

$$P\alpha P^{\circ}C\overline{H}PjP^{\circ}PePsP\gg PsPiC-C\neq PSC-PIP\gg P^{\circ}C\overline{I}C,P\ddot{e}PIPsC\overline{I}C,C-$$

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

$P\bar{h}bP\mu C...P^{\circ}PSC-P\cdot PjPrC-C-$

$P\check{Y}P\mu C\ddagger PsPIP^{\circ}PeP\ddot{e}C\bar{I}P^{\circ}\rangle PsC,P^{\circ}C''PeC-PSC\ddagger P\mu PIP\ddot{e}PjPiC\bar{H}PsPrC\bar{r}PeC,PsPj$
 $PjP\mu C,P^{\circ}P\pm PsP\rangle C-P\cdot PjC\bar{r}PiC\bar{r}C\bar{H}P\ddot{e}PSC-PIC\bar{r}P\rangle C\bar{H}PrP\ddot{e}PSP\ddot{e}PN_{\bar{e}}C\bar{r}C,PIPsC\bar{H}C\bar{H}C''C,C\bar{H}C\bar{I}C\bar{I}$
 $PIC-PrC\ddagger P^{\circ}C\bar{I}C,P^{\circ}PePsC-CHP\mu P^{\circ}PeC\ddagger C-C-:PiC-PiPsPeC\bar{I}P^{\circ}PSC,P\ddot{e}PS\rightarrow PeC\bar{I}P^{\circ}PSC,P\ddot{e}PS\rightarrow$
 $C\bar{I}P\mu C\ddagger PsPIP^{\circ}PeP\ddot{e}C\bar{I}P^{\circ}\rangle PsC,P^{\circ}.P\bar{h}C\bar{I}P^{\circ}PSC,P\ddot{e}PSPsPeC\bar{I}P\ddot{e}PrP^{\circ}P\cdot P^{\circ}C''$
 $PeP^{\circ}C,P^{\circ}P\rangle C-P\cdot P^{\circ}C,PsC\bar{H}PsPjPsP\pm PsC...P\mu C,P^{\circ}PiC-PIC\ddagger C-C''C-CHP\mu P^{\circ}PeC\ddagger C-C-.$
 $P\alpha P\mu P\pm C\bar{r}PeC\bar{I}PsC\bar{I}C,P^{\circ}C,C''PiPsC...C-PrPSP\ddot{e}Pj2-P^{\circ}C\bar{H}P\ddot{e}P\rangle C,C-P^{\circ}P\cdot PsP\rangle C\bar{r},$
 $C,P\mu C\bar{H}P^{\circ}PiP\mu PIC,P\ddot{e}C\ddagger PSP^{\circ}PrC-C\bar{I}C\bar{I}PePsPiPsPiPsPi\bar{b}\bar{H}^{\text{TM}}C\bar{I}P\cdot P^{\circ}PSP^{\circ}P\cdot C-$
 $P\cdot PjP\mu PSC\epsilon P\mu PSPSC\bar{I}PjPePsPSC\ddagger P\mu PSC,C\bar{H}P^{\circ}C\ddagger C-C-C\bar{I}P\mu C\ddagger PsPIPsC-$
 $PeP\ddot{e}C\bar{I}P^{\circ}\rangle PsC,P\ddot{e}PIC\bar{I}P\ddot{e}C\bar{H}PsPIP^{\circ}C,C\ddagger C-PeC\bar{H}PsPIC-C\epsilon P\rangle C\bar{I}C...PsPj$
 $C\bar{I}P\mu P\rangle P\mu PeC,P\ddot{e}PIPSsPiPsPiC\bar{H}P\ddot{e}PiPSC-C\ddagger P\mu PSPSC\bar{I}$
 $PeC\bar{I}P^{\circ}PSC,P\ddot{e}PSPsPeC\bar{I}P\ddot{e}PrP^{\circ}P\cdot P\ddot{e}.P\alpha P\mu P\pm C\bar{r}PeC\bar{I}PsC\bar{I}C,P^{\circ}C,\bar{b}\bar{H}C\ddagger P\mu$
 $PiPsC,C\bar{r}P\bar{H}PSP\ddot{e}PN_{\bar{e}}C-C\bar{I}P\mu P\rangle P\mu PeC,P\ddot{e}PIPS\ddot{e}PN_{\bar{e}}PSP\mu PiC\bar{r}C\bar{H}P\ddot{e}PSPsPIP\ddot{e}PN_{\bar{e}}$
 $C-PSPiC-P\pm C-C,PsC\bar{H}PeC\bar{I}P^{\circ}PSC,P\ddot{e}PSPsPeC\bar{I}P\ddot{e}PrP^{\circ}P\cdot P\ddot{e}(NP-SIXO),PN_{\bar{e}}PsPiPsP\bar{h}C-$
 $(PePsPSC\bar{I}C,P^{\circ}PSC,P^{\circ}PiC\bar{H}P\ddot{e}PiPSC-C\ddagger P\mu PSPSC\bar{I})in vitroC\bar{I}C,P^{\circ}PSPsPIP\ddot{e}C,C\bar{H}$
 $PjP\mu PSC\epsilon P\mu 1PSP^{\circ}PSPsPjPsP\rangle C\bar{I}C.P'C\bar{r}P\rangle PsPiPsPeP^{\circ}P\cdot P^{\circ}PSPs,C\%_{\bar{o}}Ps$
 $C,,P\mu P\pm C\bar{r}PeC\bar{I}PsC\bar{I}C,P^{\circ}C,P\cdot PSP^{\circ}C\ddagger PSPsC\bar{H}PjC-C\bar{H}PsC\bar{H}PiC\bar{H}P\ddot{e}PiPSC-C\ddagger C\bar{r}C''$
 $P^{\circ}PeC,P\ddot{e}PIPSC-C\bar{I}C,C\bar{H}C\bar{I}PePsPeP\ddot{e}C\bar{I}PSP\mu PSPsC-,C,P^{\circ}PeC-$
 $PIC-PrPSPsPIP\rangle P\mu PSPsC-C,,PsC\bar{H}PjP\ddot{e}PeC\bar{I}P^{\circ}PSC,P\ddot{e}PSPsPeC\bar{I}P\ddot{e}PrP^{\circ}P\cdot P\ddot{e}.Pj$
 $C,P\mu C\bar{H}P^{\circ}PiP\mu PIC,P\ddot{e}C\ddagger PSP\ddot{e}C...PePsPSC\ddagger P\mu PSC,C\bar{H}P^{\circ}C\ddagger C-C\bar{I}C...$
 $C,,P\mu P\pm C\bar{r}PeC\bar{I}PsC\bar{I}C,P^{\circ}C,PSP\mu PiC\bar{H}P\ddot{e}PiPSC-C\ddagger C\bar{r}C''C-PSC\epsilon C-C,,P\mu C\bar{H}PjP\mu PSC,P\ddot{e},$
 $C\%_{\bar{o}}PsP\pm P\mu C\bar{H}C\bar{r}C,C\bar{H}C\bar{r}C\ddagger P^{\circ}C\bar{I}C,C\bar{H}C\bar{r}PjP\mu C,P^{\circ}P\pm PsP\rangle C-P\cdot PjC-PiC\bar{r}C\bar{H}P\ddot{e}PSC-PI$
 $P^{\circ}P\pm PsPiC-C\bar{H}P\ddot{e}PjC-PrP\ddot{e}PSC-PI,C,P^{\circ}PeP\ddot{e}C...C\bar{I}Pe$
 $PiC\bar{r}P^{\circ}PSC-PSPPrP\mu P\cdot P^{\circ}PjC-PSP^{\circ}P\cdot P^{\circ},$
 $PiC-PiPsPeC\bar{I}P^{\circ}PSC,P\ddot{e}PSPiC\bar{r}P^{\circ}PSC-PSC,,PsC\bar{I}C,,PsC\bar{H}P\ddot{e}P\pm PsP\cdot P\ddot{e}P\rangle C,C\bar{H}P^{\circ}PSC\bar{I}C,,P\mu C\bar{H}$
 $P^{\circ}P\cdot P^{\circ},PsC\bar{H}PsC,P^{\circ}C,C,,PsC\bar{I}C,,PsC\bar{H}P\ddot{e}P\pm PsP\cdot P\ddot{e}P\rangle C,C\bar{H}P^{\circ}PSC\bar{I}C,,P\mu C\bar{H}P^{\circ}P\cdot P^{\circ},$
 $PsC\bar{H}PsC,P\ddot{e}PrP\ddot{e}PSPjPsPSPsC,,PsC\bar{I}C,,P^{\circ}C,PrP\mu PeP^{\circ}C\bar{H}P\pm PsPeC\bar{I}P\ddot{e}P\rangle P^{\circ}P\cdot P^{\circ}P^{\circ}P\pm Ps$
 $PiC\bar{r}C\bar{H}P\ddot{e}PSPSC\bar{r}PeP\rangle P\mu PsP\cdot P\ddot{e}PrC,,PsC\bar{I}C,,PsC\bar{H}P\ddot{e}P\rangle P^{\circ}P\cdot P^{\circ}.$

$P\bar{h}bP\rangle C-PSC-C\ddagger PSP^{\circ}P\mu C,,P\mu PeC,P\ddot{e}PIPSC-C\bar{I}C,C\bar{H}C,P^{\circ}P\pm P\mu P\cdot PiP\mu PeP^{\circ}$

$P\mu PsPrP^{\circ}PiC\bar{H}P^{\circ}$

$P\cdot C,,P\mu PeC,P\ddot{e}PIPSC-C\bar{I}C,C\bar{H}C,,P\mu P\pm C\bar{r}PeC\bar{I}PsC\bar{I}C,P^{\circ}C,C\bar{r}P\pm C\bar{r}P\rangle P^{\circ}$
 $PiC-PrC,PIP\mu C\bar{H}PrP\bar{H}P\mu PSP^{\circ}C\bar{r}C,,P^{\circ}P\cdot C-3C,C\bar{H}C\bar{H}PsC...PsC\bar{I}PSPsPIPSP\ddot{e}C...$
 $PrPsC\bar{I}P\rangle C-PrP\bar{H}P\mu PSCH(PrPIP^{\circ}PsC\bar{I}PSPsPIPSC-PrPsC\bar{I}P\rangle C-PrP\bar{H}P\mu PSPSC\bar{I}APEXC-FACTC-$
 $PrPsPrP^{\circ}C,PePsPIP\mu PrPsC\bar{I}P\rangle C-PrP\bar{H}P\mu PSPSC\bar{I}CONFIRMS,PsPiP\ddot{e}C\bar{I}P^{\circ}PSC-PSP\ddot{e}P\bar{H}C\ddagger P\mu),$
 $C\bar{I}PeC-PIPeP\rangle C\bar{H}C\ddagger P^{\circ}P\rangle P\ddot{e}4101PiP^{\circ}C\ddagger C-C''PSC,P^{\circ}C-P\cdot PiC-PiP\mu C\bar{H}C\bar{r}C\bar{H}P\ddot{e}PeP\mu PjC-C''C\bar{H}C-$
 $PiPsPrP^{\circ}PiC\bar{H}PsC\bar{H}.PjPePsP\bar{H}PSPsPjC\bar{r}P\cdot C\ddagger P\ddot{e}C...PsC\bar{I}PSPsPIPSP\ddot{e}C...PrPsC\bar{I}P\rangle C-PrP\bar{H}P\mu PSCH$
 $C,,P^{\circ}P\cdot P\ddot{e}3C,,P\mu P\pm C\bar{r}PeC\bar{I}PsC\bar{I}C,P^{\circ}C,P\pm C-P\rangle C\bar{H}C\epsilon P\mu C,,P\mu PeC,P\ddot{e}PIPSsP\cdot PSP\ddot{e}P\bar{H}C\bar{I}PIP^{\circ}PI$
 $C\bar{I}P\ddot{e}C\bar{H}PsPIP^{\circ}C,PePsPIC\bar{r}PePsPSC\ddagger P\mu PSC,C\bar{H}P^{\circ}C\ddagger C-C\bar{H}C\bar{I}P\mu C\ddagger PsPIPsC-PeP\ddot{e}C\bar{I}P\rangle PsC,P\ddot{e}C-$
 $PiC-PrC,C\bar{H}P\ddot{e}PjC\bar{r}PIP^{\circ}PIC-C-PSP^{\circ}PSP^{\circ}P\rangle P\mu P\bar{H}PSPsPjC\bar{r}C\bar{H}C-PIPSC-PiPsC\bar{H}C-PIPSC\bar{I}PSPsP-$
 $P^{\circ}P\rangle PsPiC\bar{r}C\bar{H}P\ddot{e}PSPsP\rangle PsPj.P\mu P\mu C\bar{H}PIP\ddot{e}PSPSPsC\bar{H}PeC-PSC\ddagger P\mu PIPsC\bar{H}C,PsC\ddagger PePsC\bar{H}$
 $P\mu C,,P\mu PeC,P\ddot{e}PIPSsC\bar{I}C,C-PIPrPsC\bar{I}P\rangle C-PrP\bar{H}P\mu PSPSC\bar{I}C...APEXC-FACTP\pm C\bar{r}P\rangle P^{\circ}$
 $C\ddagger P^{\circ}C\bar{I}C,PeP^{\circ}PiP^{\circ}C\ddagger C-C''PSC,C-PI,C\bar{r}C\bar{I}PeP\ddot{e}C...PiC\bar{H}PsC,C\bar{I}PiPsPjPsC\bar{I}C,P^{\circ}PSPSC-C...$
 $C,C\bar{H}C\bar{H}PsC...PjC-C\bar{I}C\bar{I}C\ddagger C-PIPePsPSC\ddagger P\mu PSC,C\bar{H}P^{\circ}C\ddagger C-C\bar{I}C\bar{I}P\mu C\ddagger PsPIPsC-PeP\ddot{e}C\bar{I}P\rangle PsC,P\ddot{e}$
 $PIC\bar{I}P\ddot{e}C\bar{H}PsPIP^{\circ}C,C\ddagger C-PeC\bar{H}PsPIC-PSP\mu PiP\mu C\bar{H}P\mu PIP\ddot{e}C\%_{\bar{o}}C\bar{r}PIP^{\circ}P\rangle P^{\circ}6,0PjPi/PrP\rangle$

(357 PjPePjPsP»CH/P»). PJ PrPsPrP°C,PePsPIPsPjCr PrPsCfP»C-PrP¶PµPSPSC- CONFIRMS C,,P°P·Pë 3, CḡPµP·CrP»CHC,P°C,Pë C¶PePsPiPs CfC,P°P»Pë PrPsCfC,CrPiPSC- PiC-CfP»C¶ PiPµCḡCεPsC— CḡPµC”CfC,CḡP°C†C-C— C,,PµP±CrPeCfPsCfC,P°C,Cr, PiPµCḡPIPePSPSPsCḡ PeC-PSC†PµPIPsCḡ C,PsC†PePsCḡ PµC,,PµPeC,PëPIPsPSCfC,C- P±CrP»P° C†P°CfC,PeP° PiP°C†C-C”PSC,C-PI, Cr C¶PePëC... PePsPSC†PµPSC,CḡP°C†C-C¶ CfPµC†PsPIPsC— PePëCfP»PsC,Pë PI CfPëCḡPsPIP°C,C†C- PeCḡPsPIC- PSPµ PiPµCḡPµPIPeC%oCrPIP°P»P° 6,0 PjPi/PrP» PSP° PjPsPjPµPSC, PsCfC,P°PSPSCHPsPiPs PIC-P·PëC,Cr. PJ C†C- PrPsCfP»C-PrP¶PµPSPSC¶ PSPµ PIPeP»CḡC†P°P»Pë PiP°C†C-C”PSC,C-PI, C¶PeC- PiPµCḡPµPSPµCfP»Pë C,CḡP°PSCfPiP»P°PSC,P°C†C-Cḡ PsCḡPiP°PSC-PI (PrPëPI. CḡPsP·PrC-P» B«PhCfPsP±P»PëPIPsCfC,C- P·P°CfC,PsCfCrPIP°PSPSC¶B»).

P”PsCfP»C-PrP¶PµPSPSC¶ APEX. P”PsCfP»C-PrP¶PµPSPSC¶ PµC,,PµPeC,PëPIPsPSCfC,C- C,,PµP±CrPeCfPsCfC,P°C,Cr P· PePsPSC,CḡPsP»PµPj PiP»P°C†PµP±Ps C,P° P°P»PsPiCrCḡPëPSPsP»Cr C,,P°P·Pë 3 (Allopurinol and Placebo-Controlled Efficacy Study of Febuxostat, APEX) P±CrP»Ps CḡP°PSPPrPsPjC-P·PsPIP°PSPëPj PiPsPrPIC-PNëPSPëPj CfP»C-PiPëPj, P±P°PiP°C,PsC†PµPSC,CḡPsPIPëPj C,CḡPëPIP°P»C-CfC,Cḡ 28 C,PëP¶PSC-PI. P’CfCHPsPiPs P±CrP»Ps CḡP°PSPPrPsPjC-P·PsPIP°PSPs 1072 PiP°C†C-C”PSC,Pë: PiP»P°C†PµP±Ps (n=134), C,,PµP±CrPeCfPsCfC,P°C, 80 PjPi 1 CḡP°P· PSP° PrPsP±Cr (n=267), C,,PµP±CrPeCfPsCfC,P°C, 120 PjPi 1 CḡP°P· PSP° PrPsP±Cr (n=269), C,,PµP±CrPeCfPsCfC,P°C, 240 PjPi 1 CḡP°P· PSP° PrPsP±Cr (n=134) P°P±Ps P°P»PsPiCrCḡPëPSPsP» (300 PjPi 1 CḡP°P· PSP° PrPsP±Cr (n=258) PrP»C¶ PiP°C†C-C”PSC,C-PI C-P· PiPsC†P°C,PePsPIPsCḡ CfPëCḡPsPIP°C,PePsPIPsCḡ PePsPSC†PµPSC,CḡP°C†C-C”Cḡ PeCḡPµP°C,PëPSC-PSCr ≤ 1,5 PjPi/PrP» P°P±Ps 100 PjPi 1 CḡP°P· PSP° PrPsP±Cr (n=10) PrP»C¶ PiP°C†C-C”PSC,C-PI C-P· PiPsC†P°C,PePsPIPsCḡ CfPëCḡPsPIP°C,PePsPIPsCḡ PePsPSC†PµPSC,CḡP°C†C-C”Cḡ PeCḡPµP°C,PëPSC-PSCr > 1,5 PjPi/PrP» C- ≤ 2,0 PjPi/PrP»). P”P»C¶ PsC†C-PSPePë P±PµP·PiPµPePë C,,PµP±CrPeCfPsCfC,P°C, PiCḡPëP·PSP°C†P°P»Pë PI PrPsP·C- 240 PjPi (Cr 2 CḡP°P·Pë PIPëC%oPµ PjP°PeCfPëPjP°P»CHPSPsC— CḡPµPePsPjPµPSPPrPsPIP°PSPsC— PrPsP·Pë).

P”PsCfP»C-PrP¶PµPSPSC¶ APEX PiPsPeP°P·P°P»Ps CfC,P°C,PëCfC,PëC†PSPs PrPsCfC,PsPIC-CḡPSCr PiPµCḡPµPIP°PiCr PsP±PsC... CḡPµP¶PëPjC-PI P»C-PeCrPIP°PSPSC¶ PiCḡPµPiP°CḡP°C,PsPj C,,PµP±CrPeCfPsCfC,P°C, 80 PjPi 1 CḡP°P· PSP° PrPsP±Cr C- C,,PµP±CrPeCfPsCfC,P°C, 120 PjPi 1 CḡP°P· PSP° PrPsP±Cr PiPsCḡC-PIPsC¶PSPs P· P°P»PsPiCrCḡPëPSPsP»PsPj Cr P·PIPeC†P°PNëPSC-PNë PrPsP·C- 300 PjPi (n = 258)/100 PjPi (n=10) Cr P·PjPµPSCεPµPSPSC- CfPëCḡPsPIP°C,PePsPIPsC— PePsPSC†PµPSC,CḡP°C†C-C— CfPµC†PsPIPsC— PePëCfP»PsC,Pë PSPëP¶C†Pµ 6 PjPi/PrP» (357 PjPePjPsP»CH/P») (PrPëPI. C,P°P±P». 1 C- CḡPëCf. 1).

