeP°CḡPēPīCḡP°P·PēPSC† PSP° C, PμCḡC, PēP»CHPSC-C†C, CH P»CḡPrPēPSPē PSPμ
 P±C†PI PIPēPIC†PμPSPēPN₆. Pj PrPsCḡP»C-PrP¶PμPSPSCḡC... PSP° C%C†CḡP°C...
 CḡPīPsC†C, PμCḡC-PiP°P»PsC†Cḡ P·PSPēP¶PμPSPSCḡ C, PμCḡC, PēP»CHPSPsC†C, C- C, P°
 PīPsPeP°P·PSPēPeC-PI P·P°PīP»C-PrPSPμPSPSCḡ C† CḡP°PjPsPe (PrPēPI. CḡPsP·PrC-P»
 B«P°P°PSC- PrPsPeP»C-PSC-C†PSPēC... PrPsCḡP»C-PrP¶PμPSCḡ P· P±PμP·PīPμPePēB»).

*P—PrP°C, PSC-C†C, CH PIPīP»PēPIP°C, Pē PSP° CēPIPēPrPeC-C†C, CH CḡPμP°PeC†C-C— PīCḡPē
 PePμCḡC†PIP°PSPSC- P°PIC, PsC, CḡP°PSCḡPīPsCḡC, PsPj P°P±PsB C-PSCēPēPjPē
 PjPμC...P°PSC-P·PjP°PjPē.*

PḡP°CḡPēPīCḡP°P·PēPS PjP°C” CḡP»P°P±PePēPN₆ P°P±Ps PīPsPjC-CḡPSPēPN₆ PIPīP»PēPI PSP°
 P·PrP°C, PSC-C†C, CH PīP°C†C-C”PSC, C-PI PePμCḡC†PIP°C, Pē P°PIC, PsC, CḡP°PSCḡPīPsCḡC, PsPj
 C, P° PīCḡP°C†CḡPIP°C, Pē P· C-PSCēPēPjPē PjPμC...P°PSC-P·PjP°PjPē. PμP°C†C-C”PSC, C-PI
 PīPsC, CḡC-P±PSPs P·P°C†C, PμCḡPμPiC, Pē PIC-Pr CḡPsP±PsC, Pē P· PSPμP±PμP·PīPμC†PSPēPjPē
 PjPμC...P°PSC-P·PjP°PjPē, PIPeP»CḡC†PSPs P· P°PIC, PsC, CḡP°PSCḡPīPsCḡC, PsPj, PrPsPīPsPePē
 PIPsPSPē PSPμ P±C†PrC†C, CH C†C-P»PePsPj PIPiPμIPSPμPSC-, C%Ps
 P»C-PeP°CḡCḡCHPePēPN₆ P·P°C†C-P± P PμP°PiC-P»P° PSPμ PjP°C” PSP° PSPēC...
 PSPμPiP°C, PēIPSPsPiPs PIPīP»PēPIC†.

PḡPīPsC†C-P± P·P°C†C, PsC†C†PIP°PSPSCḡ C, P° PrPsP·Pē.

P"PsP·CfPIP°PSPSCl

P PμPePsPjPμPSPPrPsPIP°PSP° PīPsC±P°C,PePsPIP° PrPsP·P° PeP°CḡPēPīCḡP°P·PēPSCr
CfC,P°PSPsPIPēC,Ch 1,5 PjPi PsPrPēPS CḡP°P· PSP° PrPsP±Cf. P—PīPsPrPsPj PrPsP·Cf Cf
CḡP°P·C- PīPsC,CḡPμP±Pē PjPsP¶PSP° PīPsPIC-P»ChPSPs PīC-PrPIPēC‰CfPIP°C,Pē PīPs
1,5 PjPi PrPs PjP°PeCfPēPjP°P»ChPSPsC— PrPsP·Pē 6 PjPi/PrPsP±Cf. PkP°PNēPSPēP¶C±P°
PμC,,PμPeC,PēPIPSP° PrPsP·P° PjP°C" PīC-PrC,CḡPēPjCfPIP°C,PēCfCμ P·PīC-PrPSPs P·
PeP»C-PSC-C±PSPsCḡ PsC†C-PSPePsCḡ P»C-PeP°CḡCμ. P§PμCḡPμP· PrPsPIPīPēPNē
PīPμCḡC-PsPr PSP°PīC-PIPIPēPIPμPrPμPSPSCl PeP°CḡPēPīCḡP°P·PēPSCr C,P° PNēPsPiPs
P°PeC,PēPIPSPēC... PjPμC,P°P±PsP»C-C,C-PI P·PjC-PSPē PI PrPsP·CfPIP°PSPSC- PSPμ
P±CfPrCfC,Ch PīPsPIPSC-CfC,Cḡ PIC-PrPsP±CḡP°P¶P°C,PēCfCμ PI PīP»P°P·PjC-
PīCḡPsC,CμPīPsPj PeC-P»ChPePsC... C,PēP¶PSC-PI. P—P° CfC,P°PSPsPj PīP°C†C-C"PSC,P°
C,CḡPμP±P° CfPīPsCfC,PμCḡC-PiP°C,Pē CfC,PsCfPsPIPSPs PīPsCμPIPē PīPsP±C-C±PSPēC...
CḡPμP°PeC†C-PNē C,P° PIC-PrPīPsPIC-PrC- PSP° P»C-PeCfPIP°PSPSCl PīCḡPsC,CμPīPsPj
PeC-P»ChPePsC... C,PēP¶PSC-PI PīC-CfP»Cμ PīPsC±P°C,PeCf PīCḡPēPNēPsPjCf
PeP°CḡPēPīCḡP°P·PēPSCr C,P° PīC-CfP»Cμ PePsP¶PSPsC— P·PjC-PSPē PrPsP·CfPIP°PSPSCl
(PrPēPI. CḡPsP·PrC-P» B«PαP°CḡPjP°PePsPeC-PSPμC,PēPeP°B».).