P”PsCfP»C-PrP¶PµPSPSC¶ FACT. P”PsCfP»C-PrP¶PµPSPSC¶ PµC,,PµPeC,PëPIPsPSCfC,C- C,,PµP±CrPeCfPsCfC,P°C,Cr P· P°P»PsPiCrCḡPëPSPsP»-PePsPSC,CḡPsP»PµPj (The Febuxostat Allopurinol Controlled Trial, FACT) C,,P°P·Pë 3 P±CrP»Ps CḡP°PSPPrPsPjC-P·PsPIP°PSPëPj PiPsPrPIC-PNëPSPëPj CfP»C-PiPëPj, P±P°PiP°C,PsC†PµPSC,CḡPsPIPëPj C,CḡPëPIP°P»C-CfC,Cḡ 52 C,PëP¶PSC-. P’CfCHPsPiPs P±CrP»Ps CḡP°PSPPrPsPjC-P·PsPIP°PSPs 760 PiP°C†C-C”PSC,C-PI: C,,PµP±CrPeCfPsCfC,P°C, 80 PjPi 1 CḡP°P· PSP° PrPsP±Cr (n = 256), C,,PµP±CrPeCfPsCfC,P°C, 120 PjPi 1 CḡP°P· PSP° PrPsP±Cr (n = 251) C,P° P°P»PsPiCrCḡPëPSPsP» 300 PjPi 1 CḡP°P· PSP° PrPsP±Cr (n = 253).

P”PsCfP»C-PrP¶PµPSPSC¶ FACT PiPsPeP°P·P°P»Ps CfC,P°C,PëCfC,PëC†PSPs PrPsCfC,PsPIC-CḡPSCr PiPµCḡPµPIP°PiCr PsP±PsC... CḡPµP¶PëPjC-PI бḡ” C,,PµP±CrPeCfPsCfC,P°C, 80 PjPi 1 CḡP°P· PSP° PrPsP±Cr C- C,,PµP±CrPeCfPsCfC,P°C, 120 PjPi 1 CḡP°P· PSP° PrPsP±Cr бḡ” PiPsCḡC-PIPsC¶PSPs P· P°P»PsPiCrCḡPëPSPsP»PsPj Cr P·PIPeC†P°PNëPSC-PNë PrPsP·C- 300 PjPi Cr P·PjPµPSCεPµPSPSC- C- PiC-PrC,CḡPëPjC†C- CfPëCḡPsPIP°C,PePsPIPsC— PePsPSC†PµPSC,CḡP°C†C-C— CfPµC†PsPIPsC— PePëCfP»PsC,Pë

PSPëP¶C±Pµ 6 PjPi/PrP» (357 PjPePjPsP»CHb/P»).

PJ C,P°P±P»PëC†C- 1 PïC¶PµPrC†C,P°PIP»PµPSPs C¶PµP·C†P»CHbC,P°C,Pë PsC†C-PSPëPë
PïPµC¶PIPëPSPSPsC— PeC-PSC†PµPIPsC— C,Psc†PePë PµC,,PµPeC,PëPIPsC†C,C-.

PŸP°P±P»PëC†C¶ 1

PŸP°C†C,PeP° PïP°C†C-C"PSC,C-PI C-P· PePsPSC†PµPSC,C¶P°C†C-C"CH C†PµC±PsPIPsC—
PePëC†P»PsC,Pë PI C†PëC¶PsPIP°C,C†C- PeC¶PsPIC- < 6,0 PjPi/PrP»

(357 PjPePjPsP»CHb/P») PïC-Pr C±P°C† C,C¶CHbPsC... PsC†C,P°PSPSC-C...
C%oPsPjC-C†C¶C±PSPëC... PIC-P·PëC,C-PI

P"PsC†P»C-PrP¶PµPSPSC¶	P±PµP±C†PeC†PsC†C,P°C, 80 PjPi 1 C¶P°P· PSP° PrPsP±C†	P±PµP±C†PeC†PsC†C,P°C, 120 PjPi 1 C¶P°P· PSP° PrPsP±C†	P¶P»PsPïC†C¶PëPSPsP» 300/100 PjPi 1 C¶P°P· PSP° PrPsP±C† ¹
APEX (28 C,PëP¶PSC-PI)	48 %* (n=262)	65 %*,# (n=269)	22 % (n=268)
FACT (52 C,PëP¶PSC-)	53 %* (n=255)	62 %* (n=250)	21 % (n=251)
PhP±b¶™C"PrPSP°PSC- C¶PµP·C†P»CHbC,P°C,Pë	51 %* (n=517)	63 %*,# (n=519)	22 % (n=519)
¹ P PµP·C†P»CHbC,P°C,Pë C† PïP°C†C-C"PSC,C-PI, C¶PeC- PsC,C¶PëPjC†PIP°P»Pë 100 PjPi 1 C¶P°P· PSP° PrPsP±C† (n = 10: PïP°C†C-C"PSC,Pë P· PïPsC±P°C,PePsPIPsC¶ C†PëC¶PsPIP°C,PePsPIPsC¶ PePsPSC†PµPSC,C¶P°C†C-C"CH PeC¶PµP°C,PëPSC-PSC† > 1,5 PjPi/PrP» C- ≤ 2,0 PjPi/PrP») P°P±Ps 300 PjPi 1 C¶P°P· PSP° PrPsP±C† (n=509), C† PïC¶PsC†PµC†C- P°PSP°P»C-P·C† P±C†P»Pë PsP±b¶™C"PrPSP°PSC-. * p < 0,001 PïPsC¶C-PIPsC¶PSPs P· P°P»PsPïC†C¶PëPSPsP»PsPj, # p < 0,001 PïPsC¶C-PIPsC¶PSPs P· PrPsP·PsC¶ 80 PjPi.			

PµC¶Pë P·P°C†C,PsC†C†PIP°PSPSC- C,,PµP±C†PeC†PsC†C,P°C,C† P·PjPµPSC¶PµPSPSC¶
C†PëC¶PsPIP°C,PePsPIPsC— PePsPSC†PµPSC,C¶P°C†C-C— C†PµC±PsPIPsC— PePëC†P»PsC,Pë
P±C†P»Ps C¶PIPëPrPePëPj C,P° C†C,C¶PëPjC†PIP°P»PsC†CH PrPsPIPiPs. P—PjPµPSC¶PµPSPSC¶
PePsPSC†PµPSC,C¶P°C†C-C— C†PµC±PsPIPsC— PePëC†P»PsC,Pë PI C†PëC¶PsPIP°C,C†C-
PeC¶PsPIC- PrPs < 6,0 PjPi/PrP» (357 PjPePjPsP»CHb/P») PIC-PrP·PSP°C±P°P»PsC†C¶ PIP¶Pµ
PSP° PrC¶C†PiPsPjC† C,PëP¶PSC- PrPsC†P»C-PrP¶PµPSPSC¶ C- P·P±PµC¶C-PiP°P»PsC†C¶
PSP°PrP°P»C- PïC¶PsC,C¶PiPsPj P»C-PeC†PIP°PSPSC¶. P¶P° C¶PëC†. 1 PïPsPeP°P·P°PSPs
C†PµC¶PµPrPSC- PePsPSC†PµPSC,C¶P°C†C-C— C†PµC±PsPIPsC— PePëC†P»PsC,Pë PI
C†PëC¶PsPIP°C,C†C- PeC¶PsPIC- P·P°P»PµP¶PSPs PIC-Pr C±P°C†C† PrP»C¶ PePsP¶PSPsC—
C,PµC¶P°PïPµPIC,PëC±PSPsC— PïC¶C†PïPë P»C-PeC†PIP°PSPSC¶ PI PsP±PsC...
PsC†PSPsPIPsPëC... PrPsC†P»C-PrP¶PµPSPSC¶C... C,,P°P·Pë 3.

P PëC†C†PSPsPe 1

PŸPµC¶PµPrPSC- PePsPSC†PµPSC,C¶P°C†C-C— C†PµC±PsPIPsC— PePëC†P»PsC,Pë PI
C†PëC¶PsPIP°C,C†C- PeC¶PsPIC- P·P° PrP°PSPëPjPë PsP±b¶™C"PrPSP°PSPëC...
PsPïPsC¶PSPëC... PrPsC†P»C-PrP¶PµPSC¶C (C,,P°P·P° 3)

PuCTHPëPjC-C,PeP°: 509 PiP°CTC-C"PS C,C-PI PsC,CTHPëPjCrPIP°P»Pë P°P»PsPiCrCTHPëPSPsP» Cr PrPsP·C- 300 PjPi 1 CTHP°P· PSP° PrPsP±Cr; 10 PiP°CTC-C"PS C,C-PI C-P· CTHPëCTHPsPIP°C,PePsPIPsCTH PePsPSC†PμPSC,CTHP°CTC-C"CTH PeCTHPμP°C,PëPSC-PSCr > 1,5 PjPi/PrP» C- < 2,0 PjPi/PrP» PsC,CTHPëPjCrPIP°P»Pë P°P»PsPiCrCTHPëPSPsP» Cr PrPsP·C- 100 PjPi 1 CTHP°P· PSP° PrPsP±Cr (10 C-P· 268 PiP°CTC-C"PS C,C-PI Cr PrPsCTP»C-PrP¶PμPSPSC- APEX). PαPμP±CrPeCTPSCrC,P°C, Cr PrPsP·C- 240 PjPi PiCTHPëP·PSP°C†P°P»Pë PrP»C¶ PsCTC-PSPePë P±PμP·PiPμPePë PiCTHPë PrPsP·C-, C°%Ps Cr 2 CTHP°P·Pë PiPμCTHPμPIPëC°CrPIP°P»P° PjP°PeCTPëPjP°P»CHbPSCr CTHPμPePsPjPμPSPPrPsPIP°PSCr.

P"PsCTP»C-PrP¶PμPSPSC¶ CONFIRMS. P"PsCTP»C-PrP¶PμPSPSC¶ CONFIRMS P±CrP»Ps CTHP°PSPPrPsPjC-P·PsPIP°PSPëPj PePsPSC,CTHPsP»CHbPsPIP°PSPëPj PrPsCTP»C-PrP¶PμPSPSC¶Pj C,,P°P·Pë 3 C,CTHPëPIP°P»C-CTC,CTH 26 C,PëP¶PSC-PI, C¶PePμ PiCTHPsPIPsPrPëP»Pë PrP»C¶ PsCTC-PSPePë P±PμP·PiPμPePë C,P° PμC,,PμPeC,PëPIPsPSCrC,C- C,,PμP±CrPeCTPSCrC,P°C,Cr PI PrPsP·P°C... 40 PjPi C- 80 PjPi PiPsCTH-C-PIPsC¶PSPs P· P°P»PsPiCrCTHPëPSPsP»PsPj Cr PrPsP·P°C... 300 PjPi C- 200 PjPi PrP»C¶ PiP°CTC-C"PS C,C-PI C-P· PiPsPrP°PiCTHPsCTH C- PiC-PiPμCTHCrCTHPëPePμPjC-C"CTH. P'CTCHbPsPiPs P±CrP»Ps CTHP°PSPPrPsPjC-P·PsPIP°PSPs 2269 PiP°CTC-C"PS C,C-PI: C,,PμP±CrPeCTPSCrC,P°C, 40 PjPi 1 CTHP°P· PSP° PrPsP±Cr (n=757), C,,PμP±CrPeCTPSCrC,P°C, 80 PjPi 1 CTHP°P· PSP° PrPsP±Cr (n=756) C,P° P°P»PsPiCrCTHPëPSPsP» 300/200 PjPi 1 CTHP°P· PSP° PrPsP±Cr (n=756). P©PsPSP°PNëPjPμPSC€Pμ 65 % PiP°CTC-C"PS C,C-PI PjP°P»Pë PiPsCTHCrC€PμPSPSC¶ C,,CrPSPeCTC-C— PSPëCTHPsPe PIC-Pr P»PμPiPePsPiPs PrPs PiPsPjC-CTHPSPsPiPs CTc,CrPiPμPSC¶ (C-P· PeP»C-CTHPμPSCrPsPj PeCTHPμP°C,PëPSC-PSCr 30B¶"89 PjP»/C...PI). P¶CTHPsC,,C-P»P°PeC,PëPeP° PSP°PiP°PrC-PI PiPsPrP°PiCTHPë P±CrP»P° PsP±PsPIB¶™ C¶P·PePsPIPsCTH PiCTHPsC,C¶PiPsPj 26 C,PëP¶PSC-PI.

PSP°CTC,PeP° PiP°CTC-C"PS C,C-PI C-P· PePsPSC†PμPSC,CTHP°CTC-C"CTH CTcPμC†PsPIPsC— PePëCTP»PsC,Pë PI CTPëCTHPsPIP°C,CTC- PeCTHPsPIC- < 6,0 PjPi/PrP» (357 PjPePjPsP»CHb/P») PI PsCTC,P°PSPSC-PNë PIC-P·PëC, CTc,P°PSPsPIPëP»P° 45 % PrP»C¶ C,,PμP±CrPeCTPSCrC,P°C,Cr 40 PjPi, 67 % B¶" PrP»C¶ C,,PμP±CrPeCTPSCrC,P°C,Cr 80 PjPi C- 42 % B¶" PrP»C¶ P°P»PsPiCrCTHPëPSPsP»Cr 300/200 PjPi PIC-PrPiPsPIC-PrPSPs.

PuPμCTHIPëPSPSP° PeC-PSC†PμPIP° C,PsC†PeP° C¿ PiC-PrPiCTH¿PiC- PiP°CTC-C"PS C,C-PI C-P· PiPsCTH¿C¿C€PμPSPSC¶PjPë C,,C¿PSPeCTC-C— PSPëCTHPsPe

PJ PrPsCTP»C-PrP¶PμPSPSC- APEX PsCTC-PSCrPIP°P»Pë PμC,,PμPeC,PëPIPsC-CTc,CHb P·P°CTc,PsCTcCrPIP°PSPSC¶ PiCTHPμPiP°CTHP°C,Cr P· CrC†P°CTc,CTH 40 PiP°CTC-C"PS C,C-PI C-P· PiPsCTHCrC€PμPSPSC¶PjPë C,,CrPSPeCTC-C— PSPëCTHPsPe (C,PsP±C,Ps P· PiPsC†P°C,PePsPIPsCTH CTPëCTHPsPIP°C,PePsPIPsCTH PePsPSC†PμPSC,CTHP°CTC-C"CTH PeCTHPμP°C,PëPSC-PSCr > 1,5 PjPi/PrP» C- ≤ 2,0 PjPi/PrP»). PÿP°PePëPj PiP°CTC-C"PS C,P°Pj, CTHP°PSPPrPsPjC-P·PsPIP°PSPëPj Cr PiCTHCrPiCr P°P»PsPiCrCTHPëPSPsP»Cr, PrPsP·Cr PiCTHPμPiP°CTHP°C,Cr P·PjPμPSC€CrPIP°P»Pë PrPs 100 PjPi 1 CTHP°P· PSP° PrPsP±Cr. PμPμCTHIPëPSPSP° PeC-PSC†PμPIP° C,PsC†PeP° PμC,,PμPeC,PëPIPsPSCrC,C- P±CrP»P° PrPsCTC¶PiPSCrC,P° Cr PiCTHCrPiC- P· C,,PμP±CrPeCTPSCrC,P°C,PsPj Cr 44 % PiP°CTC-C"PS C,C-PI (80 PjPi 1 CTHP°P· PSP° PrPsP±Cr), 45 % (120 PjPi 1 CTHP°P· PSP° PrPsP±Cr) C-

60 % (240 PjPi 1 CTHP°P· PSP° PrPsP±Cr) PiPsCTH-C-PIPsC¶PSPs P· 0 % Cr PiCTHCrPiP°C... P°P»PsPiCrCTHPëPSPsP»Cr 100 PjPi 1 CTHP°P· PSP° PrPsP±Cr C- PiP»P°CT†PμP±Ps.

$$P''PsC\dot{I}P \gg C-PrP \ll P_{\mu}PSPSCII \text{ APEX. } P_{\mu}CHPsC, CIIPIsPj \text{ 8-C, } P\ddot{E}P \ll PSP_{\mu}PIPsPiPs$$

PiC₇PsC,,C-P»P°PeC,PëC±PSPsPiPs PiPμC₇C-PsPrCr PiP°C†C-C"PSC,Pë P·
C,PμC₇P°PiPμPIC,PëC±PSPsC— PiC₇CrPiPë C,,PμP±CrPeC†PsC†C,P°C,Cr 120 PjPi (36 %), C₄PeC-
PiPsC,C₇PμP±CrPIP°P»Pë C,PμC₇P°PiC-C— PSP°PiP°PrC-PI PiPsPrP°PiC₇Pë,
PiPsC₇C-PIPSC₇PIP°P»PëC†C₄ P· PiP°C†C-C"PSC,P°PjPë, C₄PeC- P·P°C†C,PsC†PsPICrPIP°P»Pë
C,,PμP±CrPeC†PsC†C,P°C, 80 PjPi (28 %), P°P»PsPiCrC₇PëPSPsP» 300 PjPi (23 %) C,P°
PiP»P°C†PμP±Ps (20 %). P§P°C†C,PsC,P° PSP°PiP°PrC-PI P±CrP»P° PIPëC%PsC₇ PiC-C†P»C₄
PiC₇PsC,,C-P»P°PeC,PëC±PSPsPiPs PiPμC₇C-PsPrCr C- P· C†P°C†PsPj PiPsC†C,CrPiPsPIPs
P·PSPëP¶C†PIP°P»P°C†C₄. P'C-Pr 46 PrPs 55 % PiP°C†C-C"PSC,C-PI PiC₇PsPIPsPrPëP»Pë
P»C-PeCrPIP°PSPSC₄ PSP°PiP°PrC-PI PiPsPrP°PiC₇Pë P· 8 C,PëP¶PSC₄ C- P·

28 C,PëP¶PSC₄. PkP°PiP°PrPë PiPsPrP°PiC₇Pë, C%Ps PIPëPSPëPeP»Pë PiC₇PsC,C₄PiPsPj
PsC†C,P°PSPSC-C... 4-C... C,PëP¶PSC-PI PIPëPiC₇PsP±CrPIP°PSC₇ (24b₇"

28 C,PëP¶PSC-PI), C†PiPsC†C,PμC₇C-PiP°P»PëC†C₄ Cr 15 % PiP°C†C-C"PSC,C-PI
(C,,PμP±CrPeC†PsC†C,P°C, 80, 120 PjPi), 14 % PiP°C†C-C"PSC,C-PI (P°P»PsPiCrC₇PëPSPsP» 300
PjPi) C- 20 % PiP°C†C-C"PSC,C-PI (PiP»P°C†PμP±Ps).

P"PsC†P»C-PrP¶PμPSPSC₄ FACT. PμC₇PsC,C₄PiPsPj 8-C,PëP¶PSPμPIPsPiPs
PiC₇PsC,,C-P»P°PeC,PëC±PSPsPiPs PiPμC₇C-PsPrCr PiP°C†C-C"PSC,Pë P·
C,PμC₇P°PiPμPIC,PëC±PSPsC— PiC₇CrPiPë C,,PμP±CrPeC†PsC†C,P°C,Cr 120 PjPi (36 %), C₄PeC-
PiPsC,C₇PμP±CrPIP°P»Pë C,PμC₇P°PiC-C— PSP°PiP°PrC-PI PiPsPrP°PiC₇Pë,
PiPsC₇C-PIPSC₇PIP°P»PëC†C₄ P· PiP°C†C-C"PSC,P°PjPë PsP±PsC...
C,PμC₇P°PiPμPIC,PëC±PSPëC... PiC₇CrPi, PrPμ P·P°C†C,PsC†PsPICrPIP°P»Pë
C,,PμP±CrPeC†PsC†C,P°C, 80 PjPi (22 %) C,P° P°P»PsPiCrC₇PëPSPsP» 300 PjPi (21 %).
PμC-C†P»C₄ 8-C,PëP¶PSPμPIPsPiPs PiC₇PsC,,C-P»P°PeC,PëC±PSPsPiPs PiPμC₇C-PsPrCr
C†P°C†C,PsC,P° PSP°PiP°PrC-PI P·P±C-P»CHC€PëP»P°C†C₄ C- P· C†P°C†PsPj
PiPsC†C,CrPiPsPIPs P·PSPëP·PëP»P°C†C₄ (64 % C- 70 % PiP°C†C-C"PSC,C-PI, C₄PeC-
PsC,C₇PëPjCrPIP°P»Pë P»C-PeCrPIP°PSPSC₄ P· PiC₇PëPIPsPrCr PSP°PiP°PrC-PI PiPsPrP°PiC₇Pë
P· 8b₇"52 C,PëP¶PSC₄). PkP°PiP°PrPë PiPsPrP°PiC₇Pë PiC₇PsC,C₄PiPsPj PsC†C,P°PSPSC-C... 4-
C... C,PëP¶PSC-PI PIPëPiC₇PsP±CrPIP°PSC₇ (49b₇"52 C,PëP¶PSC-)
C†PiPsC†C,PμC₇C-PiP°P»PëC†C₄ Cr 6b₇"8 % PiP°C†C-C"PSC,C-PI (C,,PμP±CrPeC†PsC†C,P°C,
80 PjPi, 120 PjPi) C- PI

11 % PiP°C†C-C"PSC,C-PI (P°P»PsPiCrC₇PëPSPsP» 300 PjPi).

P§P°C†C,PeP° PiP°C†C-C"PSC,C-PI, C₄PeC- PiPsC,C₇PμP±CrPIP°P»Pë P»C-PeCrPIP°PSPSC₄
P·P°PiPsC†C,C₇PμPSC₇ PiPsPrP°PiC₇Pë (PrPsC†P»C-PrP¶PμPSPSC₄ APEX C- FACT), P±CrP»P°
PSPëP¶C†PsC₇ Cr PiC₇CrPiP°C..., PrPμ C†PμC₇PμPrPSC₄ PePsPSC†PμPSC,C₇P°C†C-C₄
C†PμC†PsPIPsC— PePëC†P»PsC,Pë PI C†PëC₇PsPIP°C,C†C- PeC₇PsPIC- PiC-C†P»C₄
P»C-PeCrPIP°PSPSC₄ P·PjPμPSC€C†PIP°P»P°C†C₄ PrPs < 6,0 PjPi/PrP», < 5,0 PjPi/PrP» P°P±Ps
< 4,0 PjPi/PrP» PiPsC₇C-PIPSC₄PSPs P· PiC₇CrPiP°PjPë, Cr C₄PePëC... C†PμC₇PμPrPSC-PN₆
C₇C-PIPμPSC₇ C†PμC†PsPIPsC— PePëC†P»PsC,Pë C†C,P°PSPsPIPëPI ≥ 6,0 PjPi/PrP» PI
PsC†C,P°PSPSC- 32 C,PëP¶PSC- P»C-PeCrPIP°PSPSC₄ (P· 20b₇"

24 C,PëP¶PSC₄ PiPs 49b₇"52 C,PëP¶PrPμPSC₇).

PμC-Pr C†P°C† PrPsC†P»C-PrP¶PμPSPSC₄ CONFIRMS C†P°C†C,PeP° PiP°C†C-C"PSC,C-PI,
C₄PeC- PiPsC,C₇PμP±CrPIP°P»Pë P»C-PeCrPIP°PSPSC₄ PSP°PiP°PrC-PI PiPsPrP°PiC₇Pë (1
PrPμPSC₇ PePsP¶PSC- 6 PjC-C†C₄C†C-PI), C†C,P°PSPsPIPëP»P° 31 % C- 25 % Cr
PiC₇CrPiP°C..., C₄PeC- PsC,C₇PëPjCrPIP°P»Pë PIC-PrPiPsPIC-PrPSPs C,,PμP±CrPeC†PsC†C,P°C,
80 PjPi C- P°P»PsPiCrC₇PëPSPsP». P'C-PrPjC-PSPSPsC†C,PμPN₆ Cr
C†PiC-PIPIC-PrPSPsC€PμPSPSC- PiP°C†C-C"PSC,C-PI, C₄PeC- PiPsC,C₇PμP±CrPIP°P»Pë

P»C-PeCfPIP°PSPSClI PSP°PīP°PrC-PI PīPsPrP°PiCḡPē, PjC-P¶ PiCḡCfPīP°PjPē, ClIPeC-P·P°CfC,PsCfPsPICfPIP°P»Pē C,,PμP±CfPeCfPsCfC,P°C, 80 PjPi C- 40 PjPi, PSPμ PIC-PrP·PSP°CfP°P»PsCfCfI.

P"PsPIPiPsCfC,CḡPsPePsPIC- CḡPsP·CēPēCḡPμPSC- PIC-PrPeCḡPēC,C-PrPsCfP»C-PrP¶PμPSPSClI

P"PsCfP»C-PrP¶PμPSPSClI EXCEL (C02-021). P"PsCfP»C-PrP¶PμPSPSClI EXCEL P±CfP»Ps C,CḡPēCḡC-CfPSPēPj PIC-PrPeCḡPēC,PēPj PjCfP»CHC,PēCfPμPSC,CḡPsPIPēPj CḡP°PSPrPsPjC-P·PsPIP°PSPēPj, CḡPsP·CēPēCḡPμPSPēPj P°P»PsPīCfCḡPēPSPsP»-PePsPSC,CḡPsP»CHPsPIP°PSPēPj PrPsCfP»C-PrP¶PμPSPSClI Pj P±PμP·PīPμPePē C,,P°P·Pē 3, ClIPePμ PīCḡPsPIPsPrPēP»PsCfCfI PrP»ClI PsCfC-PSPePē P±PμP·PīPμPePē P· CfCfP°CfC,Cḡ PīP°CfC-C"PSC,C-PI, ClIPeC- PīCḡPsPNeCēP»Pē PsCfPSPsPIPsC- PrPsCfP»C-PrP¶PμPSPSClI C,,P°P·Pē 3 (APEX P°P±Ps FACT). P'CfCHPsPiPs PI PrPsCfP»C-PrP¶PμPSPSClI P±CfP»Ps PIPeP»CHCfPμPSPs 1086 PīP°CfC-C"PSC,C-PI: C,,PμP±CfPeCfPsCfC,P°C, 80 PjPi 1 CḡP°P·PSP° PrPsP±Cf (n=649), C,,PμP±CfPeCfPsCfC,P°C, 120 PjPi 1 CḡP°P·PSP° PrPsP±Cf (n=292) C,P° P°P»PsPīCfCḡPēPSPsP» 300/100 PjPi 1 CḡP°P·PSP° PrPsP±Cf (n=145). PμCḡPēP±P»PēP·PSPs PrP»ClI 69 % PīP°CfC-C"PSC,C-PI PePsCḡPμPeCfC-ClI C,PμCḡP°PīC-C— PrP»ClI PrPsCfCfIPiPSPμPSPSClI PsCfC,P°C,PsCfPSPsPiPs CfC,P°P±C-P»CHPsPSPsPiPs P»C-PeCfPIP°PSPSClI PSPμ P±CfP»P° PīPsC,CḡC-P±PSP°. PμP°CfC-C"PSC,Pē, CḡC-PIPsC-CfPēCḡPsPIP°C,PePsPIPsC— PePsPSCfPμPSC,CḡP°CfC-C— CfPμCfPsPIPsC— PePēCfP»PsC,Pē Cf ClIPePēC... PīCḡPē C,CḡPēCḡP°P·PsPIPsPjCf PīPsCfP»C-PrPsPIPsPjCf PIPēPjC-CḡCḡPIP°PSPSC- CfC,P°PSPsPIPēP»Pē > 6,0 PjPi/PrP», P±CfP»Pē PIPēPeP»CHCfPμPSC- P· PrPsCfP»C-PrP¶PμPSPSClI.

P C-PIPsC- CfPēCḡPsPIP°C,PePsPIPsC— PePsPSCfPμPSC,CḡP°CfC-C— CfPμCfPsPIPsC— PePēCfP»PsC,Pē P· PīP»PēPSPsPj CfP°CfCf PSPμ P·PjC-PSPēP»PēCfCfI (PSP°PīCḡPēPeP»P°Pr, Cf

91 % C- 93 % PīP°CfC-C"PSC,C-PI, ClIPeC- CfPīPsCfP°C,PeCf P·P°CfC,PsCfPsPICfPIP°P»Pē C,,PμP±CfPeCfPsCfC,P°C, Cf PrPsP·P°C... PIC-PrPīPsPIC-PrPSPs 80 PjPi C-

120 PjPi, CḡC-PIPsC- CfPēCḡPsPIP°C,PePsPIPsC— PePsPSCfPμPSC,CḡP°CfC-C— CfPμCfPsPIPsC— PePēCfP»PsC,Pē CfC,P°PSPsPIPēP»Pē < 6,0 PjPi/PrP» PSP° 36-PjCf PjC-CfCfCfC-).

P—P° PrP°PSPēPjPē C,CḡPēCḡC-CfPSPsPiPs CfPīPsCfC,PμCḡPμP¶PμPSPSClI Cf PjPμPSCē PSC-P¶ 4 % PīP°CfC-C"PSC,C-PI, ClIPeC- PīPsC,CḡPμP±CfPIP°P»Pē P»C-PeCfPIP°PSPSClI PSP°PīP°PrC-PI, PIC-PrP·PSP°CfPμPSPs P·PjPμPSCēPμPSPSClI CfP°CfC,PsC,Pē PSP°PīP°PrC-PI PīPsPrP°PiCḡPē PSP° 16bḡ"24 PjC-CfCfCfC- C- 30bḡ"36 PjC-CfCfCfC- (C,PsP±C,Ps P±C-P»CHCē PSC-P¶ Cf 96 % PīP°CfC-C"PSC,C-PI PSPμPsP±C...C-PrPSC-CfC,CH Cf P»C-PeCfPIP°PSPSC- PSP°PīP°PrC-PI PIC-PrCfCfC,PSClI).

Pj 46 % C- 38 % PīP°CfC-C"PSC,C-PI, ClIPeC- PsC,CḡPēPjCfPIP°P»Pē PsCfC,P°C,PsCfPSPμ CfC,P°P±C-P»CHPsPμ P»C-PeCfPIP°PSPSClI C,,PμP±CfPeCfPsCfC,P°C,PsPj PIC-PrPīPsPIC-PrPSPs PI PrPsP·C- 80 P°P±Ps 120 PjPi 1 CḡP°P·PSP° PrPsP±Cf, CfPīPsCfC,PμCḡC-PiP°P»PsCfCfI PīPsPIPsPμ P·PSPēPePSPμPSPSClI PīPμCḡPIPēPSPSPsPiPs PīP°P»CHPīPsPIP°PSPsPiPs C,PsC,,CfCfCfI PIC-Pr PīPsCfP°C,PeCf PrPs PsCfC,P°PSPSCHPsPiPs PIC-P·PēC,Cf.

P"PsCfP»C-PrP¶PμPSPSClI FOCUS (TMX-01-005) P±CfP»Ps Pībḡ™ ClI,C,PēCḡC-CfPSPēPj PIC-PrPeCḡPēC,PēPj PjCfP»CHC,PēCfPμPSC,CḡPsPIPēPj CḡPsP·CēPēCḡPμPSPēPj

PrPsCfP»C-PrP¶PµPSPSC¶Pj P±PµP·PīPµPePē C,,P°P·Pē 2, C%Ps PīC¶PsPIPsPrPēP»PsCfC¶ P·CfC±P°CfC,C¶ PīP°C†C-C"PSC,C-PI, C¶PeC- P·P°PeC-PSC±PēP»Pē 4-C,PēP¶PSPµPIPePNē PīC¶PēPNēPsPj C,,PµP±CfPeCfPsCfC,P°C,Cf P· PīPsPrPIC-PNēPSPēPj CfP»C-PīPēPj PrPsP·CfPIP°PSPSC¶Pj Cf PIPēPīC¶PsP±CfPIP°PSPSC- TMX-00-004. P"PsCfP»C-PrP¶PµPSPSC¶PIPeP»C¶C±P°P»Ps 116 PīP°C†C-C"PSC,C-PI, C¶PeC- PsC,C¶PēPjCfPIP°P»Pē CfPīPsC±P°C,PeCf C,,PµP±CfPeCfPsCfC,P°C, 80 PjPi 1 C¶P°P· PSP° PrPsP±Cf. P"»C¶ 62 % PīP°C†C-C"PSC,C-PI PrP»C¶ PīC-PrC,C¶PēPjPePē C¶C-PIPS¶ CfPēC¶PsPIP°C,PePsPIPsC— PePsPSC†PµPSC,C¶P°C†C-C— CfPµC±PsPIPsC— PePēCfP»PsC,Pē PjPµPSC¶Pµ 6,0 PjPi/PrP» PePsC¶PµPeC†C-C¶ PrPsP·Pē PSPµ P±CfP»P° PīPsC,C¶C-P±PSP°, P° 38 % PīP°C†C-C"PSC,C-PI PīPsC,C¶PµP±CfPIP°P»Pē PePsC¶PµPeC†C-C— PrPsP·Pē PrP»C¶ PrPsCfC¶PiPSPµPSPSC¶PsCfC,P°C,PsC±PSPsC— CfC,P°P±C-P»CHbPSPsC— PePsPSC†PµPSC,C¶P°C†C-C—.

P¶P°CfC,PeP° PīP°C†C-C"PSC,C-PI C-P· C¶C-PIPS¶Pj CfPēC¶PsPIP°C,PePsPIPsC— PePsPSC†PµPSC,C¶P°C†C-C— CfPµC±PsPIPsC— PePēCfP»PsC,Pē PjPµPSC¶Pµ 6,0 PjPi/PrP» (357 PjPePjPsP»CHb/P») PSP° PjPsPjPµPSC, PsCfC,P°PSPSCHbPsPiPs PIC-P·PēC,Cf CfC,P°PSPsPIPeP»P° P±C-P»CHbC¶Pµ 80 % (81b¶"100 %) PrP»C¶ PePsP¶PSPsC— P· PīC¶CfPī P·P° PrPsP·PsC¶ C,,PµP±CfPeCfPsCfC,P°C,Cf.

Pj C,,P°P·C- 3 PeP»C-PSC-C±PSPēC... PrPsCfP»C-PrP¶PµPSC¶ Cf PīP°C†C-C"PSC,C-PI, C¶PeC- PsC,C¶PēPjCfPIP°P»Pē C,,PµP±CfPeCfPsCfC,P°C,, CfPīPsCfC,PµC¶C-PiP°P»PēCfC¶ PSPµP·PSP°C±PSC- P·PjC-PSPē PīPµC±C-PSPePsPIPeC... PīPsPeP°P·PSPēPeC-PI (5,0 %). P¶P°CfC,PsC,P° PrP°PSPēC... P·PjC-PS P±CfP»P° CfC...PsP¶P° P· C,P°PePsC¶ PīC¶Pē P·P°CfC,PsCfCfPIP°PSPSC- P°P»PsPīCfC¶PēPSPsP»Cf (4,2 %) (PrPēPI. C¶PsP·PrC-P» B«PhCfPsP±P»PēPIPsCfC,C- P·P°CfC,PsCfCfPIP°PSPSC¶B»). Pj PrPsPIPiPsCfC,C¶PsPePsPIPeC... PIC-PrPeC¶PēC,PēC... C¶PsP·C¶PēC¶PµPSPēC... PrPsCfP»C-PrP¶PµPSPSC¶C... Cf PīP°C†C-C"PSC,C-PI, C¶PeC- PsC,C¶PēPjCfPIP°P»Pē C,,PµP±CfPeCfPsCfC,P°C, (5,5 %) P°P±Ps P°P»PsPīCfC¶PēPSPsP» (5,8 %) PīC¶PsC,C¶PiPsPj C,C¶PēPIP°P»PsPiPs C±P°CfCf, PIC-PrP·PSP°C±P°P»PsCfC¶ PīC-PrPIPeC%PµPSPSC¶ C¶C-PIPS¶ P¶P¶" (> 5,5 PjPeP¶Ph/PjP») (PrPēPI. C¶PsP·PrC-P» B«PhCfPsP±P»PēPIPsCfC,C- P·P°CfC,PsCfCfPIP°PSPSC¶B»).

PµC-CfP»C¶C¶PµC"CfC,C¶P°C†C-PNēPSC- PrPsPIPiPsCfC,C¶PsPePsPIC- PrPsCfP»C-PrP¶PµPSPSC¶

P"PsCfP»C-PrP¶PµPSPSC¶ CARES C¶PIP»C¶P»Ps CfPsP±PsC¶ P±P°PiP°C,PsC†PµPSC,C¶PsPIPµ C¶P°PSPPrPsPjC-P·PsPIP°PSPµ PīPsPrPIC-PNēPSPs CfP»C-PīPµ PrPsCfP»C-PrP¶PµPSPSC¶ PIC-PrCfCfC,PSPsCfC,C- PjPµPSC¶PsC— PµC,,PµPeC,PēPIPSsCfC,C-, PīC-Pr C±P°Cf C¶PePsPiPs PīPsC¶C-PIPS¶PIP°P»Pē C¶PµP·CfP»CHbC,P°C,Pē CfPµC¶C†PµPIPs-CfCfPrPēPSPSPēC... P·P°C...PIPsC¶C¶PIP°PSC¶ PīC¶Pē P·P°CfC,PsCfCfPIP°PSPSC- C,,PµP±CfPeCfPsCfC,P°C,Cf C,P° P°P»PsPīCfC¶PēPSPsP»Cf Cf PīP°C†C-C"PSC,C-PI P· PīPsPrP°PīC¶PsC¶ C,P° PsCfPSPsPIPSēPjPē CfPµC¶C†PµPIPs- CfCfPrPēPSPSPēPjPē P·P°C...PIPsC¶C¶PIP°PSPSC¶PjPē PI P°PSP°PjPSPµP·C-, PIPeP»C¶C±P°C¶Pē C-PSC,,P°C¶PeC, PjC-PsPeP°C¶PrP°, PīPsCfPīC-C,P°P»C-P·P°C†C-C¶ P· PīC¶PēPIPsPrCf PSPµCfC,P°P±C-P»CHbPSPsC— CfC,PµPSPsPeP°C¶PrC-C-, PīC¶PsC†PµPrCfC¶ PePsC¶PsPSP°C¶PSPsC— P°P±Ps C†PµC¶PµP±C¶P°P»CHbPSPsC— C¶PµPIP°CfPeCfP»C¶C¶PēP·P°C†C-C-, C-PSCfCfP»CHbC,, PīPsCfPīC-C,P°P»C-P·P°C†C-C¶ P· PīC¶PēPIPsPrCf C,C¶P°PSP·PēC,PsC¶PSPsC— C-C¶PµPjC-C±PSPsC— P°C,P°PePē, P·P°C...PIPsC¶C¶PIP°PSPSC¶ PīPµC¶PēC,,PµC¶PēC±PSPēC... CfCfPrPēPS P°P±Ps C†CfPeC¶PsPIPePNē PrC-P°P±PµC, P· PsP·PSP°PeP°PjPē PjC-PeC¶PsP°PSPiC-PsPīP°C,C-C— P°P±Ps PjP°PeC¶PsP°PSPiC-PsPīP°C,C-C—. P"»C¶ PrPsCfC¶PiPSPµPSPSC¶ C¶C-PIPS¶ sUA PjPµPSC¶Pµ 6 PjPi/PrP» PrPsP·Cf C,,PµP±CfPeCfPsCfC,P°C,Cf C,PēC,C¶CfPIP°P»Pē P·

40 PjPi PrPs 80 PjPi (PSPμP·P°P»PμP¶PSPs PIC-Pr C„CfPSPeC†C-C— PSPëCĤPsPe), P° PrPsP·Cf P°P»PsPiCfCĤPëPSPsP»Cf C,PëC,CĤCfPIP°P»Pë P· PeCĤPsPePsPj 100 PjPi P· 300 PrPs 600 PjPi PrP»CĬ PiP°C†C-C”PSC,C-PI C-P· PSPsCĤPjP°P»CHPSPsCĤ C„CfPSPeC†C-C”CĤ PSPëCĤPsPe C,P° PSPëCĤPePsPIPsCĤ PSPμPrPsCfC,P°C,PSC-CfC,CĤ P»PμPiPePsPiPs CfC,CfPiPμPSCĬ C,P° P· 200 PrPs 400 PjPi PrP»CĬ PiP°C†C-C”PSC,C-PI C-P· PSPëCĤPePsPIPsCĤ PSPμPrPsCfC,P°C,PSC-CfC,CĤ PiPsPjC-CĤPSPsPiPs CfC,CfPiPμPSCĬ C,CĬP¶PePsCfC,C-.

PμPμCĤPIPëPSPSPsCĤ PeC-PSC†PμPIPsCĤ C,PsC†PePsCĤ PI PrPsCfP»C-PrP¶PμPSPSC- CARES P±CfPI C†P°Cf PiPμCĤC€PsC— PiPsCĬPIPë MACE (PIP°P¶P»PëPIC- PiPsP±C-C†PSC- CfPμCĤC†PμPIPs-CfCfPrPëPSPSC- CĬPIPëC%P°), CfPeP»P°PrPsPIPsC— PSPμP»PμC,P°P»CHPSPsPiPs C-PSC„P°CĤPeC,Cf PjC-PsPeP°CĤPrP°, PSPμP»PμC,P°P»CHPSPsPiPs C-PSCfCfP»CHC,Cf, P»PμC,P°P»CHPSPsPiPs PSP°CfP»C-PrPeCf PIC-Pr CfPμCĤC†PμPIPs-CfCfPrPëPSPSPëC... PiP°C,PsP»PsPiC-PNë C,P° PSPμCfC,P°P±C-P»CHPSPsC— CfC,PμPSPsPeP°CĤPrC-C— P· PSPμPIC-PrPeP»P°PrPSPsCĤ PePsCĤPsPSP°CĤPSPsCĤ CĤPμPIP°CfPeCfP»CĬCĤPëP·P°C†C-C”CĤ.