*PμPμCḡPμC...C-Pr P· C-PSCēPēC... P°PSC,PēPīCfPēC...PsC,PēPeC-PI PSP°
PeP°CḡPēPīCḡP°P·PēPS*

PμCḡPē PīPμCḡPμC...PsPrC- P· C-PSCēPēC... P°PSC,PēPīCfPēC...PsC,PēPeC-PI PSP°
PeP°CḡPēPīCḡP°P·PēPS PīPsC,CḡC-P±PSPs PICḡP°C...PsPICfPIP°C,Pē PīPsCfC,CfPīPsPIPμ
PīPμCḡPμC...CḡPμCfPSPμ C,PēC,CḡCfPIP°PSPSCl P· PīPsCfC,CfPīPsPIPēPj
PīCḡPēPīPēPSPμPSPSClPj P·P°CfC,PsCfCfPIP°PSPSCl PīPsPīPμCḡPμPrPSCḡPsC—
C,PμCḡP°PīC-C— PīC-Pr C±P°Cf PīPsC±P°C,PeCf PīCḡPēPNēPsPjCf PeP°CḡPēPīCḡP°P·PēPSCr.

PμPμCḡPμC...C-Pr P· PeP°CḡPēPīCḡP°P·PēPSCē PSP° C-PSCēPēPNē P°PSC,PēPīCfPēC...PsC,PēPe

PμCḡPē PīPμCḡPμC...PsPrC- P· PeP°CḡPēPīCḡP°P·PēPSCr PSP° C-PSCēPēPNē
P°PSC,PēPīCfPēC...PsC,PēPe PīPsCfC,CfPīPsPIPμPīPs PīPμCḡPμC...CḡPμCfPSPsPiPs
C,PēC,CḡCfPIP°PSPSCl PSPμ PIC-PrP±CfPIP°C,PēPjPμC,ChCfCμ C,PsPjCf PīCḡPēPNēPsPj
PSPsPiPsPiPs P°PSC,PēPīCfPēC...PsC,PēPeP° PjPsP¶PSP° PīPsC±PēPSP°C,Pē P· PNēPsPiPs
PSP°PNēPSPēP¶C±PsC— PrPsP·Pē PīC-Pr C±P°Cf PīCḡPēPīPēPSPμPSPSCl
PIPēPePsCḡPēCfC,P°PSPSCl PeP°CḡPēPīCḡP°P·PēPSCr. PμPsC,CḡC-P±PSPs
PICḡP°C...PsPICfPIP°C,Pē, C‰Ps PePsPSC†PμPSC,CḡP°C†C-Cμ PeP°CḡPēPīCḡP°P·PēPSCr C,P°
PNēPsPiPs P°PeC,PēPIPSPēC... PjPμC,P°P±PsP»C-C,C-PI PI PīP»P°P·PjC- P·PjPμPSCēPēC,ChCfCμ
PSP° 50 % PīCḡPēP±P»PēP·PSPs PīCḡPsC,CμPīPsPj 1 C,PēP¶PSCl (PrPēPI. CḡPsP·PrC-P»
B«PαP°CḡPjP°PePsPeC-PSPμC,PēPeP°B»).

PμCḡPsPīCēCfPe PīCḡPēPNēPsPjCē C,P°P±P»PμC,PsPe

PμCḡPē PīCḡPsPīCfCfPeCf PīCḡPēPNēPsPjCf C,P°P±P»PμC,PePē PīP°C†C-C"PSC, PīPsPIPēPSPμPS
PSPμPīP°PNēPSPs PīCḡPēPNēPSClC,Pē PīCḡPsPīCfC‰PμPSCr C,P°P±P»PμC,PeCf. PhPrPSP°Pe
CμPeC‰Ps CfP¶Pμ PjP°PNēP¶Pμ PSP°CfC,P°PI C±P°Cf PīCḡPēPNēPsPjCf PSP°CfC,CfPīPSPsC—
C,P°P±P»PμC,PePē, PīCḡPsPīCfC‰PμPSCr C,P°P±P»PμC,PeCf PSPμ PIP°CḡC,Ps
PīCḡPēPNēPjP°C,Pē, P° CfP»C-Pr PīCḡPēPNēPSClC,Pē PSP°CfC,CfPīPSCr PrPsP·Cf P·PīC-PrPSPs
P·C- P·PIPēC±P°PNēPSPēPj PīCḡP°C,,C-PePsPj. PkPμ CḡPμPePsPjPμPSPPrCfC",ChCfCμ
PīCḡPēPNēPjP°C,Pē PīPsPrPIC-PNēPSCr PrPsP·Cf, C‰PsP± PePsPjPīPμPSCfCfPIP°C,Pē
PīCḡPsPīCfC‰PμPSCr PrPsP·Cf.

PhCfPsP±P»PēPIC- PīCḡCfPīPē PīP°C†C-C"PSC,C-PI

PμPsCḡCžC€PμPSPSCḡ C,,CžPSPeC†C-C— PSPëCḡPsPe

PμP°C†C-C" PSC,Pë P· PīPsCḡC†C€PμPSPSCḡPj C,,C†PSPeC†C-C— PSPëCḡPsPe P»PμPiPePsPiPs C†Pë C†PμCḡPμPrPSCḡPsPiPs C†C,C†PīPμPSCḡ C,CḡP¶PēPsC†C,C- (PeP»C-CḡPμPSC† PeCḡPμP°C,PëPSC-PSC† (CrCl) ≥ 30 PjP»/C...PI C,P° < 89 PjP»/C...PI) PSPμ PīPsC,CḡPμP±C†CḡC,Cḡ P¶PēPsPrPSPëC... PePsCḡPëPīC†PIP°PSCḡ PrPsP·Pë. P'PμP·PīPμC†PSC-C†C,Cḡ C,P° PμC,,PμPeC,PëPIPSC-C†C,Cḡ P·P°C†C,PsC†C†PIP°PSPSCḡ PeP°CḡPëPīCḡP°P·PëPSC† PrP»Cḡ PīP°C†C-C" PSC,C-PI C-P· C,CḡP¶PēPëPj PīPsCḡC†C€PμPSPSCḡPj C,,C†PSPeC†C-C— PSPëCḡPsPe (CrCl < 30 PjP»/C...PI) PSPμ PsC†C-PSCḡPIP°P»PëC†Cḡ. PμP°C†C-C" PSC,P°Pj C-P· C,CḡP¶PēPëPj PīPsCḡC†C€PμPSPSCḡPj C,,C†PSPeC†C-C— PSPëCḡPsPe PSPμ CḡPμPePsPjPμPSP†C†C",CḡC†Cḡ PīCḡPëPNēPsPj PeP°CḡPëPīCḡP°P·PëPSC† (PrPëPI. CḡPsP·PrC-P» B«PαP°CḡPjP°PePsPeC-PSPμC,PëPeP°B»).