PĤC-PSC†PμPIC- PiPsPeP°P·PSPëPePë (PiPμCĤPIPëPSPSC- C,P° PIC,PsCĤPëPSPSC-) P°PSP°P»C-P·CfPIP°P»Pë PIC-PrPiPsPIC-PrPSPs PrPs P°PSP°P»C-P·Cf PSP°C†C-P»PμPSPSCĬ PSP° P»C-PeCfPIP°PSPSCĬ (P†PŸPŸ), PIPeP»CĤC†P°CĤC†Pë PICfC-C... CfCfP±'C”PeC,C-PI, CĬPeC- P±CfP»Pë CĤP°PSPPrPsPjC-P·PsPIP°PSC- C,P° PsC,CĤPëPjP°P»Pë PiCĤPëPSP°PNëPjPSC- PsPrPSCf PrPsP·Cf PiCĤPμPiP°CĤP°C,Cf Cf C...PsPrC- PiPsPrPIC-PNëPSPsPiPs CfP»C-PiPsPiPs PrPsCfP»C-PrP¶PμPSPSCĬ.

P—P°PiP°P»PsPj 56,6 % PiP°C†C-C”PSC,C-PI PiCĤPëPiPëPSPëP»Pë PiCĤPsP±PSPμ P»C-PeCfPIP°PSPSCĬ PiPμCĤPμPrC†P°CfPSPs, P° 45 % PiP°C†C-C”PSC,C-PI P·P°PIPμCĤC€PëP»Pë PSPμ PICfC- PIC-P·PëC,Pë PrPsCfP»C-PrP¶PμPSPSCĬ.

P—P°PiP°P»PsPj, 6190 PiP°C†C-C”PSC,C-PI P·PSP°C...PsPrPëP»PëCfCĬ PiC-Pr CfPiPsCfC,PμCĤPμP¶PμPSPSCĬPj PiCĤPsC,CĬPiPsPj 32 PjC-CfCĬC†C-PI, CfPμCĤPμPrPSCĬ C,CĤPëPIP°P»C-CfC,CĤ PIPiP»PëPICf CfC,P°PSPsPIPëP»P° 728 PrPSC-PI PrP»CĬ PiP°C†C-C”PSC,C-PI PiCĤCfPiPë C„PμP±CfPeCfPsCfC,P°C,Cf (n=3098) C,P° 719 PrPSC-PI PrP»CĬ PiP°C†C-C”PSC,C-PI PiCĤCfPiPë P°P»PsPiCfCĤPëPSPsP»Cf (n=3092).

PμPμCĤPIPëPSPSP° PeC-PSC†PμPIP° C,PsC†PeP° MACE CfPiPsCfC,PμCĤC-PiP°P»P°CfCĬ P· P°PSP°P»PsPiC-C†PSPëPjPë PiPsPeP°P·PSPëPeP°PjPë Cf PiCĤCfPiP°C... P»C-PeCfPIP°PSPSCĬ C„PμP±CfPeCfPsCfC,P°C,PsPj C,P° P°P»PsPiCfCĤPëPSPsP»PsPj (10,8 % PiCĤPsC,Pë 10,4 % PiP°C†C-C”PSC,C-PI PIC-PrPiPsPIC-PrPSPs; CfPiC-PIPIC-PrPSPsC€PμPSPSCĬ CĤPëP·PëPeCf [HR] 1,03; PrPIPsCfC,PsCĤPsPSPSC-PNë PiPsPIC,PsCĤPSPëPNë 95 % PrPsPIC-CĤC†PëPNë C-PSC,PμCĤPIP°P» [CI]

0,89БĤ“1,21).

PμCĤPë P°PSP°P»C-P·C- PsPeCĤPμPjPëC... PePsPjPiPsPSPμPSC,C-PI MACE C†P°CfC,PsC,P° P»PμC,P°P»CHPSPsCfC,C- PIC-Pr CfPμCĤC†PμPIPs-CfCfPrPëPSPSPëC... PiP°C,PsP»PsPiC-PNë P±CfP»P° PIPëC%PsCĤ Cf PiCĤCfPiC- C„PμP±CfPeCfPsCfC,P°C,Cf, PSC-P¶ P°P»PsPiCfCĤPëPSPsP»Cf (4,3 % PiCĤPsC,Pë 3,2 % PiP°C†C-C”PSC,C-PI; PŸPŸPŸ 1,34; 95 % P”P† 1,03БĤ“1,73). PŸP°CfC,PsC,P° C-PSC€PëC... PiPsPrC-PNë MACE P±CfP»P° CfC...PsP¶P° Cf PiCĤCfPiP°C... C„PμP±CfPeCfPsCfC,P°C,Cf C,P° P°P»PsPiCfCĤPëPSPsP»Cf, C,PsP±C,Ps PSPμP»PμC,P°P»CHPSPsPiPs C-PSC„P°CĤPeC,Cf PjC-PsPeP°CĤPrP° (3,6 % PiCĤPsC,Pë 3,8 % PiP°C†C-C”PSC,C-PI; PŸPŸPŸ 0,93; 95 % P”P† 0,72БĤ“1,21), PSPμP»PμC,P°P»CHPSPsPiPs C-PSCfCfP»CHC,Cf (2,3 % PiCĤPsC,Pë 2,3 % PiP°C†C-C”PSC,C-PI; PŸPŸPŸ 1,01; 95 % P”P† 0,73БĤ“1,41) C,P° C,PμCĤPjC-PSPsPIPsC— CĤPμPIP°CfPeCfP»CĬCĤPëP·P°C†C-C— C†PμCĤPμP·

PSPμCÍC,P°P±C-P»CHbPSCr CÍC,PμPSPsPeP°CḡPrC-Cḡ (1,6 % PíCḡPsC,Pë 1,8 % PíP°C†C-C"PSC,C-PI; P\$PŸPŸ 0,86; 95 % P"P† 0,59ḡḡ"1,26).

P\$P°CÍC,PsC,P° P»PμC,P°P»CHbPSPsCÍC,C- P· CÍCÍC-C... PíCḡPëC†PëPS C,P°PePsP¶ P±CÍP»P° PIPëC%PsCḡ CÍ PíCḡCÍPíC- C,,PμP±CÍPeCÍPsCÍC,P°C,CÍ, PSC-P¶ P°P»PsPíCÍCḡPëPSPsP»CÍ (7,8 % PíCḡPsC,Pë 6,4 % PíP°C†C-C"PSC,C-PI; P\$PŸPŸ 1,22; 95 % P"P† 1,01ḡḡ"1,47), C%Ps Pí PsCÍPSPsPIPSPsPjCÍ P·CÍPjPsPIP»CḡPIP°P»PsCÍC¶ P±C-P»CHbC€ PIPëCÍPsPePëPj CḡC-PIPSPμPj P»PμC,P°P»CHbPSPsCÍC,C- PIC-Pr CÍPμCḡC†PμPIPs-CÍCÍPrPëPSPSPëC... PíP°C,PsP»PsPíC-PNë CÍ C†C-PNë PíCḡCÍPíC- (PrPëPI. CḡPsP·PrC-P» B«PḡCÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PsCÍCÍPIP°PSPSC¶B»).

PŸPμPjPíPë PíCḡPëPNëPSC¶C,PsC— PíPsCÍPíC-C,P°P»C-P·P°C†C-C— P· PíCḡPëPIPsPrCÍ CÍPμCḡC†PμPIPsC— PSPμPrPsCÍC,P°C,PSPsCÍC,C-, PíPsCÍPíC-C,P°P»C-P·P°C†C-C— P· PíCḡPëPIPsPrCÍ P°CḡPëC,PjC-C—, C%Ps PSPμ PíPsPíḡḡ™ C¶P·P°PSP° C-P· C-C€PμPjC-C"Cḡ, PIPμPSPsP·PSPëPjPë C,CḡPsPjP±PsPμPjP±PsP»C-C†PSPëPjPë PíPsPrC-C¶PjPë, C- PíPsCÍPíC-C,P°P»C-P·P°C†C-C— P· PíCḡPëPIPsPrCÍ PíPμCḡPμC...C-PrPSPëC... C-C€PμPjC-C†PSPëC... PSP°PíP°PrC-PI P±CÍP»Pë PíPsCḡC-PIPSC¶PSPSPëPjPë PrP»C¶ C,,PμP±CÍPeCÍPsCÍC,P°C,CÍ C,P° P°P»PsPíCÍCḡPëPSPsP»CÍ.

P"P°CÍP»C-PrP¶PμPSPSC¶ FASTB P±CÍP»Ps PíCḡPsCÍPíPμPeC,PëPIPsPëPj CḡP°PSPPrPsPjC-P·PsPIP°PSPëPj PIC-PrPeCḡPëC,PëPj PrPsCÍP»C-PrP¶PμPSPSC¶Pj P· PjP°CÍPeCÍPIP°PSPSC¶Pj PeC-PSC†PμPIPsC— C,PsC†PePë, PIB C¶PePsPjCÍ PíPsCḡC-PIPSCḡPIP°P»Pë PíCḡPsC,,C-P»CH P±PμP·PíPμPePë C,,PμP±CÍPeCÍPsCÍC,P°C,CÍ PNë P°P»PsPíCÍCḡPëPSPsP»CÍ PrP»C¶ CÍPμCḡC†PμPIPs-CÍCÍPrPëPSPSPsC— CÍPëCÍC,PμPjPë CÍ PíP°C†C-C"PSC,C-PI P· C...CḡPsPSC-C†PSPsCḡ PíC-PíPμCḡCÍCḡPëPePμPjC-C"Cḡ (PI CÍPjPsPIP°C..., PePsP»Pë PIC-PrPeP»P°PrPμPSPSC¶ CÍCḡP°C,C-PI CÍP¶Pμ PIC-PrP±CÍP»PsCÍC¶) C- C,,P°PeC,PsCḡP°PjPë CḡPëP·PëPeCÍ CÍPμCḡC†PμPIPs- CÍCÍPrPëPSPSPëC... P·P°C...PIPsCḡCḡPIP°PSCḡ (PŸPŸP—) (C,PsP±C,PsB PíP°C†C-C"PSC,Pë PIC-PePsPj PIC-Pr 60 CḡPsPeC-PI C- PíCḡPëPSP°PNëPjPSC- P· PsPrPSPëPj C-PSC€PëPj C,,P°PeC,PsCḡPsPj CḡPëP·PëPeCÍB PŸPŸP—).B PμP°C†C-C"PSC,Pë, C¶PeC- PIC-PrPíPsPIC-PrP°P»Pë PeCḡPëC,PμCḡC-C¶Pj PIPeP»CḡC†PμPSPSC¶ CÍ PrPsCÍP»C-PrP¶PμPSPSC¶,B PsC,CḡPëPjCÍPIP°P»Pë P»C-PeCÍPIP°PSPSC¶ P°P»PsPíCÍCḡPëPSPsP»PsPj PrPs CḡP°PSPPrPsPjC-P·P°C†C-C— C-, C¶PeC%Ps P±CÍP»Ps PíPsC,CḡC-P±PSPs, C—Pj PePsCḡPëPíCÍPIP°P»Pë PrPsP·CÍ P· CÍCḡP°C...CÍPIP°PSPSC¶PjB PeP»C-PSC-C†PSPsC—B PsC†C-PSPePë, CḡPμPePsPjPμPSPPrP°C†C-PNë P,,PICḡPsPíPμPNëCÍCHbPePsC— PíCḡPsC,PëCḡPμPIPjP°C,PëC†PSPsC— P»C-PíPë (EULAR) C- P·P°C,PIPμCḡPrP¶PμPSPsC— CÍC...PμPjPë PrPsP·CÍPIP°PSPSC¶. PḡP°PíCḡPëPeC-PSC†C- PíC-PrPíPsC,PsPIC†PsC— C,,P°P·Pë P·P°CÍC,PsCÍCÍPIP°PSPSC¶ P°P»PsPíCÍCḡPëPSPsP»CÍ PíP°C†C-C"PSC,Pë P· CḡC-PIPSPμPj CÍPëCḡPsPIP°C,PePsPIPsC— PePsPSC†PμPSC,CḡP°C†C-C— CÍPμC†PsPIPsC— PePëCÍP»PsC,Pë (sUA) < 0,36 PjPjPsP»CHb/P» (< 6 PjPi/PrP») P°P±Ps PíP°C†C-C"PSC,Pë, C¶PeC- PsC,CḡPëPjCÍPIP°P»Pë PjP°PeCÍPëPjP°P»CHbPSCr PíPμCḡPμPSPsCÍPSCr PrPsP·CÍ P°P±PsB PjP°PeCÍPëPjP°P»CHbPSCr PrPsP·PIPsP»PμPSCr PrPsP·CÍ P°P»PsPíCÍCḡPëPSPsP»CÍ, P±CÍP»Pë CḡP°PSPPrPsPjC-P·PsPIP°PSC- CÍ CÍPíC-PIPIC-PrPSPsC€PμPSPSC- 1:1 PrP»C¶ PsC,CḡPëPjP°PSPSC¶ P»C-PeCÍPIP°PSPSC¶ P°P±Ps C,,PμP±CÍPeCÍPsCÍC,P°C,PsPj, P°P±Ps P°P»PsPíCÍCḡPëPSPsP»PsPj. PμPμCḡPIPëPSPSPsCḡ PeC-PSC†PμPIPsCḡ C,PsC†PePsCḡ PrPsCÍP»C-PrP¶PμPSPSC¶ FAST P±CÍPI C†P°CÍ PrPs PíPμCḡC€PsPíPs PSP°CÍC,P°PSPSC¶ P±CÍPrCHb-C¶PePsC—B PíPsPrC-C—, C%Ps PIC...PsPrPëC,CH PrPs CÍPeP»P°PrPsPIPsC—B PeC-PSC†PμPIPsC— C,PsC†PePë Antiplatelet Trialistsḡḡ™ Collaborative

(P_hP P_ŷP_ŷ), PI C,PsPjC_r C_hP_eC_rP»C-:

- PiPsC_rPiC-C,P°P»C-P·P°C_hC-C_h P· PiC_hP_ePIPsPrC_r PSP_hP»P_hC,P°P»CH_hPSPsPiPs
C-PSC,,P°C_hPeC,C_r PjC-PsPeP°C_hPrP°B (P_hP_h) / PiPsC_rC,C_hPsPiPsB PePsC_hPsPSP°C_hPSPsPiPs
C_rP_ePSPPrC_hPsPjC_rB (P°P_hP_ŷ) P· PiPsP·P_eC,P_ePIPsPsC_h C_hP_hP°PeC_hC-C°C_h PSP°
P±C-PsPjP°C_hPeP_hC_hP_e;

- PSP_hP»P_hC,P°P»CH_hPSP_ePN_e C-PSC_rC_rP»CH_hC,;

- P»P_hC,P°P»CH_hPSP_ePN_e PSP°C_rP»C-PrPsPe C_r C_hP_hP·C_rP»CH_hC,P°C,C- C_rP_hC_hC_hP_hPIPs-
C_rC_rPrP_ePSPSPsPiPs C_rC_rPeP»P°PrPSP_hPSPSC_h.

P_hP_hC_hPIP_ePSPSP_ePN_e P°PSP°P»C-P· PiC_hC_rPSC,C_rPIP°PIC_rC_h PSP° PiC-PrC...PsPrC-, C%_{oo}Ps
PIC_hP°C...PsPIC_rPIP°PI PrP°PSC- PiP°C_hC-C°PSC,C-PI, C_hPeC-B PsC,C_hP_ePjC_rPIP°P»P_e
P»C-PeC_rPIP°PSPSC_h.

Pj C_hC-P»PsPjC_r P±C_rP»P_e C_hP°PSPPrPsPjC-P·PsPIP°PSC- 6128 PiP°C_hC-C°PSC,C-PI, P·
C_hPeP_eC... 3063 PsC,C_hP_ePjC_rPIP°P»P_e C,,P_hP±C_rPeC_rPsC_rC,P°C,B C-B

3065 -B P°P»PsPiC_rC_hP_ePSPsP».

Pj PiP_hC_hPIP_ePSPSPsPjC_r P°PSP°P»C-P·C- PrP°PSP_eC... PiP°C_hC-C°PSC,C-PI, C_hPeC-
PsC,C_hP_ePjC_rPIP°P»P_e P»C-PeC_rPIP°PSPSC_h, C,,P_hP±C_rPeC_rPsC_rC,P°C, PSP_h
PiPsC_rC,C_rPiP°PIC_rC_h P°P»PsPiC_rC_hP_ePSPsP»C_r P·P° C_hP°C_rC,PsC,PsC_h
PIP_ePSP_ePePSP_hPSPSC_h PiP_hC_hPIP_ePSPSPsC— PeC-PSC_hP_hPIPsC— C,PsC_hPeP_e, C_hPeP°
C_rPiPsC_rC,P_hC_hC-PiP°P»P°C_rC_h C_r

172 PiP°C_hC-C°PSC,C-PI (1,72/100 PiP°C_hC-C°PSC,Ps-C_hPsPeC-PI) C_r PiC_hC_rPiC-
C,,P_hP±C_rPeC_rPsC_rC,P°C,C_r PiPsC_hC-PIPsC_hPSPs P· 241 PiP°C_hC-C°PSC,PsPj (2,05/100
PiP°C_hC-C°PSC,Ps-C_hPsPeC-PI) C_r PiC_hC_rPiC- P°P»PsPiC_rC_hP_ePSPsP»C_r, P·C-
C_rPePsC_hP_ePiPsPIP°PSP_ePj PIC-PrPSPsC_eP_hPSPSC_hPj C_hP_eP·P_ePeC-PI [P°P]

0,85 (95 %, P°P_h: 0,70, 1,03), C_h °0,001. P_hPSP°P»C-P· PrP°PSP_eC... PiP°C_hC-C°PSC,C-PI,
C_hPeC- PsC,C_hP_ePjC_rPIP°P»P_e P»C-PeC_rPIP°PSPSC_h, PrP»C_h PiP_hC_hPIP_ePSPSPsC—
PeC-PSC_hP_hPIPsC— C,PsC_hPeP_e C_r PiC-PrPiC_hC_rPiC- PiP°C_hC-C°PSC,C-PI P· P_hP_h,
C-PSC_rC_rP»CH_hC,PsPj P°P±Ps P°P_hP_ŷ PI P°PSP°PjPSP_hP·C- PSP_h
PiC_hPsPrP_hPjPsPSC_rC,C_hC_rPIP°PI C_rC_rC,C,C°PIP_sC— C_hC-P·PSP_eC_hC- PjC-P¶
PiC_hC_rPiP°PjP_e P»C-PeC_rPIP°PSPSC_h: 635 (9,5 %) PiP°C_hC-C°PSC,C-PI P·
PiPsPrC-C_hPjP_e C_r PiC_hC_rPiC- C,,P_hP±C_rPeC_rPsC_rC,P°C,C_r C- 83 (11,8 %)
PiP°C_hC-C°PSC,C-PI P· PiPsPrC-C_hPjP_e C_r PiC_hC_rPiC- P°P»PsPiC_rC_hP_ePSPsP»C_r;
C_rPePsC_hP_ePiPsPIP°PSP_h PIC-PrPSPsC_eP_hPSPSC_h C_hP_eP·P_ePeC-PI [P°P] 1,02 (95 % P°P_h:
0,74-1.42); C_h = 0,202.

P»C-PeC_rPIP°PSPSC_h C,,P_hP±C_rPeC_rPsC_rC,P°C,PsPj PSP_h P±C_rP»Ps PiPsPIb_h™ C_hP·P°PSP_h P·C-
P·P±C-P»CH_hC_eP_hPSPSC_hPj P»P_hC,P°P»CH_hPSPsC_rC,C- PIC-Pr P_ŷP_ŷP— P°P±Ps P· C-PSC_ePeC...
PiC_hP_eC_hPePS C_hPe C_r C_hC-P»PsPjC_r, C,P°Pe C- PI PiC-PrPiC_hC_rPiC- PiP°C_hC-C°PSC,C-PI P·
P_hP_h, C-PSC_rC_rP»CH_hC,PsPj P°P±Ps P°P_hP_ŷ PI P°PSP°PjPSP_hP·C-. P—P°PiP°P»PsPj, C_r
PiC_hC_rPiC- C,,P_hP±C_rPeC_rPsC_rC,P°C,C_r P±C_rP»Ps PjP_hPSC_eP_h P»P_hC,P°P»CH_hPSP_eC...
PSP°C_rP»C-PrPeC-PI (62 P»P_hC,P°P»CH_hPSP_eC... PIP_ePiP°PrPeP_e PIC-Pr P_ŷP_ŷP— C-

108 P»P_hC,P°P»CH_hPSP_eC... PIP_ePiP°PrPeC-PI P· C-PSC_ePeC...B PiC_hP_eC_hPePS), PSC-P¶ C_r
PiC_hC_rPiC- P°P»PsPiC_rC_hP_ePSPsP»C_r (82 P»P_hC,P°P»CH_hPSP_eC... PIP_ePiP°PrPeP_e PIC-Pr

P°Ps PrPsCfP»C-PrP¶PµPSPSCf P±CfP»Ps PIPeP»CfCfPµPSPs 346 PīP°C†C-C°PSC,C-PI C-P·
PiPµPjP°C,PsP»PsPiC-C†PSPëPjPë P·P»PsCfPeC-CfPSPëPjPë PSPsPiPsCfC,PIPsCfPµPSPSCfPjPë,
CfPeC- PsC,CfPëPjCfPIP°P»Pë C...C-PjC-PsC,PµCfP°PiC-Cf C- PjP°P»Pë
CfPµCfPµPrPSC-PNë/PIPëCfPsPePëPNë CfC,CfPiC-PSCH CfPëP·PëPeCf CfPsP·PIPëC,PeCf
PŸP·Pµ. PŸPµCfPµPrPSC° P·PSP°C†PµPSPSCf AUC sUA₁₋₈ (PjPi × C†/PrP») P±CfP»Ps
P·PSP°C†PSPs PSPëP¶C†PëPj PiCfPë PiCfPëPNëPsPjC- C„PµP±CfPeCfPsCfC,P°C,Cf (514,0 B±
225,71 PīPsCfC-PIPSCfPSPs C-P· 708,0 B± 234,42; CfPµCfPµPrPSC° PSP°PNëPjPµPSCëPëC...
PePIP°PrCfP°C,C-PI PrP»Cf CfC-P·PSPëC†C-: -196,794 [95 % PrPsPIC-CfC†PsPiPs
C-PSC,PµCfPIP°P»Cf: -238,600; -154,988]; p < 0,0001). PµCfC-Pj C,PsPiPs, CfPµCfPµPrPSC-PNë
CfPëCfPsPIP°C,PePsPIPëPNë CfC-PIPµPSCH CfPµC†PsPiPsC— PePëCfP»PsC,Pë P±CfPI
P·PSP°C†PSPs PSPëP¶C†PëPNë PiCfPë P·P°CfC,PsCfCfPIP°PSPSC- C„PµP±CfPeCfPsCfC,P°C,Cf,
PiPsC†PëPSP°CfC†Pë P· PiPµCfCëPëC... 24 PiPsPrPëPS P»C-PeCfPIP°PSPSCf C- PI P±CfPrCH-
CfPePëPNë PSP°CfC,CfPiPSPëPNë PjPsPjPµPSC, C†P°CfCf. PŸC,P°C,PëCfC,PëC†PSPs
P·PSP°C†CfC°PëC... PIC-PrPjC-PSPSPsCfC,PµPNë P·P° CfPµCfPµPrPSC-Pj PIPjC-CfC,PsPj
CfPëCfPsPIP°C,PePsPiPsPiPs PeCfPµP°C,PëPSC-PSCf (%) PjC-P¶ C„PµP±CfPeCfPsCfC,P°C,PsPj
C- P°P»PsPiCfCfPëPSPsP»PsPj PSPµ P±CfP»Ps (-0,83 B± 26,98 PīPsCfC-PIPSCfPSPs P· -4,92 B±
16,70 PIC-PrPiPsPIC-PrPSPs; CfPµCfPµPrPSC° PSP°PNëPjPµPSCëPëC... PePIP°PrCfP°C,C-PI
PrP»Cf CfC-P·PSPëC†C-: 4,0970 [95 % PrPsPIC-CfC†PsPiPs C-PSC,PµCfPIP°P»Cf: -0,6467;
8,8406]; p=0,0903). P— CfCfP°C...CfPIP°PSPSCfPj PIC,PsCfPëPSPSPëC... PeC-PSC†PµPIPëC...
C,PsC†PsPe, CfC,P°C,PëCfC,PëC†PSPs P·PSP°C†CfC°PëC... PIC-PrPjC-PSPSPsCfC,PµPNë P·P°
C†P°CfC,PsC,PsCH CfPsP·PIPëC,PeCf P»P°P±PsCHP°C,PsCHPSPs

PiC-PrC, PIPμCḡPrP¶PμPSPSPiPs PŸP>Pμ PSPμ P±CfP»Ps (8,1 % C- 9,2 % PrP»Cḡ C,,PμP±CfPeCfPsCfC,P°C,Cf C- P°P»PsPiCfCḡPēPSPSP»Cf PIC-PrPiPsPIC-PrPSPs; PIC-PrPSPsCfPSPēPNē CḡPēP·PēPe: 0,875 [95 % PrPsPIC-CḡCfPsPiPs C-PSC,PμCḡPIP°P»Cf: 0,4408; 1,7369]; p=0,8488) C- PeP»C-PSC-PePē CḡPēPSPrCḡPsPjCf CḡPsP·PiP°PrCf PiCfC...P»PēPSPē PSPμ P±CfP»Ps (1,7 % C- 1,2 % PrP»Cḡ C,,PμP±CfPeCfPsCfC,P°C,Cf PNē P°P»PsPiCfCḡPēPSPSP»Cf PIC-PrPiPsPIC-PrPSPs; PIC-PrPSPsCfPSPēPNē CḡPēP·PēPe: 0,994 [95 % PrPsPIC-CḡCfPsPiPs C-PSC,PμCḡPIP°P»Cf: 0,9691; 1,0199]; p=1,0000). P§P°CfC,PsC,P° PICfC-C... PsP·PSP°Pe C- CḡPēPjPiC,PsPjC-PI, C%oPs PIPēPSPēPeP»Pē PiC-Pr CfP°Cf P»C-PeCfPIP°PSPSCḡ, P° C,P°PePsP¶ PiPsP±C-CfPSPēC... CḡPμP°PeCfC-PNē CfC,P°PSPsPIPēP»P° 67,6 % PiPsCḡC-PIPSCḡPSPs P· 64,7 % C- 6,4 % PiPsCḡC-PIPSCḡPSPs P· 6,4 % PrP»Cḡ C,,PμP±CfPeCfPsCfC,P°C,Cf C- P°P»PsPiCfCḡPēPSPSP»Cf PIC-PrPiPsPIC-PrPSPs. Pj PrPsCfP»C-PrP¶PμPSPSC- FLORENCE C,,PμP±CfPeCfPsCfC,P°C, PiCḡPsPrPμPjPsPSCfC,CḡCfPIP°PI PSP°PNēPeCḡP°C%oCf C- CēPIPēPrCēCf PrC-Cḡ C%oPsPrPs P·PSPēP¶PμPSPSCḡ CḡC-PIPSCḡ CḡPμCfPsPIPsC— PePēCfP»PsC,Pē PI CḡPēCḡPsPIP°C,CfC- PeCḡPsPIC- PiPsCḡC-PIPSCḡPSPs P· P°P»PsPiCfCḡPēPSPSP»PsPj. P°P°PSC- C%oPsPrPs PiPsCḡC-PIPSCḡPSPSCḡ C,,PμP±CfPeCfPsCfC,P°C,Cf C- CḡP°CfP±CfCḡPēPeP°P·Pē PSP° PrP°PSPēPNē CfP°Cf PIC-PrCfCfC,PSC-. P·C,,PμPeC,PēPIPSC-CfC,Cḡ C,P° P±PμP·PiPμPeP° P·P°CfC,PsCfCfPIP°PSPSCḡ C,,PμP±CfPeCfPsCfC,P°C,Cf PSPμ P±CfP»Pē PICfC,P°PSPsPIP»PμPSC- PrP»Cḡ PiP°CfC-C°PSC,C-PI C-P· PiPsCfC,CḡPēPj C,CḡP¶PePēPj PŸP>Pμ, PSP°PiCḡPēPeP»P°Pr PiP°CfC-C°PSC,C-PI, Cf CḡPePēC... C-PSCēC- PIPēPrPē C,PμCḡP°PiC-C— PrP»Cḡ P·PSPēP¶PμPSPSCḡ CfCḡP°C,C-PI PSPμ PrC-CḡC,Cḡ.

PαP°CḡPjP°PePsPeC-PSPμC,PēPeP°

Pj P·PrPsCḡPsPIPēC... PrPsP±CḡPsPIPsP»CḡCfC-PI PjP°PeCfPēPjP°P»CḡPSP° PePsPSCfPμPSC,CḡP°CfC-Cḡ Cf PiP»P°P·PjC- PeCḡPsPIC- (PŸ_{max}) C,P° PiP»PsC%oP° PiC-Pr PeCḡPēPIPsCḡ (AUC) P·P±C-P»CḡCēCfPIP°P»PēCfCḡ PiCḡPsPiPsCḡCfC-PNēPSPs PrPsP·C- PiC-CfP»Cḡ PsPrPSPsCḡP°P·PsPIPsPiPs C,P° P±P°PiP°C,PsCḡP°P·PsPIPsPiPs P·P°CfC,PsCfCfPIP°PSPSCḡ C,,PμP±CfPeCfPsCfC,P°C,Cf Cf PrPsP·P°C... PIC-Pr 10 PrPs 120 PjPi. PμCḡPē PrPsP·P°C... PIC-Pr 120 PrPs 300 PjPi P·P±C-P»CḡCēPμPSPSCḡ AUC P±CfP»Ps P±C-P»CḡCēPēPj, PSC-P¶ PiCḡPsPiPsCḡCfC-PNēPSPs PrPsP·C-. PμCḡPē P·P°CfC,PsCfCfPIP°PSPSC- PrPsP· 10Bḡ“240 PjPi PePsP¶PSC- 24 PiPsPrPēPSPē PSP°PePsPiPēCfPμPSPSCḡ C,,PμP±CfPeCfPsCfC,P°C,Cf PSPμ PIC-PrP·PSP°CfP°P»PsCfCḡ. PμPμCḡPμPrP±P°CfCfPIP°PSPēPNē CḡPμCḡPμPrPSC-PNē C,PμCḡPjC-PSP°P»CḡPSPēPNē PiPμCḡC-PsPr PSP°PiC-PIPIPēPIPμPrPμPSPSCḡ (t_{1/2}) C,,PμP±CfPeCfPsCfC,P°C,Cf CfC,P°PSPsPIPēPI PiCḡPēP±P»PēP·PSPs 5Bḡ“8 PiPsPrPēPS. P’CfPI PiCḡPsPIPμPrPμPSPēPNē PiPsPiCfP»CḡCfC-PNēPSPēPNē P°PSP°P»C-P· C,,P°CḡPjP°PePsPeC-PSPμC,PēPePē/C,,P°CḡPjP°PePsPrPēPSP°PjC-PePē P·P° PrP°PSPēPjPē, PsC,CḡPēPjP°PSPēPjPē P· CfCfP°CfC,Cḡ 211 PiP°CfC-C°PSC,C-PI C-P· PiC-PiPμCḡCfCḡPēPePμPjC-C°Cḡ C- PiPsPrP°PiCḡPsCḡ, CḡPeC- P·P°CfC,PsCfCfPICfPIP°P»Pē C,,PμP±CfPeCfPsCfC,P°C, Cf PrPsP·P°C... 40Bḡ“240 PjPi 1 CḡP°P· PSP° PrPsP±Cf. P’ CfC-P»PsPjCf PsC,CḡPēPjP°PSC- P·PSP°CfPμPSPSCḡ C,,P°CḡPjP°PePsPeC-PSPμC,PēCfPSPēC... PiP°CḡP°PjPμC,CḡC-PI PIC-PrPiPsPIC-PrP°CḡC,Cḡ C,P°PePēPj Cf P·PrPsCḡPsPIPēC... PrPsP±CḡPsPIPsP»CḡCfC-PI, CḡPeC-, PsC,P¶Pμ, C° C...PsCḡPsCēPsCḡ PjPsPrPμP»P»Cḡ PrP»Cḡ PsCfC-PSPePē C,,P°CḡPjP°PePsPeC-PSPμC,PēPePē/C,,P°CḡPjP°PePsPrPēPSP°PjC-PePē PiCḡPμPiP°CḡP°C,Cf Cf PiP°CfC-C°PSC,C-PI C-P· PiPsPrP°PiCḡPsCḡ.

P’CfPjPsPeC,CfPIP°PSPSCḡ. PαPμP±CfPeCfPsCfC,P°C, CēPIPēPrPePs (t_{max} (CfP°Cf PrPsCfCḡPiPSPμPSPSCḡ PjP°PeCfPēPjP°P»CḡPSPsC— PePsPSCfPμPSC,CḡP°CfC-C—)

1,0Bḡ“1,5 PiPsPrPēPSPē) C- PrPsP±CḡPμ (PiCḡPēPSP°PNēPjPSC- 84 %)

PICÍPjPsPeC,CrC" C,CHCÍCÍ. P_μCT_μPē PsPrPSPsCT_μP°P·PsPIPsPjCr C,P°
P±P°PiP°C,PsCT_μP°P·PsPIPsPjCr P·P°CÍC,PsCÍCrPIP°PSPSC- C,,P_μP±CrPeCÍPsCÍC,P°C,Cr
PīP_μCT_μPsCT_μP°P»CH_μPSPs Cr PrPsP·P°C... 80 PjPi P°P±Ps 120 PjPi 1 CT_μP°P·PSP° PrPsP±Cr P_{max}
PIC-PrPīPsPIC-PrPSPs CÍC,P°PSPsPIPēC,CH_μ 2,8B_μ"3,2 PjPePi/PjP» C,P° 5,0B_μ"5,3 PjPePi/PjP». P_μP±CÍPsP»CH_μC,PsCÍ P±C-PsPrPsCÍC,CrPīPSC-CÍC,CH_μ C,P°P±P»P_μC,PsPe
C,,P_μP±CrPeCÍPsCÍC,P°C,Cr PSP_μ P°PSP°P»C-P·CrPIP°P»Pē. P_μCT_μPē
P±P°PiP°C,PsCT_μP°P·PsPIPsPjCr P·P°CÍC,PsCÍCrPIP°PSPSC- Cr PrPsP·C- 80 PjPi 1 CT_μP°P·PSP°
PrPsP±Cr P°P±Ps PīCT_μPē PsPrPSPsCT_μP°P·PsPIPsPjCr P·P°CÍC,PsCÍCrPIP°PSPSC- Cr PrPsP·C-
120 PjPi Cr PīPsC"PrPSP°PSPSC- P·P_μPēCT_μPSPsCT_μ C-P_μP_μCT_μ P_{max}
P·PjP_μPSCēCÍPIP°P»P°CÍCÍ PSP°

49 % C,P° 38 %, P° AUC B_μ" PSP° 18 % C,P° 16 % PIC-PrPīPsPIC-PrPSPs. P_μPrPSP°Pe C†P_μ PSP_μ
CÍCrPīCT_μPsPIPsPrP_μCÍPIP°P»PsCÍCÍ PeP»C-PSC-C†PSPs P·PSP°C†CÍC%PēPjPē P·PjC-PSP°PjPē
CÍC,CrPīP_μPSCÍ P·PjP_μPSCēP_μPSPSCÍ CT_μC-PIPSCÍ CÍP_μC†PsPIPsC— PePēCÍP»PsC,Pē Cr
CÍPēCT_μPsPIP°C,C†C- PeCT_μPsPIC- (PīCT_μPē P±P°PiP°C,PsCT_μP°P·PsPIPsPjCr
P·P°CÍC,PsCÍCrPIP°PSPSC- Cr PrPsP·C- 80 PjPi). P_μC,P_μP±CrPeCÍPsCÍC,P°C,
PjPsP_μPSP° P·P°CÍC,PsCÍPsPICrPIP°C,Pē PSP_μP·P°P»P_μP_μPSPs PIC-Pr PIP_μPēPIP°PSPSCÍ
C-P_μC-

P PsP·PīPsPrC-P». P_μP_μCT_μP_μPrP±P°C†CÍPIP°PSPēP_μ PsP±B_μ" C" Pj CT_μPsP·PīPsPrC-P»Cr PI
CT_μC-PIPSPsPIP°P_μPSPsPjCr CÍC,P°PSC- (V_{ss}/F) PrP»CÍ C,,P_μP±CrPeCÍPsCÍC,P°C,Cr
P·PjC-PSC_μC" C,CHCÍCÍ PIC-Pr 29 PrPs 75 P» PīC-CÍP»CÍ PīP_μCT_μPsCT_μP°P»CH_μPSPsPiPs
P·P°CÍC,PsCÍCrPIP°PSPSCÍ Cr PrPsP·C- 10B_μ"300 PjPi. P_μC,CrPīC-PSC_μ
P·PīB_μ" CÍP·CÍPIP°PSPSCÍ C,,P_μP±CrPeCÍPsCÍC,P°C,Cr P·P±C-P»PeP°PjPē PīP»P°P·PjPē
PeCT_μPsPIC- (PīPsP»PsPIPsPēPj C†PēPSPsPj P·P°P»CH_μP±C†PjC-PSPsPj)
CÍC,P°PSPsPIPēC,CH_μ 99,2 % C- PSP_μ P·PjC-PSC_μC" C,CHCÍCÍ PīCT_μPē
PīC-PrPIPēC%P_μPSPSC- PrPsP·Pē P· 80 PrPs 120 PjPi. P" P»CÍ P°PeC,PēPIPSPēC...
PjP_μC,P°P±PsP»C-C,C-PI C,,P_μP±CrPeCÍPsCÍC,P°C,Cr CÍC,CrPīC-PSC_μ
P·PīB_μ" CÍP·CÍPIP°PSPSCÍ P·P±C-P»PeP°PjPē PīP»P°P·PjPē PeCT_μPsPIC-
PePsP»PēPIP°C" C,CHCÍCÍ PIC-Pr 82 PrPs 91 %.

P_μP_μC,P°P±PsP»C-P·Pj. P_μP_μP±CrPeCÍPsCÍC,P°C, P°PeC,PēPIPSPs
PjP_μC,P°P±PsP»C-P·CÍC" C,CHCÍCÍ CēP»CÍC...PsPj PePsPSB_μ" CT_μPiP°C†C-C— P·
CÍC†P°CÍC,CT_μ
CÍCT_μPēPrPēPSPPrPēC,,PsCÍC,,P°C,PiP»CT_μPeCÍCT_μPsPSC-P»C,CT_μP°PSCÍC,,P_μCT_μP°P·Pē (PjP" P_μ-
PiP»CT_μPeCÍCT_μPsPSC-P»C,CT_μP°PSCÍC,,P_μCT_μP°P·Pē) C,P° PsPePēCÍPSP_μPSPSCÍ P·
CÍC†P°CÍC,CT_μ C,,P_μCT_μPjP_μPSC,C-PI CÍPēCÍC,P_μPjPē C†PēC,PsC...CT_μPsPjCr P 450 (CYP).
PjCÍCT_μPsPiPs C-PrP_μPSC,PēC,,C-PePsPIP°PSPs 4 C,,P°CT_μPjP°PePsP»PsPiC-C†PSPs
P°PeC,PēPIPSPēC... PiC-PrCT_μPsPeCÍPēP»CH_μPSPēC... PjP_μC,P°P±PsP»C-C,Pē
C,,P_μP±CrPeCÍPsCÍC,P°C,Cr, 3 P·PSPēC... P±C†P»Pē PIPēCÍPIP»P_μPSC- Cr PīP»P°P·PjC-
PeCT_μPsPIC- P»CT_μPrPēPSPē. P"PsCÍP»C-PrP_μPSPSCÍ *in vitro* PSP° PjC-PeCT_μPsCÍPsPjP°C...
PīP_μC†C-PSPePē P»CT_μPrPēPSPē P·P°CÍPIC-PrC†PēP»Pē, C%Ps C†C- PsPePēCÍPSP_μPSC-
PjP_μC,P°P±PsP»C-C,Pē CrC,PIPsCT_μCT_μC,CHCÍCÍ PīP_μCT_μP_μPIP°P_μPSPs PiC-Pr PrC-C"CT_μ
CYP1P_μ1, CYP1P_μ2, CYP2P_μ8 P°P±Ps CYP2P_μ9, C,PsPrC- CÍPe C,,P_μP±CrPeCÍPsCÍC,P°C,Cr
PiP»CT_μPeCÍCT_μPsPSC-Pr CrC,PIPsCT_μCT_μC,CHCÍCÍ PiPsP»PsPIPsPēPj C†PēPSPsPj PiC-Pr
PrC-C"CT_μ PjP" P_μ-PiP»CT_μPeCÍCT_μPsPSC-P»C,CT_μP°PSCÍC,,P_μCT_μP°P·Pē 1P_μ1, 1P_μ8 C,P° 1P_μ9.