PμPsCḡCžC€PμPSPSCḡ C,,CžPSPeC†C-C— PīPμC†C-PSPePë

PμP°C†C-C" PSC,Pë P· PīPsCḡC†C€PμPSPSCḡ C,,C†PSPeC†C-C— PīPμC†C-PSPePë P»PμPiPePsPiPs P°P±Ps C†PμCḡPμPrPSCḡPsPiPs C†C,C†PīPμPSCḡ C,CḡP¶PēPsC†C,C- (5Bḡ"9 P·P° C€PeP°P»PsCḡ P§P°PNēP»PrP° Bḡ" PμBḡ™ Cḡ) PSPμ PīPsC,CḡPμP±C†CḡC,Cḡ P¶PēPsPrPSPëC... PePsCḡPëPīC†PIP°PSCḡ PrPsP·Pë. P'PμP·PīPμC†PSC-C†C,Cḡ C,P° PμC,,PμPeC,PëPIPSC-C†C,Cḡ P·P°C†C,PsC†C†PIP°PSPSCḡ PeP°CḡPëPīCḡP°P·PëPSC† B PrP»Cḡ PīP°C†C-C" PSC,C-PI C-P· C,CḡP¶PēPëPj PīPsCḡC†C€PμPSPSCḡPj C,,C†PSPeC†C-C— PīPμC†C-PSPePë (10Bḡ"15 P·P° C€PeP°P»PsCḡ P§P°PNēP»PrP° Bḡ" PμBḡ™ Cḡ) PSPμ PsC†C-PSCḡPIP°P»PëC†Cḡ. PμP°C†C-C" PSC,P°Pj C-P· C,CḡP¶PēPëPj PīPsCḡC†C€PμPSPSCḡPj C,,C†PSPeC†C-C— PīPμC†C-PSPePë PSPμ CḡPμPePsPjPμPSP†C†C",CḡC†Cḡ PīCḡPëPNēPsPj PeP°CḡPëPīCḡP°P·PëPSC† (PrPëPI. CḡPsP·PrC-P» B«PαP°CḡPjP°PePsPeC-PSPμC,PëPeP°B»).

PμP°C†C-C" PSC,Pë P»C-C,PSCHPsPiPs PIC-PeCž

P"PsC†C,C†PīPSPëC... PrP°PSPëC... C†C,PsC†PsPIPSPs P»C-PeC†PIP°PSPSCḡ PeP°CḡPëPīCḡP°P·PëPSPsPj PīP°C†C-C" PSC,C-PI P»C-C,PSCHPsPiPs PIC-PeC† (≥ 65 CḡPsPeC-PI) PSPμPrPsC†C,P°C,PSCHPsB PrP»Cḡ PIPëCḡPIP»PμPSPSCḡ PIC-PrPjC-PSPSPC†C,PμPNē C—C...PSCHPsC— PIC-PrPīPsPIC-PrC- PSP° P»C-PeC†PIP°PSPSCḡ PIC-Pr PIC-PrPīPsPIC-PrC- PīP°C†C-C" PSC,C-PI PjPsP»PsPrC€PsPiPs PIC-PeC† (PrPëPI. CḡPsP·PrC-P» B«PαP°CḡPjP°PePsPeC-PSPμC,PëPeP°B»). PμC-PrP±C-Cḡ PrPsP·Pë PrP»Cḡ PīP°C†C-C" PSC,C-PI P»C-C,PSCHPsPiPs PIC-PeC† PjP°C" P±C†C,Pë P±C-P»CHC€ PsP±PμCḡPμP¶PSPëPj.

PŸPīPsC†C-P± P·P°C†C,PsC†C†PIP°PSPSCḡ

P»C-PeP°CḡC†CḡPePëPNē P·P°C†C-P± P PμP°PiC-P»P° P·P°C†C,PsC†PsPIC†PIP°C,Pë PīPμCḡPsCḡP°P»CHPSPs 1 CḡP°P· PSP° PrPsP±C† PI PsPrPëPS C- C,PsPNē C†P°PjPëPNē C†P°C† PSPμP·P°P»PμP¶PSPs PIC-Pr PIP¶PëPIP°PSPSCḡ C—P¶C-.

PμCḡPë P·P°C†C,PsC†C†PIP°PSPSC- PeP°CḡPëPīCḡP°P·PëPSC† C†P»C-Pr C†PSPëPeP°C,Pë PIP¶PëPIP°PSPSCḡ P°P»PePsPiPsP»Cḡ (PrPëPI. CḡPsP·PrC-P» B«P'P·P°C" PjPsPrC-Cḡ P· C-PSC€PëPjPë P»C-PeP°CḡC†CḡPePëPjPë P·P°C†PsP±P°PjPë C,P° C-PSC€C- PIPëPrPë PIP·P°C" PjPsPrC-PNēB»).

P"C-C,Pë.

P'PμP·PīPμPeC† C,P° PμC,,PμPeC,PëPIPSC-C†C,Cḡ P·P°C†C,PsC†C†PIP°PSPSCḡ

PeP°CḡPēPīCḡP°P·PēPSCř PrP»Cḡ PrC-C,PμPNē (PIC-PePsPj PrPs 18 CḡPsPeC-PI) PSPμ
PICřC,P°PSPsPIP»PμPSPs. PkPμPjP°C” PrP°PSPēC....

PμPμCḡPμPrPsP·CzPIP°PSPSCḡ.