P'PēPIP_μPrP_μPSPSCÍ. P_μP_μP±CrPeCÍPsCÍC,P°C, PIPēPIPsPrPēC,CHCÍCÍ P·
PsCT_μPIP°PSC-P·PjCr C†P_μCT_μP_μP· PīP_μC†C-PSPeCr C,P° PSPēCT_μPeP°PjPē. P_μC-CÍP»CÍ
PīP_μCT_μPsCT_μP°P»CH_μPSPsPiPs P·P°CÍC,PsCÍCrPIP°PSPSCÍ ¹⁴P_μ-C,,P_μP±CrPeCÍPsCÍC,P°C,Cr Cr
PrPsP·C- 80 PjPi PīCT_μPēP±P»PēP·PSPs 49 % PIPēPIPsPrPēP»PsCÍCÍ C-P· CÍP_μC†P_μCT_μ Cr

PIPëPiP»CΠPrC- PSPμP·PjC-PSPμPSPsPiPs C,,PμP±CfPeCfPsCfC,P°C,Cf (3 %),
P°C†PëP»PiP»CfPeCfCfPsPSC-PrCf PrC-CfCfPsC— CfPμCfPsPIPëPSPë (30 %), PIC-PrPsPjPëC...
PsPePëCfPSPμPSPëC... PjPμC,P°P±PsP»C-C,C-PI C,P° C—C... PePsPSbTM CfPiP°C,C-PI (13 %)
C,P° C-PSCëPëC... PSPμPIC-PrPsPjPëC... PjPμC,P°P±PsP»C-C,C-PI (3 %). P₇CfC-Pj
PSPëCfPePsPIPsC— PμPeCfPeCfPμC†C-C—, PìCfPëP±P»PëP·PSPs 45 % PrPsP·Pë
PIPëPIPsPrPëP»PsCfCΠ P· PeP°P»PsPj Cf PIPëPiP»CΠPrC- PSPμP·PjC-PSPμPSPsPiPs
C,,PμP±CfPeCfPsCfC,P°C,Cf

(12 %), P°C†PëP»PiP»CfPeCfCfPsPSC-PrCf PrC-CfCfPsC— CfPμCfPsPIPëPSPë (1 %),
PIC-PrPsPjPëC... PsPePëCfPSPμPSPëC... PjPμC,P°P±PsP»C-C,C-PI C,P° C—C...
PePsPSbTM CfPiP°C,C-PI (25 %) C,P° C-PSCëPëC... PSPμPIC-PrPsPjPëC...
PjPμC,P°P±PsP»C-C,C-PI (7 %).

PkPëCfPePsPIP° PSPμPrPsCfC,P°C,PSC-CfC,Cf

PμCfPë P±P°PiP°C,PsCfP°P·PsPIPsPjCf P·P°CfC,PsCfCfPIP°PSPSC-
C,,PμP±CfPeCfPsCfC,P°C,Cf PI PrPsP·C- 80 PjPi PSPμ P±CfP»Ps PIC-PrP·PSP°CfPμPSPs P·PjC-PS
P₇_{max} C,,PμP±CfPeCfPsCfC,P°C,Cf Cf PìP°C†C-C"PSC,C-PI P· P»PμPiPePsCf, PìPsPjC-CfPSPsCf
P°P±Ps C,CΠP¶PePsCf PSPëCfPePsPIPsCf PSPμPrPsCfC,P°C,PSC-CfC,Cf
PìPsCfC-PIPsCΠPSPs P· PìP°C†C-C"PSC,P°PjPë P· PSPsCfPjP°P»CfPSPsCf C,,CfPSPeC†C-C"Cf
PSPëCfPsPe. P₇PμCfPμPrPSCΠ P·P°PiP°P»CfPSP° AUC C,,PμP±CfPeCfPsCfC,P°C,Cf
P·P±C-P»CfCëCfPIP°P»P°CfCΠ PìCfPëP±P»PëP·PSPs Cf 1,8 CfP°P·P°: PIC-Pr 7,5 PjPePi ×
PiPsPrPëPSP°/PjP» Cf PìP°C†C-C"PSC,C-PI P· PSPsCfPjP°P»CfPSPsCf C,,CfPSPeC†C-C"Cf
PSPëCfPsPe PrPs 13,2 PjPePi × PiPsPrPëPSP°/PjP» Cf PìP°C†C-C"PSC,C-PI P· C,CΠP¶PePsCf
PSPëCfPePsPIPsCf PSPμPrPsCfC,P°C,PSC-CfC,Cf. C_{max} C,P° AUC P°PeC,PëPIPsPëC...
PjPμC,P°P±PsP»C-C,C-PI PìC-PrPIPëC%oCfPIP°P»PëCfCΠ Cf 2 C- 4 CfP°P·Pë
PIC-PrPìPsPIC-PrPSPs. PμCfPsC,Pμ PìP°C†C-C"PSC,P°Pj C-P· PSPëCfPePsPIPsCf
PSPμPrPsCfC,P°C,PSC-CfC,Cf P»PμPiPePsPiPs P°P±Ps PìPsPjC-CfPSPsPiPs CfC,CfPìPμPSCΠ
PePsCfPμPeC†C-CΠ PrPsP·Pë P»C-PeP°CfCfCfPePsPiPs P·P°CfPsP±Cf PSPμ
PìPsC,CfC-P±PSP°.

PμPμCfC-PSPePsPIP° PSPμPrPsCfC,P°C,PSC-CfC,Cf

PμCfPë P±P°PiP°C,PsCfP°P·PsPIPsPjCf P·P°CfC,PsCfCfPIP°PSPSC-
C,,PμP±CfPeCfPsCfC,P°C,Cf Cf PrPsP·C- 80 PjPi PSPμ P±CfP»Ps PIC-PrP·PSP°CfPμPSPs
CfCfC,C,C"PIPëC... P·PjC-PS P₇_{max} C,P° AUC C,,PμP±CfPeCfPsCfC,P°C,Cf C- P₇PsPiPs
PjPμC,P°P±PsP»C-C,C-PI Cf PìP°C†C-C"PSC,C-PI P· P»PμPiPePsCf (PeP»P°Cf P₇ P·P°
CëPeP°P»PsCf P₇P°P₇P»PrP°bTM "PμbTM Cf) C,P° PìPsPjC-CfPSPsCf (PeP»P°Cf P' P·P°
CëPeP°P»PsCf P₇P°P₇P»PrP°bTM "PμbTM Cf) PìPμCfC-PSPePsPIPsCf
PSPμPrPsCfC,P°C,PSC-CfC,Cf PìPsCfC-PIPsCΠPSPs P· PìP°C†C-C"PSC,P°PjPë P·
PSPsCfPjP°P»CfPSPsCf C,,CfPSPeC†C-C"Cf PìPμCfC-PSPePë. P"PsCfP»C-PrP¶PμPSPSCΠ
P»C-PeP°CfCfCfPePsPiPs P·P°CfPsP±Cf Cf PìP°C†C-C"PSC,C-PI P· C,CΠP¶PePsCf
PìPμCfC-PSPePsPIPsCf PSPμPrPsCfC,P°C,PSC-CfC,Cf (PeP»P°Cf P₇ P·P° CëPeP°P»PsCf
P₇P°P₇P»PrP°bTM "PμbTM Cf) PSPμ PìCfPsPIPsPrPëP»Pë.

P'C-Pe

PμCfPë P±P°PiP°C,PsCfP°P·PsPIPsPjCf PìPμCfPsCfP°P»CfPSPsPjCf
P·P°CfC,PsCfCfPIP°PSPSC- C,,PμP±CfPeCfPsCfC,P°C,Cf PSPμ P±CfP»Ps PIC-PrP·PSP°CfPμPSPs
CfCfC,C,C"PIPëC... P·PjC-PS AUC C,,PμP±CfPeCfPsCfC,P°C,Cf C,P° P₇PsPiPs
PjPμC,P°P±PsP»C-C,C-PI Cf PìP°C†C-C"PSC,C-PI P»C-C,PSChPsPiPs PIC-PeCf
PìPsCfC-PIPsCΠPSPs P· PjPsP»PsPrPëPjPë P·PrPsCfPsPIPëPjPë PrPsP±CfPsPIPsP»CfC†CΠPjPë.

PŸC,P°C,CH

PµCŸPë P±P°PiP°C,PsCŸP°P·PsPIPsPjCř PiPµCŸPsCŸP°P»CHßPSPsPjCř
P·P°CŸC,PsCŸCřPIP°PSPSC- C,,PµP±CřPeCŸPsCŸC,P°C,Cř PŸ_{max} C,P° AUC
C,,PµP±CřPeCŸPsCŸC,P°C,Cř Cř P¶C-PSPsPe P±CřP»Pë PSP° 24 % C,P° 12 % PIPëC%PëPjPë
PIC-PrPiPsPIC-PrPSPs, PSC-P¶ Cř C±PsP»PsPIC-PeC-PI. PhPrPSP°Pe PŸ_{max} C,P° AUC,
CŸPePsCŸPëPiPsPIP°PSC- P·P° PjP°CŸPsCŸ C,C-P»P°, P±CřP»Pë CŸC...PsP¶C- PrP»C¶
PsP±PsC... PiCŸCřPi, C,PsPjCř P·PjC-PSP° PrPsP·Pë C,,PµP±CřPeCŸPsCŸC,P°C,Cř
P·P°P»PµP¶PSPs PIC-Pr CŸC,P°C,C- PSPµ PiPsC,CŸC-P±PSP°.

PŸP»C-PSC-C±PSC- C...P°CŸP°PeC,PµCŸPëCŸC,PëPePë

PµPsPeP°P·P°PSPSC¶

P,,P'P PhPαP·P' Cř PrPsP·C- 80 PjPi C,P° 120 PjPi

P>C-PeCřPIP°PSPSC¶ C...CŸPsPSC-C±PSPsC— PiC-PiPµCŸCřCŸPëPePµPjC-C— PiCŸPë
P·P°C...PIPsCŸCŸPIP°PSPSC¶C..., C%Ps CŸCřPiCŸPsPIPsPrP¶CřCŸC,CHßCŸC¶
PIC-PrPeP»P°PrP°PSPSC¶Pj PeCŸPëCŸC,P°P»C-PI CřCŸP°C,C-PI, Cř C,PsPjCř C±PëCŸP»C-
PiCŸPë PSP°C¶PIPsPSCŸC,C- C,PsC,,CřCŸC-PI C,P°/P°P±Ps PiPsPrP°PiCŸPëC±PSPsPiPs
P°CŸC,CŸPëC,Cř PI PrP°PSPëP№ C±P°CŸ C±Pë PI P°PSP°PjPSPµP·C-.

P,,P'P PhPαP·P' Cř PrPsP·C- 120 PjPi

P>C-PeCřPIP°PSPSC¶ C,P° PiCŸPsC,,C-P»P°PeC,PëPeP° PiC-PiPµCŸCřCŸPëPePµPjC-C— Cř
PrPsCŸPsCŸP»PëC... PiP°C†C-C" PSC,C-PI, C¶PeC- PiC-PrPrP°CŸC,CHßCŸC¶
C...C-PjC-PsC,PµCŸP°PiC-C— P· PiCŸPëPIPsPrCř PiPµPjP°C,PsP»PsPiC-C±PSPëC...
P·P»PsC¶PeC-CŸPSPëC... PSPsPIPsCřC,PIPsCŸPµPSCHß P· PiPsPjC-CŸPSPëPj P°P±Ps
PIPëCŸPsPePëPj CŸPëP·PëPePsPj CŸPëPSPrCŸPsPjCř P»C-P·PëCŸCř PiCřC...P»PëPSPë (PŸP>P¶).

P,,P'P PhPαP·P' PiPsPeP°P·P°PSPëP№ PrPsCŸPsCŸP»PëPj PiP°C†C-C" PSC,P°Pj.

PµCŸPsC,PëPiPsPeP°P·P°PSPSC¶

P"C-PiPµCŸC±CřC,P»PëPIC-CŸC,CHß PrPs P°PeC,PëPIPsPSC— CŸPµC±PsPIPëPSPë P°P±Ps PrPs
P±CřPrCHß-C¶PePsC— C-PSC€PsC— PrPsPiPsPjC-P¶PSPsC— CŸPµC±PsPIPëPSPë
PiCŸPµPiP°CŸP°C,Cř, P·P°P·PSP°C±PµPSPsC— Cř CŸPsP·PrC-P»C- B«PŸPeP»P°PrB».

***P'P·P°C" PjPsPrC-C¶ P· C-PSC€PëPjPë P»C-PeP°CŸCŸCHßPePëPjPë P·P°CŸPsP±P°PjPë C,P°
C-PSC€C- PIPëPrPë PIP·P°C" PjPsPrC-PNë***

PßPµCŸPeP°PiC,PsPiC¿CŸPëPS/P°P·P°C,C-PsPiCŸPëPS

P'C-PrPiPsPIC-PrPSPs PrPs PjPµC...P°PSC-P·PjCř CŸPIPsC"C— PrC-C—
C,,PµP±CřPeCŸPsCŸC,P°C, PiCŸPëPiPSC-C±CřC" PeCŸP°PSC,PëPSPsPeCŸPëPrP°P·Cř, C,PsPjCř
CŸCřPiCřC,PSC" P·P°CŸC,PsCŸCřPIP°PSPSC¶ PSPµ CŸPµPePsPjPµPSPrCřC"C,CHßCŸC¶.
PµCŸPëPiPSC-C±PµPSPSC¶ PeCŸP°PSC,PëPSPsPeCŸPëPrP°P·Pë PjPsP¶Pµ PiCŸPëP·PIPsPrPëC,Pë

PrPs PiC-PrPIPëC%PµPSPSC¼ PePsPSC†PµPSC, CĤP°C†C-C— PsP±PsC... PiCĤPµPiP°CĤP°C, C-PI
Cf PiP»P°P·PjC- PeCĤPsPIC-, C%Ps PjPsP¶Pµ CfPiCĤPëC†PëPSC¼C, Pë
PjC-C”P»PsC, PsPeCfPëC†PSCf CĤPµP°PeC†C-CĤ. Pj CĤP°P·C- PsPrPSPsC†P°CfPSPsPiPs
PIPIPµPrPµPSPSC¼ C,, PµP±CfPeCfPsCfC, P°C, Cf PrPsP·Pë
PjPµCĤPeP°PiC, PsPiCfCĤPëPSCf/P°P·P°C, C-PsPiCĤPëPSCf CfP»C-Pr P·PjPµPSCëPëC, Pë PrPs 20
% P°P±Ps PjPµPSCëPµ PIC-Pr CĤP°PSC-CëPµ PiCĤPëP·PSP°C†PµPSPsC— PrPsP·Pë (PrPëPI.
CĤPsP·PrC-P» B«PhCfPsP±P»PëPIPsCfC, C- P·P°CfC, PsCfCfPiP°PSPSC¼B»).

PhPrPµPePiP°C, PSC-CfC, CĤ P·P°PiCĤPsPiPsPSPsPiP°PSPsC— PePsCĤPµPeC†C-C— PrPsP·Pë,
C¼PeP° P±P°P·CfPiP°P»P°CfC¼ PSP° PjPsPrPµP»CĤPiP°PSPSC- C, P°
C-PjC-C, P°C†C-PNëPSPsPjCf P°PSP°P»C-P·C- PrPsPeP»C-PSC-C†PSPëC... PrP°PSPëC... PSP°
C%CrCĤP°C..., P±CfP»P° PiC-PrC, PiPµCĤPrP¶PµPSP° CĤPµP·CfP»CĤC, P°C, P°PjPë
PeP»C-PSC-C†PSPsPiPs PrPsCfP»C-PrP¶PµPSPSC¼ PiP·P°C”PjPsPrC-C—
P»C-PeP°CĤCfCĤPePëC... P·P°CfPsP±C-PI Cf P·PrPsCĤPsPiPëC... PrPsP±CĤPsPiPsP»CĤC†C-PI,
C¼PeC- PsC, CĤPëPjCfPiP°P»Pë P°P·P°C, C-PsPiCĤPëPS 100 PjPi PsPeCĤPµPjPs C, P°
P·PSPëP¶PµPSCf PrPsP·Cf P°P·P°C, C-PsPiCĤPëPSCf (25 PjPi) Cf PePsPjP±C-PSP°C†C-C— P·
C,, PµP±CfPeCfPsCfC, P°C, PsPj (40 P°P±Ps

120 PjPi). P”PsCfP»C-PrP¶PµPSPSC¼ PiP·P°C”PjPsPrC-C— C,, PµP±CfPeCfPsCfC, P°C, Cf PiC-Pr
C†P°Cf C†PëC, PsC, PsPeCfPëC†PSPsC— C...C-PjC-PsC, PµCĤP°PiC-C— PSPµ PiCĤPsPiPsPrPëP»Pë.
Pj PiCĤPsC†PµCfC- PsPiPsCĤPSPsPiPs PrPsCfP»C-PrP¶PµPSPSC¼ PiP°C†C-C”PSC, P°Pj C-P·
PŸP·Pµ P· PrPµPeC-P»CĤPePsPjP° CĤPµP¶PëPjP°PjPë C...C-PjC-PsC, PµCĤP°PiC-C—
PiCĤPëP·PSP°C†P°PICfC¼ C,, PµP±CfPeCfPsCfC, P°C, Cf PrPsP·C- 120 PjPi,
PiPeP»CĤC†P°CĤC†Pë PjPsPSPsPeP»PsPSP°P»CĤPSC- P°PSC, PëC, C-P»P°. PhPrPSP°Pe PiC-Pr
C†P°Cf C†CĤPsPiPs PrPsCfP»C-PrP¶PµPSPSC¼ PiP·P°C”PjPsPrC-C— P»C-PeP°CĤCfCĤPePëPµ
PiCĤPµPiP°CĤP°C, BĤ”P»C-PeP°CĤCfCĤPePëPµ PiCĤPµPiP°CĤP°C, C-
P»C-PeP°CĤCfCĤPePëPµ PiCĤPµPiP°CĤP°C, BĤ”P·P°C...PiPsCĤCĤPiP°PSPSC¼ PSPµ
PrPsCfP»C-PrP¶CfPiP°P»Pë. PŸPsPjCf PjPsP¶P»PëPIC-CfC, CĤ PiP·P°C”PjPsPrC-C— P·
P±CfPrCĤ-C¼PePëPjPë C†PëC, PsC, PsPeCfPëC†PSPëPjPë PiCĤPµPiP°CĤP°C, P°PjPë, C%Ps
CfCfPjC-CfPSPs PiCĤPëP·PSP°C†P°CĤC, CĤCfC¼, PiPëPeP»CĤC†P°C, Pë PSPµ PjPsP¶PSP°.

P PsP·PëPiP»C-C, P°P·PsPS/CfCžP±CfC, CĤP°C, Pë CYP2C8

PµPµP±CfPeCfPsCfC, P°C, C” CfP»P°P±PePëPj C-PSPiC-P±C-C, PsCĤPsPj CYP2C8 *in vitro*. Pj
PiCĤPsC†PµCfC- PrPsCfP»C-PrP¶PµPSPSC¼ Cf P·PrPsCĤPsPiPëC...
PrPsP±CĤPsPiPsP»CĤC†C-PI PiP°CĤP°P»PµP»CĤPSPµ P·P°CfC, PsCfCfPiP°PSPSC¼ 120 PjPi
C,, PµP±CfPeCfPsCfC, P°C, Cf 1 CĤP°P· PSP° PrPsP±Cf C, P° PsPrPSPsCĤP°P·PsPiPsC—
PiPµCĤPsCĤP°P»CĤPSPs PiCĤPëPµPSC¼C, PsC— PrPsP·Pë CĤPsP·PëPiP»C-C, P°P·PsPSCf 4 PjPi
PSPµ PiPiP»PëPiP°P»Ps PSP° C,, P°CĤPjP°PePsPeC-PSPµC, PëPeCf CĤPsP·PëPiP»C-C, P°P·PsPSCf
C- PNëPsPiPs PjPµC, P°P±PsP»C-C, Cf N-PrPµP·PjPµC, PëP»CĤPsP·PëPiP»C-C, P°P·PsPSCf, C%Ps
PrPµPjPsPSCfC, CĤCfC”, C%Ps C,, PµP±CfPeCfPsCfC, P°C, PSPµ PiCĤPëPiPSC-C†CfC”
C,, PµCĤPjPµPSC, CYP2C8 *in vivo*. PŸP°PePëPj C†PëPSPsPj, PsPrPSPsC†P°CfPSPµ
PIPIPµPrPµPSPSC¼ C,, PµP±CfPeCfPsCfC, P°C, Cf C- CĤPsP·PëPiP»C-C, P°P·PsPSCf P°P±Ps
C-PSCëPëC... CfCfP±CfC, CĤP°C, C-PI CYP2C8 PSPµ PiPëPjP°PiP°C” PePsCĤPµPeC†C-C—
PrPsP·Pë PrP»C¼ C†PëC... PiCĤPµPiP°CĤP°C, C-PI.