PŸPēPjPīC,PsPjPē

PμPsPIC-PrPsPjP»CḡP»PsCřCḡ PīCḡPs PIPēPīP°PrPePsPIPμ PiPsCřC,CḡPμ
PīPμCḡPμPrPsP·CřPIP°PSPSCḡ (48 PjPi/PrPsP±Cř) PI PsPrPSPsPiPs PīP°C†C-C”PSC,P° . PJ
C†CHbPsPiPs PīP°C†C-C”PSC,P° P·Bḡ™ CḡPIPēP»PēCřCḡ PsCḡC,PsCřC,P°P· C,P°
CřPμPrP°C,PēPIPSPēPNē PμC,,PμPeC,. PŸC,P°PS PīP°C†C-C”PSC,P° PīPsPIPSC-CřC,Cḡ
PIC-PrPSPsPIPēPICřCḡ PI C,PsPNē PḡPμ PrPμPSCḡ.

P>C-PeCřPIP°PSPSCḡ PīCḡPē PīPμCḡPμPrPsP·CřPIP°PSPSC-

P>C-PeCřPIP°PSPSCḡ PīCḡPē PīPμCḡPμPrPsP·CřPIP°PSPSC- PjP°C” P±CřC,Pē
PīC-PrC,CḡPēPjCřPIP°P»CHbPSPμ, PIPeP»CḡC†PSPs P· PīC-PrC,CḡPēPjPePsCḡ PIC-P»CHbPSPsC—
PīCḡPsC...C-PrPSPsCřC,C- PrPēC...P°P»CHbPSPēC... CēP»CḡC...C-PI, PSP°CřPēC†PμPSPSCḡPj
PePēCřPSPμPj C,P° PIPμPSC,PēP»CḡC†C-C”Cḡ, P° C,P°PePsPḡ CřPēPjPīC,PsPjP°C,PēC†PSPμ.
PŸPiPsCřC,PμCḡPμPḡPμPSPSCḡ P·P° CřPμCḡC†PμPIPs-CřCřPrPēPSPSPsCḡ CřPēCřC,PμPjPsCḡ
PjP°C” CḡPsP·PiPsC†PēPSP°C,PēCřCḡ PSPμPīP°PNēPSPs C,P° PIPeP»CḡC†P°C,Pē
PμP»PμPeC,CḡPsPeP°CḡPrC-PsPiCḡP°C,,C-C†PSPēPNē PjPsPSC-C,PsCḡPēPSPi PrP»Cḡ
PIPēCḡPIP»PμPSPSCḡ PjPsPḡP»PēPIPēC... P°CḡPēC,PjC-PNē. PJ CḡP°P·C-
PIPēPSPēPePSPμPSPSCḡ C,CḡPḡPePēC... PμPeCřC,CḡP°PīC-CḡP°PjC-PrPSPēC...
CřPēPjPīC,PsPjC-PI CřP»C-Pr P·P°CřC,PsCřCřPIP°C,Pē P°PSC,PēC...PsP»C-PSPμCḡPiC-C†PSC-
PīCḡPμPīP°CḡP°C,Pē. PkCřPeC-P»CHbPePē PeP°CḡPēPīCḡP°P·PēPS CřPēP»CHbPSPs
P·PiBḡ™ CḡP·CřC”C,CHbCřCḡ P· P±C-P»PeP°PjPē PīP»P°P·PjPē, PiPμPjPsPrC-P°P»C-P· PSPμ
P±CřPrPμ B PμC,,PμPeC,PēPIPSPēPj PrP»Cḡ P>C-PeCřPIP°PSPSCḡ
PīPμCḡPμPrPsP·CřPIP°PSPSCḡ. PμPēP»CHbPSPēPNē PjPμPrPēC†PSPēPNē PSP°PiP»CḡPḡ C,P°
PjPsPSC-C,PsCḡPēPSPi PjP°CḡC,CHb C,CḡPēPIP°C,Pē PrPsC,Pē, PrPsPePē CřC,P°PS
PīP°C†C-C”PSC,P° PSPμ PIC-PrPSPsPIPēC,CHbCřCḡ.

PḡP°CḡPēPīCḡP°P·PēPS PSPμ PjP°C” CřPīPμC†PēC,,C-C†PSPsPiPs P°PSC,PēPrPsC,Cř.

PμPsP±C-C†PSC- CḡPμP°PeC†C-C—.

PμPsP±C-C†PSPēPjPē CḡPμP°PeC†C-CḡPjPē, PīCḡPs CḡPeC- PSP°PNēC†P°CřC,C-CēPμ
PīPsPIC-PrPsPjP»CḡP»PsCřCḡ PīCḡPē P·P°CřC,PsCřCřPIP°PSPSC- PeP°CḡPēPīCḡP°P·PēPSCř PI
PrC-P°PīP°P·PsPSC- PrPsP· (1,5Bḡ“6 PjPi), P±CřP»Pē P°PeP°C,PēP·C-Cḡ (19 %) C,P°
PīP°CḡPeC-PSCřPsPSC-P·Pj (17,5 %). P’C-P»CHbCēC-CřC,CHb CḡPμP°PeC†C-PNē P±CřP»Pē
P»PμPiPePsPiPs C†Pē CřPμCḡPμPrPSCḡPsPiPs CřC,CřPīPμPSCḡ C,CḡPḡPePsCřC,C-.

PŸP°P±P»PēC†PSPēPNē PīPμCḡPμP»C-Pe PīPsP±C-C†PSPēC... CḡPμP°PeC†C-PNē

PμPsP±C-C†PSC- P»C-PeP°CḡCřCHbPeC- CḡPμP°PeC†C-C— (PμP>P) PSP° PsCřPSPsPIC-
PsP±Bḡ™ C”PrPSP°PSPēC... PrP°PSPēC... P· PrPsCřP»C-PrPḡPμPSPSCḡ P>C-PeCřPIP°PSPSCḡ
CēPēP·PsC,,CḡPμPSC-C— PeP°CḡPēPīCḡP°P·PēPSPsPj PīCḡPμPrCřC,P°PIP»PμPSPs P·P°
CřPēCřC,PμPjP°PjPē PsCḡPiP°PSC-PI C- P· PIPēPePsCḡPēCřC,P°PSPSCḡPj
PIC-PrPīPsPIC-PrPSPsPiPs C,PμCḡPjC-PSP° Cř C,P°P±P»PēC†C- 3.