PŸPµPsC,, C-P»C-PS

PµCĤPsPiPµPrPµPSPs PrPsCfP»C-PrP¶PµPSPSC¼ PiP·P°C”PjPsPrC-C—
C,, PµP±CfPeCfPsCfC, P°C, Cf P· CfC†P°CfC, CĤ P·PrPsCĤPsPiPëC... PrPsP±CĤPsPiPsP»CĤC†C-PI
PrP»C¼ PsC†C-PSPëPë PiPiP»PëPICf PiCĤPëPiPSC-C†PµPSPSC¼
PeCfP°PSC, PëPSPsPeCfPëPrP°P·Pë PSP° P·P±C-P»CĤCëPµPSPSC¼ CĤC-PIPSC¼
C, PµPsC,, C-P»C-PSCf PI C†PëCĤPeCfP»CĤCĤC†C-PNë PeCĤPsPIC-, C%Ps

°C₇PēPS

P_αP_μP±C₇P_eC₇P_sC₇C, P° C, P_jP_sP₇PSP° P_sPrPSPsC₇P°C₇PSPs P·P°C₇C, P_sC₇P_sPIC₇P₇P° C, Pē P·
P_eP_sP»C...C-C₇PēPSPsP_j P°P±P_s C-PSP₇P_sP_jP_μC, P°C₇PēPSPsP_j P±P_μP· P·P_jC-PSPē PrP_sP·Pē
P_iC₇P_μP_iP°C₇P° C, C-PI.

P₇P°P_eP_sP₇ PSP_μ P_iP_sC, C₇C-P±PSPs P·P_jC-PSC₇P₇P° C, Pē PrP_sP·C₇ C,, P_μP±C₇P_eC₇P_sC₇C, P° C, C₇
P_iC₇Pē P_sPrPSPsC₇P°C₇PSPsP_jC₇ P·P°C₇C, P_sC₇C₇P₇P°PSPSC- P·
P_iC-P₇C₇P_sC...P»P_sC₇P_sC, C-P°P·PēPrP_sP_j.

P_hPrPSPsC₇P°C₇PSP_μ P·P°C₇C, P_sC₇C₇P₇P°PSPSC₇ C,, P_μP±C₇P_eC₇P_sC₇C, P° C, C₇ P·
P₇P°C₇C,, P°C₇PēPSPsP_j PSP_μ P_iPēP_jP°P_iP° C” P·P_jC-PSPē PrP_sP·Pē P_sC₇C, P°PSPSCH₇P_sP_iP_s.
P—P°C₇C, P_sC₇C₇P₇P°PSPSC₇ C₇ P·PrP_sC₇P_sP_iPēC... PrP_sP±C₇P_sP_iP_sP»CHC₇C-PI
C,, P_μP±C₇P_eC₇P_sC₇C, P° C, C₇ (80 P_jP_i P°P±P_s 120 P_jP_i 1 C₇P°P· PSP° PrP_sP±C₇) P·
P₇P°C₇C,, P°C₇PēPSPsP_j PSP_μ P_iP_iP»PēP₇P° C” PSP° C,, P°C₇P_jP°P_eP_sP_eC-PSP_μC, PēP_eC₇
P_sC₇C, P°PSPSCH₇P_sP_iP_s. P_hPrPSPsC₇P°C₇PSP_μ P·P°C₇C, P_sC₇C₇P₇P°PSPSC₇ P·
C,, P_μP±C₇P_eC₇P_sC₇C, P° C, P_sP_j C, P°P_eP_sP₇ PSP_μ P_iP_iP»PēP₇P°P»P_s PSP° P_hP_hP_h C, P°
P°P_eC, PēP_iPSC-C₇C, CH C,, P°P_eC, P_sC₇P° VP₇P₇.

P”P_μP·PēP_iC₇P°P_jC-PS/C₇C₇P±C₇C, C₇P° C, Pē CYP2D6

P—P° PrP°PSPēP_jPē, P_sC, C₇PēP_jP°PSPēP_jPē *in vitro*, C,, P_μP±C₇P_eC₇P_sC₇C, P° C, C”
C₇P»P°P±P_ePēP_j C-PSP_iC-P±C-C, P_sC₇P_sP_j CYP2D6. P_j P_iC₇P_sC₇P_μC₇C-
PrP_sC₇P»C-PrP₇P_μPSC₇ P· C₇C₇P°C₇C, C₇ P·PrP_sC₇P_sP_iPēC... PrP_sP±C₇P_sP_iP_sP»CHC₇C-PI,
C₇P_eC- P_sC, C₇PēP_jC₇P₇P°P»Pē 120 P_jP_i C,, P_μP±C₇P_eC₇P_sC₇C, P° C, C₇ 1 C₇P°P· PSP° PrP_sP±C₇,
C₇P_iP_sC₇C, P_μC₇C-P_iP°P»P_sC₇C₇ P·P±C-P»CHC₇P_μPSPSC₇ AUC PrP_μP·PēP_iC₇P°P_jC-PSC₇
(C₇C₇P±C₇C, C₇P° C, CYP2D6) PSP° 22 %, C%₀P_s C₇P_iC-PrC₇PēC, CH P_iC₇P_s C₇P»P°P±P_eC₇
P_iC₇PēP_iPSC-C₇C₇P₇P°P»CH₇PSC₇ PrC-C₇ C,, P_μP±C₇P_eC₇P_sC₇C, P° C, C₇ PSP° C,, P_μC₇P_jP_μPSC,
CYP2D6 *in vivo*.

P₇P°P_ePēP_j C₇PēPSPsP_j, P_iC₇Pē P_sPrPSPsC₇P°C₇PSPsP_jC₇ P·P°C₇C, P_sC₇C₇P₇P°PSPSC-
C,, P_μP±C₇P_eC₇P_sC₇C, P° C, C₇ C₇C₇P±C₇C, C₇P° C, C-PI CYP2D6 PSP_μP_jP° C”
PSP_μP_sP±C...C-PrPSPsC₇C, C- P·P_jC-PSC₇P₇P° C, Pē C—C... PrP_sP·Pē.

P_hPSC, P°C₇PēPrPSC- P·P°C₇P_sP±Pē

P_μC₇Pē P_sPrPSPsC₇P°C₇PSPsP_jC₇ P·P°C₇C, P_sC₇C₇P₇P°PSPSC- P· P°PSC, P°C₇PēPrP°P_jPē, C%₀P_s
P_jC-C₇C, C₇C, CH P_jP°P_iPSC-C₇ P_iC-PrC₇P_sP_eC₇PēPr C, P° P°P»C₇P_jC-PSC-C₇
P_iC-PrC₇P_sP_eC₇PēPr, P_iC-PrP·PSP°C₇P° C, CHC₇C₇ P·P° C, C₇PēP_jP_eP°
P_iC₇P_jP_sP_eC, C₇P₇P°PSPSC₇ C,, P_μP±C₇P_eC₇P_sC₇C, P° C, C₇ (P_iC₇PēP±P»PēP·PSPs PSP° 1
P_iP_sPrPēPSC₇) C, P° P·P_jP_μPSC₇P_μPSPSC₇ P₇_{max} PSP° 32 %, P_sPrPSP°P_e AUC
C,, P_μP±C₇P_eC₇P_sC₇C, P° C, C₇ C₇C₇C, C, C”P_iP_s PSP_μ P·P_jC-PSC₇C”C, CHC₇C₇, C, P_sP_jC₇
C,, P_μP±C₇P_eC₇P_sC₇C, P° C, P_jP_sP₇PSP° P·P°C₇C, P_sC₇P_sPIC₇P₇P° C, Pē P· P°PSC, P°C₇PēPrPSPēP_jPē
P·P°C₇P_sP±P°P_jPē.

P_hC₇P_sP±P»PēP_iP_sC₇C, C- P·P°C₇C, P_sC₇C₇P₇P°PSPSC₇

P₇P_μC₇C₇P_μP_iP_s-C₇C₇PrPēPSPSC- P·P° C...P_iP_sC₇C₇P₇P°PSPSC₇

P>C-P_eC₇P₇P°PSPSC₇ C...C₇P_sPSC-C₇PSPsC— P_iC-P_iP_μC₇C₇PēP_eP_μP_jC—C—

PJ PjPμP¶P°C... PīPsCīC,PjP°CḡPePμC,PēPSPiPsPIPsPiPs PSP°PiP»CḡPrCḡ P±CḡP»Pē
CḡC-PrPeC-CḡPSC- PīPsPIC-PrPsPjP»PμPSPSCḡ PīCḡPs CḡPμCḡPNēPsP·PSC-
P°P»PμCḡPiC-C±PSC- CḡPμP°PeC†C-C—/CḡPμP°PeC†C-C— PiC-PīPμCḡC±CḡC,P»PēPIPsCīC,C-
Cḡ C,PsPjCḡ C±PēCḡP»C- P·P°PiCḡPsP·P»PēPIPsPiPs PrP»Cḡ P¶PēC,C,Cḡ CḡPēPSPPrCḡPsPjCḡ
PŸC,C-PIPμPSCḡP°ḡḡ“P”P¶PsPSCḡPsPSP°, C,PsPeCḡPēC±PSPsPiPs
PμPīC-PrPμCḡPjP°P»CHbPSPsPiPs PSPμPeCḡPsP»C-P·Cḡ C,P° PiPsCīC,CḡPēC...
P°PSP°C,,C-P»P°PeC,PēC±PSPēC... CḡPμP°PeC†C-PNē/CēPsPeCḡ. PJ P±C-P»CHbCēPsCīC,C-
PIPēPīP°PrPeC-PI C,P°PeC- CḡPμP°PeC†C-C— CḡPiPsCīC,PμCḡC-PiP°P»PēCḡCḡ
PiCḡPsC,CḡPiPsPj PīPμCḡCēPsPiPs PjC-CḡCḡC†Cḡ P·P°CḡC,PsCḡCḡPIP°PSPSCḡ
C,,PμP±CḡPeCḡPsCīC,P°C,Cḡ. PJ PeC-P»CHbPePsC..., P°P»Pμ PSPμ Cḡ PICḡC-C...
PīP°C†C-C”PSC,C-PI CḡPiPsCīC,PμCḡC-PiP°P»PēCḡCḡ PiPsCḡCḡCēPμPSPSCḡ
PSPēCḡPePsPIPsC— C,,CḡPSPeC†C-C— C,P°/P°P±Ps PiC-PīPμCḡC±CḡC,P»PēPIC-CḡC,CHb PrPs
P°P»PsPiCḡCḡPēPSPsP»Cḡ PI P°PSP°PjPSPμP·C-. PŸCḡP¶PeC- CḡPμP°PeC†C-C—
PiC-PīPμCḡC±CḡC,P»PēPIPsCīC,C-, Cḡ C,PsPjCḡ C±PēCḡP»C- CḡPμP°PeC†C-C—, C%oPs
CḡCḡPiCḡPsPIPsPrP¶CḡCḡ,CHbCḡCḡ PμPsP·PēPSPsC,,C-P»C-C”Cḡ C- CḡPēCḡC,PμPjPSPēPjPē
CḡPēPjPiC,PsPjP°PjPē (DRESS-CḡPēPSPPrCḡPsPj), Cḡ PrPμCḡPePēC... PIPēPīP°PrPeP°C...
P±CḡP»Pē PīPsPIbḡ™CḡP·P°PSC- P· PiP°CḡCḡC±PePsCḡ, PiPμPjP°C,PsP»PsPiC-C±PSPsCḡ,

PSPëCĤPePsPIPsCĤ P°P±Ps PīPμC‡C-PSPePsPIPsCĤ PSPμPrPsCĤC,P°C,PSC-CĤC,CĤ.

PμP°C‡C-C°PSC,Pë PīPsPIPëPSPSC- P±CřC,Pë PīCĤPsC-PSC,,PsCĤPjPsPIP°PSC- PīCĤPs
PsP·PSP°PePë C,P° CĤPëPjPīC,PsPjPë PīC-PīPμCĤC‡CřC,P»PëPIPsCĤC,C-/P°P»PμCĤPīC-C—, P°
C,P°PePsP¶ P·P° PSPëPjPë CĤP»C-Pr CĤPīPsCĤC,PμCĤC-PiP°C,Pë C%PsPrPs CĤPsP·PIPëC,PeCř
C,P°PePëC... CĤPμP°PeC‡C-PNë. PμCĤPë PīPsCĤPIC- CĤPμCĤPNëPsP·PSPëC...
P°P»PμCĤPīC-C‡PSPëC... CĤPμP°PeC‡C-PNë/CĤPμP°PeC‡C-PNë
PīC-PīPμCĤC‡CřC,P»PëPIPsCĤC,C-, CĤPëPSPřCĤPsPjCř
PŸC,C-PIPμPSCĤP°BĤ“P”P¶PsPSCĤPsPSP° Pī C,PsPjCř C‡PëCĤP»C-, P·P°CĤC,PsCĤCřPIP°PSPSCĤ
C,,PμP±CřPeCĤPsCĤC,P°C,Cř C,CĤPμP±P° PSPμPīP°PNëPSPs PīCĤPëPīPëPSPëC,Pë,
PsCĤPeC-P»CHPePë CĤP°PSPSC” PīCĤPëPīPëPSPμPSPSCĤ P·P°CĤC,PsCĤCřPIP°PSPSCĤ
PīPsPeCĤP°C%CřC” PīCĤPsPiPSPsP·. PīPeC%Ps Cř PīP°C‡C-C°PSC,P°
CĤPsP·PIPëPSCřP»P°CĤCĤ P°P»PμCĤPīC-C‡PSP° CĤPμP°PeC‡C-CĤ/CĤPμP°PeC‡C-CĤ
PīC-PīPμCĤC‡CřC,P»PëPIPsCĤC,C-, Cř C,PsPjCř C‡PëCĤP»C- CĤPëPSPřCĤPsPj
PŸC,C-PIPμPSCĤP°BĤ“P”P¶PsPSCĤPsPSP°, C,P° PīPsCĤC,CĤC- P°PSP°C,,C-P»P°PeC,PëC‡PSC-
CĤPμP°PeC‡C-C—/CĤPsPe, C,Ps PīPsPIC,PsCĤPSPμ PīCĤPëP·PSP°C‡PμPSPSCĤ
C,,PμP±CřPeCĤPsCĤC,P°C,Cř PīCĤPsC,PëPīPsPeP°P·P°PSPs.

P—P°PiPsCĤC,CĤPμPSPSCĤ (PSP°PīP°Pr) PīPsPrP°PīCĤPë

P>C-PeCřPIP°PSPSCĤ C,,PμP±CřPeCĤPsCĤC,P°C,PsPj CĤP»C-Pr CĤPsP·PīPsC‡PëPSP°C,Pë
C,C-P»CHPePë Cř PīPμCĤC-PsPr PīC-CĤP»CĤ P·P°PīPsCĤC,CĤPμPSPSCĤ C...PIPsCĤPsP±Pë.
PμPμP±CřPeCĤPsCĤC,P°C, PjPsP¶Pμ CĤPīCĤPsPIPsPeCřPIP°C,Pë PSP°PīP°Pr PīPsPrP°PīCĤPë
PSP° PīPsC‡P°C,PeCř P»C-PeCřPIP°PSPSCĤ P·P° CĤP°C...CřPSPsPe P·PjC-PSPë CĤC-PIPSCĤ
CĤPμC‡PsPIPsC— PePëCĤP»PsC,Pë Cř CĤPëCĤPsPIP°C,C‡C- PeCĤPsPIC- C‡PμCĤPμP·
PIPëC...C-Pr CřCĤP°C,C-PI C-P· PrPμPīPs. PkP° PīPsC‡P°C,PeCř P»C-PeCřPIP°PSPSCĤ
C,,PμP±CřPeCĤPsCĤC,P°C,PsPj CĤPμPePsPjPμPSPřCřC”C,CHCĤCĤ PīCĤPëP·PSP°C‡PëC,Pë
PkPμP—P— P°P±Ps PePsP»C...C-C‡PëPS PSP° C,PμCĤPjC-PS PSPμ PjPμPSC€Pμ 6
PjC-CĤCĤC‡C-PI PrP»CĤ PīCĤPsC,,C-P»P°PeC,PëPePë PSP°PīP°PrC-PI PīPsPrP°PīCĤPë.

PμCĤPë CĤPsP·PIPëC,PeCř PSP°PīP°PrCř PīPsPrP°PīCĤPë PSP° C,P»C-
P·P°CĤC,PsCĤCřPIP°PSPSCĤ C,,PμP±CřPeCĤPsCĤC,P°C,Cř P»C-PeCřPIP°PSPSCĤ CĤP»C-Pr
PīCĤPsPrPsPIP¶CřPIP°C,Pë. PhPrPSPsC‡P°CĤPSPs PīPsC,CĤC-P±PSPs PīCĤPsPIPsPrPëC,Pë
PIC-PrPīPsPIC-PrPSCř C-PSPřPëPIC-PrCřP°P»CHPSCř C,PμCĤP°PīC-CĤ
P·P°PīPsCĤC,CĤPμPSPSCĤ PīPsPrP°PīCĤPë. PμCĤPë C,CĤPëPIP°P»PsPjCř
P·P°CĤC,PsCĤCřPIP°PSPSC- C,,PμP±CřPeCĤPsCĤC,P°C,Cř C‡P°CĤC,PsC,P° C,P°
C,CĤP¶PeC-CĤC,CH PSP°PīP°PrC-PI PīPsPrP°PīCĤPë P·PjPμPSC€CřCĤC,CHCĤCĤ.

P’C-PrPeP»P°PrPμPSPSCĤ PeCĤP°PSC,PëPSC-PI

Pj PīP°C‡C-C°PSC,C-PI C-P· PīCĤPëCĤPePsCĤPμPSPëPj CřC,PIPsCĤPμPSPSCĤPj CřCĤP°C,C-PI
(PSP°PīCĤPëPeP»P°Pr, PSP° C,P»C- P·P»PsCĤPeC-CĤPSPëC... PSPsPIPsCřC,PIPsCĤPμPSCĤ C,P°
C—C... P»C-PeCřPIP°PSPSCĤ P°P±Ps PīCĤPë CĤPëPSPřCĤPsPjC- P>PμC€P°-PkC-C...P°PSP°)
PjPsP¶P»PëPIPμ CĤCřC,C,C°PIPμ P·P±C-P»CHC€PμPSPSCĤ P°P±CĤPsP»CĤC,PSPsC—
PePsPSC‡PμPSC,CĤP°C‡C-C— PeCĤP°PSC,PëPSC-PI Cř CĤPμC‡C-, C%Ps Cř
CĤC-PrPeC-CĤPSPëC... PIPëPīP°PrPeP°C... CĤCřPīCĤPsPIPsPrP¶CřC”C,CHCĤCĤ C—C...
PIC-PrPeP»P°PrPμPSPSCĤPj Cř CĤPμC‡PsPIPëPIC-PrPSPëC... C€P»CĤC...P°C.... PīCHPsPiPs
PSPμ CĤPīPsCĤC,PμCĤC-PiP°P»PsCĤCĤ Pī PsPīPsCĤPSPsPjCř PeP»C-PSC-C‡PSPsPjCř
PrPsCĤP»C-PrP¶PμPSPSC- C,,PμP±CřPeCĤPsCĤC,P°C,Cř PīCĤPë PŸP·Pμ. P§PμCĤPμP·
PsP±PjPμP¶PμPSC-CĤC,CH PrPsCĤPIC-PrCř P·P°CĤC,PsCĤCřPIP°PSPSCĤ
C,,PμP±CřPeCĤPsCĤC,P°C, PSPμ PīPsPeP°P·P°PSPëPNë PīP°C‡C-C°PSC,P°Pj PīCĤPë
CĤPëPSPřCĤPsPjC- P>PμC€P°BĤ“PkC-C...P°PSP°.

PħPμCḡPeP°PiC,PsPiCžCḡPëPS/P°P·P°C,C-PsPiCḡPëPS.