PyP°P±P»PëC†C¶ 3. P¶P±P±C-C†PSC- C¶P¶P°PeC†C-C-, C%oPs PIPëPSPëPeP°CFHC,CH C†
PiP°C†C-C''PSC,C-PI C-P· C¶PëP·PsC,,C¶P¶PSC-C''CF

[illegible]¹ P PsP·P»P°PrPë CÍPSCr: P±PuP·CÍPsPSPSCll, P°PSPsPjP°P»CHbPSC- CÍPSPë, PePsC€PjP°CHPë,

P PsP·PIPëC,PsPe PeP°C,P°CĤP°PeC,Pë CÍPíPsCÍC,PμCĤC-PiP°PICÍCĬ PíC-Pr C‡P°CÍ
 PrPsPeP»C-PSC-C‡PSPëC... PrPsCÍP»C-PrP¶PμPSCĤ PeP°CĤPëPíCĤP°P·PëPSCr (PrPëPI.
 CĤPsP·PrC-P» B«P”P°PSC- PrPsPeP»C-PSC-C‡PSPëC... PrPsCÍP»C-PrP¶PμPSCĤ P·
 P±PμP·PíPμPePëB»). PŷPsPjCÍ P·P° C„PsCĤPjCÍPIP°PSPSCĬPj PeP°C,P°CĤP°PeC,Pë
 CÍPíPsCÍC,PμCĤC-PiP°P»Pë P·P° PrPsPíPsPjPsPiPsCĤ PsPiP»CĬPrC-PI C-P·
 C%oC-P»PëPSPSPSCĤ P»P°PjPíPsCĤ, P° PíP°C†C-C”PSC,Pë, CĬPeC- PIP¶Pμ PjP°P»Pë
 PeP°C,P°CĤP°PeC,CÍ, P±CÍP»Pë PIPëPeP»CĤC‡PμPSC- P· PrPsCÍP»C-PrP¶PμPSPSCĬ. PμC-Pr
 C‡P°CÍ PeP»C-PSC-C‡PSPsC— PíCĤPsPiCĤP°PjPë PrPsCÍP»C-PrP¶PμPSPSCĬ PrC-C—
 PeP°CĤPëPíCĤP°P·PëPSCr CÍ PíP°C†C-C”PSC,C-PI P· C€PëP·PsC„CĤPμPSC-C”CĤ
 PíPsPIC-PrPsPjP»CĬP»PsCÍCĬ PíCĤPs PeC-P»CĤPeP° PIPëPíP°PrPeC-PI PeP°C,P°CĤP°PeC,Pë,
 C%oPs C...P°CĤP°PeC,PμCĤPëP·CÍPIP°P»P°CÍCĬ PSPμP·PSP°C‡PSPëPj PíPsPjCÍC,PSC-PSPSCĬPj
 PeCĤPëC€C,P°P»PëPeP° P±PμP· PíPsCĤCÍC€PμPSPSCĬ P·PsCĤCÍ (13/3192; 0,4 %). P”PμCĬPeC-
 P· C†PëC... PíP°C†C-C”PSC,C-PI PjP°P»Pë C‡PëPSPSPëPePë CĤPëP·PëPeCÍ.
 PkP°PNëC‡P°CÍC,C-C€Pμ PíPsPIC-PrPsPjP»CĬP»PsCÍCĬ PíCĤPs C,P°PePëPNë PíPsP±C-C‡PSPëPNë
 PμC„PμPeC, P· P±PsPeCÍ PsCĤPiP°PSC-PI P·PsCĤCÍ, CĬPe PSPμC‡C-C,PeC-CÍC,CĤ P·PsCĤCÍ

(PĭP»P°C†PμP±Ps: 1/683, 0,1 %; PeP°CĤPĕPĭCĤP°P·PĕPS: 22/2048, 1,1 %).

P•PeCĬC,CĤP°PĭC-CĤP°PjC-PrPSC- CĬPĕPjPĭC,PsPjPĕ (P•PμPŸ)

PJ PePsCĤPsC,PePsC,CĤPĕPIP°P»PĕC... PrPsCĬP»C-PrP¶PμPSPSCĬC... C†P°CĬC,PsC,P°
PIPĕPSPĕPePSPμPSPSCĬ P•PμPŸ CĬC,P°PSPsPIPĕP»P° 27 %, 11,5 %, 30,7 % C,P° 15,1 %
PĭP°C†C-C"PSC,C-PI, CĬPeC- P»C-PeCĬPIP°P»PĕCĬCĬ PIC-PrPĭPsPIC-PrPSPs
PeP°CĤPĕPĭCĤP°P·PĕPSPsPj, PĭP»P°C†PμP±Ps, CĤPĕCĬPĭPμCĤPĕPrPsPSPsPj C,P°
P°CĤPĕPĭC-PĭCĤP°P·PsP»PsPj. PĥPeP°C,PĕP·C-CĬ CĬPĭPsCĬC,PμCĤC-PiP°P»P°CĬCĬ PI 13,6 %, 5,1 %, 9,3 % C,P° 9,9 % PĭP°C†C-C"PSC,C-PI, CĬPeC- P»C-PeCĬPIP°P»PĕCĬCĬ
PIC-PrPĭPsPIC-PrPSPs PeP°CĤPĕPĭCĤP°P·PĕPSPsPj, PĭP»P°C†PμP±Ps,
CĤPĕCĬPĭPμCĤPĕPrPsPSPsPj C,P° P°CĤPĕPĭC-PĭCĤP°P·PsP»PsPj. PμP°CĤPeC-PSCĬPsPSC-P·Pj
CĬPĭPsCĬC,PμCĤC-PiP°PICĬCĬ PI 13,6 %, 5,7 %, 22,1 % C,P° 5,3 % PĭP°C†C-C"PSC,C-PI, CĬPeC-
P»C-PeCĬPIP°P»PĕCĬCĬ PIC-PrPĭPsPIC-PrPSPs PeP°CĤPĕPĭCĤP°P·PĕPSPsPj, PĭP»P°C†PμP±Ps,
CĤPĕCĬPĭPμCĤPĕPrPsPSPsPj C,P° P°CĤPĕPĭC-PĭCĤP°P·PsP»PsPj. P"PĕCĬC,PsPSC-CĤ
CĬPĭPsCĬC,PμCĤC-PiP°P»Pĕ PI 1,8 %, 0,2 %, 3,6 % C,P° 0,7 % PĭP°C†C-C"PSC,C-PI, CĬPeC-
P»C-PeCĬPIP°P»PĕCĬCĬ PIC-PrPĭPsPIC-PrPSPs PeP°CĤPĕPĭCĤP°P·PĕPSPsPj, PĭP»P°C†PμP±Ps,
CĤPĕCĬPĭPμCĤPĕPrPsPSPsPj C,P° P°CĤPĕPĭC-PĭCĤP°P·PsP»PsPj.

PJ PĭP»P°C†PμP±PsPePsPSC,CĤPsP»CHPsPIP°PSC-PNĕ C†P°CĬC,PĕPSC-
PrPsCĬP»C-PrP¶PμPSPSCĬ PrPsPIPĭPsC,CĤPĕPIP°P»PsC— PĭC-PrC,CĤPĕPjPePĕ PμC,,PμPeC,CĬ
C†P°CĬC,PsC,P° P•PμPŸ CĬC,P°PSPsPIPĕP»P° 13,7 % CĬ PiCĤCĬPĭC-, CĬPeP° PĭCĤPĕPNĕPjP°P»P°
PeP°CĤPĕPĭCĤP°P·PĕPS, CĬ PĭPsCĤC-PIPSCĬPSPSC- P· 3,0 % CĬ PiCĤCĬPĭC-, CĬPeP°
PsC,CĤPĕPjCĬPIP°P»P° PĭP»P°C†PμP±Ps. PĥPeP°C,PĕP·C-CĬ CĬPĭPsCĬC,PμCĤC-PiP°P»P°CĬCĬ PI
3,9 % PĭP°C†C-C"PSC,C-PI, CĬPeC- P»C-PeCĬPIP°P»PĕCĬCĬ PeP°CĤPĕPĭCĤP°P·PĕPSPsPj,
PĭCĤPsC,Pĕ 2,0 % PI PiCĤCĬPĭC-, CĬPeP° PĭCĤPĕPNĕPjP°P»P° PĭP»P°C†PμP±Ps.
PμP°CĤPeC-PSCĬPsPSC-P·Pj CĬPĭPsCĬC,PμCĤC-PiP°PICĬCĬ PI 7,8 % C,P° 1,0 % CĬ
PiCĤCĬPĭP°C..., C%Ps PIC-PrPĭPsPIC-PrPSPs PĭCĤPĕPNĕPjP°P»Pĕ PeP°CĤPĕPĭCĤP°P·PĕPS C,P°
PĭP»P°C†PμP±Ps.

PJ PrPsCĬP»C-PrP¶PμPSPSC- PSPμPiP°C,PĕPIPSPĕC... CĬPĕPjPĭC,PsPjC-PI PĭCĤPs P•PμPŸ
PĭPsPIC-PrPsPjP»CĬP»PsCĬCĬ PI 14,3 % CĬ PiCĤCĬPĭC-, C%Ps PĭCĤPĕPNĕPjP°P»P°
PeP°CĤPĕPĭCĤP°P·PĕPS, C,P° PI 11,7 % CĬ PiCĤCĬPĭC-, C%Ps P»C-PeCĬPIP°P»P°CĬCĬ
CĤPĕCĬPĭPμCĤPĕPrPsPSPsPj. PĥPeP°C,PĕP·C-CĬ CĬPĭPsCĬC,PμCĤC-PiP°P»P°CĬCĬ PI 10,0 %
PĭP°C†C-C"PSC,C-PI, CĬPeC- P»C-PeCĬPIP°P»PĕCĬCĬ PeP°CĤPĕPĭCĤP°P·PĕPSPsPj, C,P° PI 5,2 %
CĬ PiCĤCĬPĭC-, C%Ps PĭCĤPĕPNĕPjP°P»P° CĤPĕCĬPĭPμCĤPĕPrPsPS. PμP°CĤPeC-PSCĬPsPSC-P·Pj
CĬPĭPsCĬC,PμCĤC-PiP°PICĬCĬ PI 5,2 % C,P° 7,4 % CĬ PiCĤCĬPĭP°C..., C%Ps
PIC-PrPĭPsPIC-PrPSPs PĭCĤPĕPNĕPjP°P»Pĕ PeP°CĤPĕPĭCĤP°P·PĕPS C,P° CĤPĕCĬPĭPμCĤPĕPrPsPS.
P'C-P»CHCĕC-CĬC,CH PIPĕPĭP°PrPeC-PI P•PμPŸ P±CĬP»Pĕ P»PμPiPePsPiPs C†Pĕ
CĬPμCĤPμPrPSCĤPsPiPs CĬC,CĬPĭPμPSCĬ C,CĬP¶PePsCĬC,C- C,P°
PePsPSC,CĤPsP»CHPIP°P»PĕCĬCĬ P·PIPĕC†P°PNĕSPĕPjPĕ P»C-PeP°CĤCĬCHPePĕPjPĕ
P·P°CĬPsP±P°PjPĕ PrP»CĬ P»C-PeCĬPIP°PSPSCĬ P•PμPŸ. P C-PIPμPSCĤ
PĭCĤPĕPĭPĕPSPμPSPSCĬ P»C-PeCĬPIP°PSPSCĬ C†PμCĤPμP· PIPĕPĭP°PrPePĕ P•PμPŸ, C%Ps
PĭPsPIbĤ™ CĬP·P°PSC- P· PμP»P , P±CĬPI PSPĕP·CHPePĕPj.

P'PμPSPsP·PSP° C,CĤPsPjP±PsPμPjP±PsP»C-CĬ (P'PŸP•)

P'PĕPĭP°PrPePĕ P'PŸP•, PIPĕP»CHC†PSPs P· PIPĕPĭP°PrPeP°PjPĕ P»PμPiPμPSPμPIPSC—
PμPjP±PsP»C— C,P° C,CĤPsPjP±PsP·CĬ PĭP»PĕP±PsPePĕC... PIPμPS,
CĬPĭPsCĬC,PμCĤC-PiP°P»PĕCĬCĬ PĭCĤPĕ PĭCĤPĕPNĕPsPjC- P°PSC,PĕPĭCĬPĕC...PsC,PĕPeC-PI.
PŖP°CĬC,PsC,P° PSPμPIC-PrPsPjP°.

Pj PeP»C-PSC-C±PSPsPjCr PrPsCfP»C-PrP¶PµPSPSC- PrP»C¶ PsC†C-PSPePë
PiPsPrPsPIP¶PµPSPSC¶ C-PSC,PµC¶PIP°P»Cr QT PiC¶Pë PiC¶PëPµPsPjC-
PeP°C¶PëPiC¶P°P·PëPSCr PSPµ P±CrP»Ps PiPsPjC-C±PµPSPs P¶PsPrPSPsPiPs
PiPsPrPsPIP¶PµPSPSC¶ C-PSC,PµC¶PIP°P»Cr QT Cr PiPsC¶C-PIPSC¶PSPSC- P· PiP»P°C†PµP±Ps
(PrPëPI. C¶PsP·PrC-P» B«PαP°C¶PjP°PePsPrPëPSP°PjC-PeP°B»). P' C-PSC€PëC...
PeP»C-PSC-C±PSPëC... PrPsCfP»C-PrP¶PµPSPSC¶C... PiPsPIC-PrPsPjP»C¶P»PsCfCH P»PëC€Pµ

ПісПс ПрПмПеС-Р»СНПеР° ПІПєПіР°ПрПеС-ПІ ПСПмР·ПСП°С±ПСПсПіПс ПіПсПрПсПІП¶ПмПСПСЦІ
 С-ПSC,РмСНПІР°Р»Ср QT ПіСНПє ПіСНПєПмПсПјС- ПеР°СНПєПіСНП°Р·ПєПSCр. РмС-Пр С±Р°СІ
 ПрПсПІПіПсС,СНПєПІР°Р»ПсПіПс ПІС-ПрПеСНПєС,ПсПіПс ПіРмСНС-ПсПрСр Р»С-ПеСрПІР°ПСПСЦІ 3
 ПіР°С±С-С"ПSC,Пє (0,4 %) ПјР°Р»Пє СІПеПсСНПєПіПсПІР°ПСПєПм П·Р° С„ПсСНПјСрР»ПсСН
 Р'Р°Р·РмС,С,Р° С-ПSC,РмСНПІР°Р» QT > 500 ПјСІ, Р° ПсПрПєПс С-Р· ПСПєС... ПјР°ПІ
 С-ПSC,РмСНПІР°Р» QT Р· ПеПсСНПєПіСрПІР°ПСПСЦІПј Р»СНПєПрРмСНПєС±С-СІ > 500 ПјСІ.
 РмПсПрПсПІП¶ПмПСПСЦІ ПСП° > 60 ПјСІ СІПеПсСНПєПіПсПІР°ПСПсПіПс Р·Р° С„ПсСНПјСрР»ПсСН
 Р'Р°Р·РмС,С,Р° С-ПSC,РмСНПІР°Р»Ср QT ПІС-Пр ПІПєС...С-ПрПСПсПіПс СНС-ПІПСЦІ
 СІПіПсСІС,РмСНС-ПіР°Р»ПсСІСІ Ср 7 ПіР°С±С-С"ПSC,С-ПІ (1 %), Р° Ср 2 ПіР°С±С-С"ПSC,С-ПІ
 (0,3 %) вН" Р· ПеПсСНПєПіСрПІР°ПСПСЦІПј Р»СНПєПрРмСНПєС±С-СІ. Пј
 ПрПсПІПіПсС,СНПєПІР°Р»ПсПјСр ПрПсСІР»С-ПрП¶ПмПСПSC- ПрР»СІ ПіС-ПрС,СНПєПјР°ПСПСЦІ
 РмС„РмПеС,Ср ПіС-Пр С±Р°СІ ПІС-ПрПеСНПєС,ПсС— СІС,Р°ПрС-С— ПіПсПрПсПІП¶ПмПСПСЦІ
 СІПеПсСНПєПіПсПІР°ПСПсПіПс Р·Р° С„ПсСНПјСрР»ПсСН Р'Р°Р·РмС,С,Р° С-ПSC,РмСНПІР°Р»Ср QT
 ПСП° > 60 ПјСІ ПІС-Пр ПІПєС...С-ПрПСПсПіПс СНС-ПІПСЦІ СІПіПсСІС,РмСНС-ПіР°Р»ПсСІСІ Ср
 12 ПіР°С±С-С"ПSC,С-ПІ (1,6 %), Р° С-ПSC,РмСНПІР°Р»Ср QT Р· ПеПсСНПєПіСрПІР°ПСПСЦІПј
 Р»СНПєПрРмСНПєС±С-СІ вН" Ср 4 ПіР°С±С-С"ПSC,С-ПІ (0,5 %). РмС-Пр С±Р°СІ
 ПіПсПрПІС-ПмПСПс СІР»С-ПіПсПіПс ПіРмСНС-ПсПрСр Р»С-ПеСрПІР°ПСПСЦІ
 ПіПсПрПсПІП¶ПмПСПСЦІ СІПеПсСНПєПіПсПІР°ПСПсПіПс Р·Р° С„ПсСНПјСрР»ПсСН Р'Р°Р·РмС,С,Р°
 С-ПSC,РмСНПІР°Р»Ср QT ПСП° > 60 ПјСІ ПІС-Пр ПІПєС...С-ПрПСПсПіПс СНС-ПІПСЦІ
 СІПіПсСІС,РмСНС-ПіР°Р»ПсСІСІ Ср 3 ПіР°С±С-С"ПSC,С-ПІ (3,1 %), СІПеС-
 Р»С-ПеСрПІР°Р»ПєСІСІ ПеР°СНПєПіСНП°Р·ПєПСПсПј, С,Р° Ср 2 ПіР°С±С-С"ПSC,С-ПІ (2 %),
 СІПеС- ПіСНПєПмПјР°Р»Пє ПіР»Р°С±РмР±Пс.

РмПсПІС-ПрПсПјР»РмПСПСЦІ ПіСНПс ПіС-ПрПсР·СНСНПІР°ПSC- ПіПсР±С-С±ПSC-
 СНРмР°ПеС±С-С—

РмПсПІС-ПрПсПјР»РмПСПСЦІ ПіСНПс ПіПсР±С-С±ПSC- СНРмР°ПеС±С-С— ПіС-СІР»СІ
 СНРмС"СІС,СНП°С±С-С— Р»С-ПеР°СНСІСНПеПсПіПс Р·Р°СІПсР±Ср ПјР°С" ПІР°П¶Р»ПєПІРм
 Р·ПСП°С±РмПСПСЦІ. Р|Рм ПрР°С" Р·ПсПіСр ПіСНПсПІПсПрПєС,Пє ПјПсПSC-С,ПсСНПєПСПі
 СІПіС-ПІПІС-ПрПСПсСєРмПСПСЦІ ПеПсСНПєСІС,СН/СНПєР·ПєПе ПіСНПє
 Р·Р°СІС,ПсСІСрПІР°ПСПSC- С±СНПсПіПс Р»С-ПеР°СНСІСНПеПсПіПс Р·Р°СІПсР±Ср.
 РмРмПрРєС±ПСПєПј С,Р° С„Р°СНПјР°С±РмПІС,ПєС±ПСПєПј ПіСНП°С±С-ПІПСПєР°Рј, Р°
 С,Р°ПеПсП¶ ПіР°С±С-С"ПSC,Р°Пј Р°Р±Пс С—С...ПSC-Пј Р·Р°ПеПсПСПСПєПј
 ПіСНПмПрСІС,Р°ПІПСПєР°Рј СІР»С-Пр ПіПсПІС-ПрПсПјР»СІС,Пє ПіСНПс СрСІС-
 ПІПєПіР°ПрПеПє ПіС-ПрПсР·СНСНПІР°ПСПєС... ПіПсР±С-С±ПСПєС... СНРмР°ПеС±С-Пм С,Р°
 ПІС-ПрСІСрС,ПСПсСІС,С- РмС„РмПеС,ПєПІПСПсСІС,С- Р»С-ПеР°СНСІСНПеПсПіПс Р·Р°СІПсР±Ср
 С±РмСНПмР· Р°ПІС,ПсПјР°С,ПєР·ПсПІР°ПSCр С-ПSC„ПсСНПјР°С±С-ПмПSCр СІПєСІС,РмПјСр Р·
 С„Р°СНПјР°ПеПсПСП°ПіР»СІПрСр Р·Р° ПіПсСІПєР»Р°ПСПСЦІПј: <https://aisf.dec.gov.ua>.

РјРмСНПјС-Пс ПіСНПєПрР°С,ПСПсСІС,С-.

5 СНПсПеС-ПІ.

ПјПсПІПє Р·Р±РмСНС-ПіР°ПСПСЦІ.

Р—Р±РмСНС-ПіР°С,Пє ПІ ПсСНПєПіС-ПСП°Р»СНПSC-Пм СрПіР°ПеПсПІС±С- ПрР»СІ
 Р·Р°С...ПєСІС,Ср ПІС-Пр ПІПіР»ПєПІСр СІПІС-С,Р»Р°.

P>C-PeP°CᄡCᄡCᄡPePëPNᄡ P·P°CᄡC-P± PSPᄡ PIPëPjP°PiP°C” CᄡPᄡPᄡCᄡC-P°P»CHᄡPSPëC...
C,PᄡPjPᄡPᄡCᄡP°C,CᄡCᄡPSPëC... CᄡPjPsPI P·P±PᄡCᄡC-PiP°PSPSCᄡ.

P—P±PᄡCᄡC-PiP°C,Pë PI PSPᄡPrPsCᄡC,CᄡPᄡPSPsPjCᄡ PrP»Cᄡ PrC-C,PᄡPNᄡ PjC-CᄡCᄡC-.

PJPᄡP°PePsPIPeP°.

PᄡPs 1,5 PjPi P°P±Ps PᄡPs 3 PjPi: PᄡPs 7 PeP°PiCᄡCᄡP» Cᄡ P±P»C-CᄡC,PᄡCᄡC-; PᄡPs 1 P°P±Ps 4
P±P»C-CᄡC,PᄡCᄡPë PI PeP°CᄡC,PSPSPSC-PNᄡ CᄡPᄡP°PePsPICᄡC-.

PᄡPs 4,5 PjPi P°P±Ps PᄡPs 6 PjPi: PᄡPs 7 PeP°PiCᄡCᄡP» Cᄡ P±P»C-CᄡC,PᄡCᄡC-; PᄡPs 4
P±P»C-CᄡC,PᄡCᄡPë PI PeP°CᄡC,PSPSPSC-PNᄡ CᄡPᄡP°PePsPICᄡC-.

PᄡP°C,PᄡPiPsCᄡC-Cᄡ PIC-PrPiCᄡCᄡPeCᄡ.

P—P° CᄡPᄡCᄡPᄡPiC,PSPj.

P’PëCᄡPsP±PSPëPe.

P’PᄡPᄡ B«P“PᄡPrPᄡPsPS P C-C...C,PᄡCᄡB», PJPiPsCᄡC%ᄡPëPSP°.

**PᄡC-CᄡCᄡPᄡP·PSP°C...PsPrPᄡPᄡPSPSCᄡ PIPëCᄡPsP±PSPëPeP° C,P° P°PrCᄡPᄡCᄡP°
PjC-CᄡCᄡCᄡ PiCᄡPsPIP°PrPᄡPᄡPSPSCᄡ PNᄡPsPiPs PrC-CᄡP»CHᄡPSPsCᄡC,C-.**

H-1103, P’CᄡPrP°PiPᄡCᄡC,, PICᄡP». P”PᄡPjCᄡPᄡC—, 19-21, PJPiPsCᄡC%ᄡPëPSP°.

B