PᄁPμP±CřPeCřPsCřC,P°C, PSPμ CḡPμPePsPjPμPSPřCřC”C,CHCřCḡ
P·P°CřC,PsCřPsPICřPIP°C,Pë PiP°C†C-C”PSC,P°Pj, CḡPeC- PsPrPSPsC†P°CřPSPs
PsC,CḡPëPjCřCḡC,CH PjPμCḡPeP°PiC,PsPiCřCḡPëPS/P°P·P°C,C-PsPiCḡPëPS,
PsCřPeC-P»CHPePë C-PSPiC-P±CřPIP°PSPSCḡ PeCřP°PSC,PëPSPsPeCřPëPrP°P·Pë
C,,PμP±CřPeCřPsCřC,P°C,PsPj PjPsPḡPμ CřPiCḡPëC†PëPSPëC,Pë PiC-PrPIPëC%PμPSPSCḡ
PePsPSC†PμPSC,CḡP°C†C-C— PjPμCḡPeP°PiC,PsPiCřCḡPëPSCř/P°P·P°C,C-PsPiCḡPëPSCř Cř
PiP»P°P·PjC- PeCḡPsPIC-, C%Ps PjPsPḡPμ PiCḡPëP·PIPμCřC,Pë PrPs CřPëP»CHPSPsC—
C,PsPeCřPëC†PSPsCřC,C-.

PİPeC%Ps PePsPjP±C-PSP°C†C-C— PSPμ CřPSPëPePSCřC,Pë,
CḡPμPePsPjPμPSPřCřC”C,CHCřCḡ P·PjPμPSCëPëC,Pë PrPsP·Cř
PjPμCḡPeP°PiC,PsPiCřCḡPëPSCř/P°P·P°C,C-PsPiCḡPëPSCř PrPs 20B %B P°P±Ps PjPμPSCëPμ
PiPsPiPμCḡPμPrPSCḡPs PiCḡPëP·PSP°C†PμPSPsC— PrPsP·Pë,B C%PsP± P·P°PiPsP±C-PiC,Pë
PjPsPḡP»PëPIPëPj PiPμPjP°C,PsP»PsPiC-C†PSPëPj PIPiP»PëPIP°Pj (PrPëPI. CḡPsP·PrC-P»
B«P’P·P°C”PjPsPrC-Cḡ P· C-PSCëPëPjPë P»C-PeP°CḡCḡPePëPjPë P·P°CřPsP±P°PjPë C,P°
C-PSCëC- PIPëPrPë PIP·P°C”PjPsPrC-PNëB»).

PḡP°C†C-C”PSC,C-PI CřP»C-Pr CḡPμC,PμP»CHPSPs PePsPSC,CḡPsP»CḡPIP°C,Pë, P° PrPsP·Cř
PjPμCḡPeP°PiC,PsPiCřCḡPëPSCř/P°P·P°C,C-PsPiCḡPëPSCř PiPsC,CḡC-P±PSPs P·PiPsPrPsPj
PePsCḡPëPiCřPIP°C,Pë PSP° PsCřPSPsPIC- PsC†C-PSPePë C,PμCḡP°PiPμPIC,PëC†PSPsC—
PIC-PrPiPsPIC-PrC- C,P° PSP°CřC,P°PSPSCḡ PjPsPḡP»PëPIPëC... C,PsPeCřPëC†PSPëC...
PμC,,PμPeC,C-PI.

*PḡP°C†C-C”PSC,Pë, CḡPeC- PiPμCḡPμPSPμCřP»Pë C,CḡP°PSCřPiP»P°PSC,P°C†C-Cḡ
PsCḡPiP°PSC-PI*

P”PsCřPIC-PrCř P·P°CřC,PsCřCřPIP°PSPSCḡ C,,PμP±CřPeCřPsCřC,P°C,Cř C†C-PNë
PeP°C,PμPiPsCḡC-C— PiP°C†C-C”PSC,C-PI PSPμPjP°C”, C,PsPjCř P·P°CřC,PsCřCřPIP°PSPSCḡ
PiCḡPμPiP°CḡP°C,Cř PSPμ PiPsPeP°P·P°PSPs.

PḡPμPsC,,C-P»C-PS

PħPrPSPsCḡP°P·PsPIPμ PsPrPSPsC†P°CřPSPμ P·P°CřC,PsCřCřPIP°PSPSCḡ
C,,PμP±CřPeCřPsCřC,P°C,Cř Cř PrPsP·C- 80 PjPi C,P° C,PμPsC,,C-P»C-PSCř Cř PrPsP·C- 400 PjPi
PSPμ PiPsPeP°P·P°P»Ps PḡPsPrPSPëC... C,,P°CḡPjP°PePsPeC-PSPμC,PëC†PSPëC...
PIP·P°C”PjPsPrC-PNë. PᄁPμP±CřPeCřPsCřC,P°C, Cř PrPsP·C- 80 PjPi PjPsPḡPSP°
P·P°CřC,PsCřPsPICřPIP°C,Pë PsPrPSPsC†P°CřPSPs P· C,PμPsC,,C-P»C-PSPsPj P±PμP·
CḡPëP·PëPeCř PiC-PrPIPëC%PμPSPSCḡ PePsPSC†PμPSC,CḡP°C†C-C— C,PμPsC,,C-P»C-PSCř Cř
PiP»P°P·PjC- PeCḡPsPIC-. P”P°PSPëC... C%PsPrPs PrPsP·Pë C,,PμP±CřPeCřPsCřC,P°C,Cř 120
PjPi PSPμPjP°C”.

P—P°C...PIPSCḡCḡPIP°PSPSCḡ PiPμC†C-PSPePë

Pj PiCḡPsC†PμCřC- PePsPjP±C-PSPsPIP°PSPsC— C,,P°P·Pë 3 PeP»C-PSC-C†PSPëC...
PrPsCřP»C-PrPḡPμPSCḡ Cř 5,0 % PiP°C†C-C”PSC,C-PI, CḡPeC- PsC,CḡPëPjCřPIP°P»Pë
C,,PμP±CřPeCřPsCřC,P°C,, CřPiPsCřC,PμCḡC-PiP°P»PëCřCḡ PSPμP·PSP°C†PSC- P·PjC-PSPë
PiPμC†C-PSPePsPIPëC... PiPsPeP°P·PSPëPeC-PI, C,PsPjCř CḡPμPePsPjPμPSPřCřC”C,CHCřCḡ
PiPμCḡPμPIC-CḡCḡC,Pë C,,CřPSPeC†C-PsPSP°P»CHPSC- PiPμC†C-PSPePsPIC-
PiPsPeP°P·PSPëPePë PrPs PiCḡPëP·PSP°C†PμPSPSCḡ C,,PμP±CřPeCřPsCřC,P°C,Cř C,P° PiC-Pr

C†P°CÍ P»C-PeCfPIP°PSPSCÍ PíCĤPë PSP°CÍPIPSpCÍC,C- PíPpPeP°P·P°PSCĤ.

P—P°C...PIPsCĤCĤPIP°PSPSCÍ C%PëC,PsPIPëPrPSPsC— P·P°P»PsP·Pë

PJ 5,5 % PíP°C†C-C”PSC,C-PI, CÍPeC- PsC,CĤPëPjCfPIP°P»Pë C,,PμP±CfPeCÍPsCÍC,P°C, PíCĤPsC,CÍPiPsPj C,CĤPëPIP°P»PsPiPs C†P°CÍCf, CÍPíPsCÍC,PμCĤC-PiP°P»PsCÍCÍ PíC-PrPIPëC%PμPSPSCÍ PíPpPeP°P·PSPëPeP° PŷPŷP” (> 5,5 PjPePĥPĥ/PjP») PíC-Pr C†P°CÍ PrPsPIPiPsCÍC,CĤPsPePsPIPëC... PIC-PrPeCĤPëC,PëC... CĤPsP·C€PëCĤPμPSPëC... PrPsCÍP»C-PrP¶PμPSCĤ. PŷPsPjCf P»C-PeP°CĤCÍCĤPePëPNë P·P°CÍC-P± CÍP»C-Pr P· PsP±PμCĤPμP¶PSC-CÍC,CĤ P·P°CÍC,PsCÍPsPICfPIP°C,Pë PíP°C†C-C”PSC,P°Pj C-P· PíPsCĤCfC€PμPSPSCÍPjPë C,,CfPSPeC†C-C— C%PëC,PsPIPëPrPSPsC— P·P°P»PsP·Pë.

P>P°PeC,PsP·P°

P>C-PeP°CĤCÍCĤPePëPNë P·P°CÍC-P± PjC-CÍC,PëC,CĤ P»P°PeC,PsP·Cf. PμP°C†C-C”PSC,P°Pj C-P· CĤC-PrPeC-CÍPSPëPjPë CÍPíP°PrPePsPIPëPjPë P·P°C...PIPsCĤCĤPIP°PSPSCÍPjPë, PíPsPIBĤ™ CÍP·P°PSPëPjPë P· PSPμPíPμCĤPμPSPsCÍPëPjC-CÍC,CĤ PiP°P»P°PeC,PsP·Pë, PSPμPrPsCÍC,P°C,PSC-CÍC,CĤ P»P°PeC,P°P·Pë P>PíPíP° P°P±Ps PíPsCĤCfC€PμPSPSCÍPj PICÍPjPsPeC,CfPIP°PSPSCÍ PíP»CĤPePsP·Pë/PiP°P»P°PeC,PsP·Pë, PíCĤPμPíP°CĤP°C, PSPμ PíPpPeP°P·P°PSPëPNë.

Pk°C,CĤC-PNë

PíPμPNë P»C-PeP°CĤCÍCĤPePëPNë P·P°CÍC-P± PjC-CÍC,PëC,CĤ PjPμPSC€Pμ 1 PjPjPsP»CĤ PSP°C,CĤC-CĤ (23 PjPi) PI 1 C,P°P±P»PμC,C†C-, C,PsP±C,Ps PíCĤP°PeC,PëC†PSPs PIC-P»CĤPSPëPNë PIC-Pr PSP°C,CĤC-CĤ.

P—P°CÍC,PsCÍCžPIP°PSPSCÍ Cž PíPμCĤC-PsPr PIP°PiC-C,PSPsCÍC,C- P°P±Ps PíPsPrCžPIP°PSPSCÍ PíCĤCžPrPrCĤ

P’P°PiC-C,PSC-CÍC,CĤ

PĥP±PjPμP¶PμPSPëPNë PrPsCÍPIC-Pr P·P°CÍC,PsCÍCfPIP°PSPSCÍ C,,PμP±CfPeCÍPsCÍC,P°C,Cf Cí PíPμCĤC-PsPr PIP°PiC-C,PSPsCÍC,C- CÍPIC-PrC†PëC,CĤ PíCĤPs PIC-PrCÍCfC,PSC-CÍC,CĤ PSPμCÍPíCĤPëCÍC,P»PëPIPsPiPs PIPíP»PëPICf PSP° PíPμCĤPμP±C-Pi PIP°PiC-C,PSPsCÍC,C- C,P° P·PrPsCĤPsPIBĤ™ CÍ PíP»PsPrP°/PSPsIPsPSP°CĤPsPrP¶PμPSPsPiPs. PJ PíCĤPsC†PμCÍC- PrPsCÍP»C-PrP¶PμPSCĤ PSP° C,PIP°CĤPëPSP°C... PSPμ P±CfP»Ps PíPsPjC-C†PμPSPs PNëPsPiPs PíCĤCÍPjPsPiPs P°P±Ps PSPμPíCĤCÍPjPsPiPs PíPsP±C-C†PSPsPiPs PIPíP»PëPICf PSP° PíPμCĤPμP±C-Pi PIP°PiC-C,PSPsCÍC,C-, CĤPsP·PIPëC,PsPe PμPjP±CĤC-PsPSP°/PíP»PsPrP° C,P° PíPμCĤPμP±C-Pi PíPsP»PsPiC-PI. PμPsC,PμPSC†C-PNëPSPëPNë CĤPëP·PëPe PrP»CÍ P»CĤPrPëPSPë PSPμPIC-PrPsPjPëPNë. PαPμP±CfPeCÍPsCÍC,P°C, PSPμ CÍP»C-Pr P·P°CÍC,PsCÍPsPICfPIP°C,Pë Cí PíPμCĤC-PsPr PIP°PiC-C,PSPsCÍC,C-.

PμPμCĤC-PsPr PíPsPrCžPIP°PSPSCÍ PíCĤCžPrPrCĤ

PkPμPIC-PrPsPjPs, C†Pë PíCĤPsPSPëPeP°C” C,,PμP±CfPeCÍPsCÍC,P°C, Cí PíCĤCfPrPSPμ PjPsP»PsPePs P»CĤPrPëPSPë. P”PsCÍP»C-PrP¶PμPSPSCÍ PSP° C,PIP°CĤPëPSP°C... PíPsPeP°P·P°P»Pë, C%Ps C,,PμP±CfPeCÍPsCÍC,P°C, PíCĤPsPSPëPeP°C” Cí PíCĤCfPrPSPμ PjPsP»PsPePs C,P° PIPëCÍPIP»CÍC” PSPμPiP°C,PëPIPSPëPNë PIPíP»PëPI PSP° CĤPsP·PIPëC,PsPe PSPsIPsPSP°CĤPsPrP¶PμPSPëC..., CÍPePëC... PíPsPrCfCĤC,CĤ C†PëPj PjPsP»PsPePsPj. P PëP·PëPe PíPsC,CĤP°PíP»CÍPSPSCÍ PíCĤPμPíP°CĤP°C,Cf PI PíCĤCfPrPSPμ PjPsP»PsPePs

PSPµ PjPsP¶Pµ P±CfC,Pë PIPëPeP»CfC†PµPSPëPNë. PαPµP±CfPeCfPsCfC,P°C, PSPµ CfP»C-Pr P·P°CfC,PsCfPsPICfPIP°C,Pë Cr PîPµCfC-PsPr PiPsPrCfPIP°PSPSC¶ PiCfCfPrPrCf.

PαPµCfC,PëP»CHPSC-CfC,CH

P"PsCfP»C-PrP¶PµPSPSC¶ C,,PµCfC,PëP»CHPSPsCfC,C- PSP° C,PIP°CfPëPSP°C... PîCfPë P·P°CfC,PsCfCfPIP°PSPSC- Cr PrPsP·C- 48 PjPi/PePi/PrPsP±Cf PSPµ PIPëC¶PIPëP»Pë P·P°P»PµP¶PSPsCfC,C- PîPsP±C-C†PSPëC... CfPµP°PeC†C-PNë PIC-Pr PrPsP·Pë. P"°C-C¶ C,,PµP±CfPeCfPsCfC,P°C,Cf PSP° CfPµPîCfPsPrCfPeC,PëPIPSCr C,,CfPSPeC†C-Cf P»CfPrPëPSPë PSPµPIC-PrPsPjP°.

P—PrP°C,PSC-CfC,CH PIPîP»PëPIP°C,Pë PSP° C¶PIPëPrPeC-CfC,CH CfPµP°PeC†C-C— PîCfPë PePµCfC¿PIP°PSPSC- P°PIC,PsC,CfP°PSCfPîPsCfC,PsPj P°P±Ps C-PSC¶PëPjPë PjPµC...P°PSC-P·PjP°PjPë.

P'CfP»Pë PîPsPIC-PrPsPjP»PµPSPSC¶ PîCfPs CfPsP·PIPëC,PsPe CfPsPSP»PëPIPsCfC,C-, P·P°PîP°PjPsCfPsC†PµPSPSC¶, PîP°CfPµCfC,PµP·C-PNë C,P° PîPsCfCfC¶PµPSPSC¶ C†C-C,PePsCfC,C- P·PsCfCf PSP° C,P»C- P·P°CfC,PsCfCfPIP°PSPSC¶ C,,PµP±CfPeCfPsCfC,P°C,Cf. PÿPsPjCf PîP°C†C-C"PSC,P°Pj, C¶PeC- P·P°CfC,PsCfPsPICfCfC,CH C,,PµP±CfPeCfPsCfC,P°C,, CfPµPePsPjPµPSPrCfC"C,CHCfC¶ P±CfC,Pë PsP±PµCfPµP¶PSPëPjPë PîCfPë PePµCfCfPIP°PSPSC- P°PIC,PsC,CfP°PSCfPîPsCfC,PSPëPjPë P·P°CfPsP±P°PjPë C,P° CfPsP±PsC,C- P· C-PSC¶PëPjPë PjPµC...P°PSC-P·PjP°PjPë PrPs C,PsPiPs C†P°CfCf, PîPsPePë PIPsPSPë PSPµ P±CfPrCfC,CH PIPîPµPIPSµPSC- Cr PIC-PrCfCfC,PSPsCfC,C- PIPëC%PµP·P°P·PSP°C†PµPSPëC... PîPsP±C-C†PSPëC... CfPµP°PeC†C-PNë.

PÿPîPsCfC-P± P·P°CfC,PsCfC¿PIP°PSPSC¶ C,P° PrPsP·Pë

P"PsP·C¿PIP°PSPSC¶

PµPsPrP°PiCfP°

P PµPePsPjPµPSPrPsPIP°PSP° PrPsP·P° P,,P'P PhPαP·P'PJ CfC,P°PSPsPIPëC,CH 80 PjPi 1 CfP°P· PSP° PrPsP±Cf PîPµCfPsCfP°P»CHPSPs, PSPµP·P°P»PµP¶PSPs PIC-Pr PIP¶PëPIP°PSPSC¶ C—P¶C-. PîPeC%Ps PePsPSC†PµPSC,CfP°C†C-C¶ CfPµC†PsPIPsC— PePëCfP»PsC,Pë PI CfPëCfPsPIP°C,C†C- PeCfPsPIC- PîPµCfPµPIPëC%CrC" 6 PjPi/PrP» (357 PjPePjPsP»CH/P») PîC-CfP»C¶ 2Bf"4 C,PëP¶PSC-PI P»C-PeCfPIP°PSPSC¶, CfP»C-Pr CfPsP·PiP»C¶PSCfC,Pë PîC-PrPIPëC%PµPSPSC¶ PrPsP·Pë P,,P'P PhPαP·P'PJ PrPs 120 PjPi 1 CfP°P· PSP° PrPsP±Cf. P·C,,PµPeC, P»C-PeP°CfCfCHPePsPiPs P·P°CfPsP±Cf PIPëC¶PIP»C¶C"C,CHCfC¶ PrPsCfPëC,CH C¶PIPëPrPePs, C%Ps CfPsP±PëC,CH PjPsP¶P»PëPIPëPj PîPsPIC,PsCfPSPµ PIPëP·PSP°C†PµPSPSC¶ PePsPSC†PµPSC,CfP°C†C-C— CfPµC†PsPIPsC— PePëCfP»PsC,Pë C†PµCfPµP· 2 C,PëP¶PSC-. PµPµC,PsCf P»C-PeCfPIP°PSPSC¶ C" P·PjPµPSC¶PµPSPSC¶ PePsPSC†PµPSC,CfP°C†C-C— CfPµC†PsPIPsC— PePëCfP»PsC,Pë Cr CfPëCfPsPIP°C,C†C- PeCfPsPIC- C,P° PîC-PrC,CfPëPjPeP° C—C— PSP° CfC-PIPS- PjPµPSC¶Pµ

6 PjPi/PrP» (357 PjPePjPsP»CH/P»).

PÿCfPëPIP°P»C-CfC,CH PîCfPsC,,C-P»P°PeC,PëPePë PSP°PîP°PrC-PI PîPsPrP°PiCfPë CfPµPePsPjPµPSPrPsPIP°PSP° PSPµ PjPµPSC¶Pµ 6 PjC-CfC¶C†C-PI.

PŸPëPSPPrCḡPsPj P»C-P·PëCÍCž PíCžC...P»PëPSPë (PŸP·Pμ)

P PμPePsPjPμPSPPrPsPIP°PSP° PrPsP·P° P„P'P PhPαP·P'PJ CÍC,P°PSPsPIPëC,CH 120 PjPi 1
CḡP°P· PSP° PrPsP±CÍ PíPμCḡPsCḡP°P»CHbPSPs, PSPμP·P°P»PμP¶PSPs PIC-Pr
PIP¶PëPIP°PSPSCÍ C—P¶C—.

P—P°CÍC,PscÍCÍPIP°PSPSCÍ P„P'P PhPαP·P'PJ CÍP»C-Pr CḡPsP·PíPsc±PëPSP°C,Pë P·P° PrPIP°
PrPSC- PrPs PíPsc±P°C,PeCÍ C†PëC,Psc,PspEcÍPëC±PSPsC— C,PμCḡP°PíC— C—
PíCḡPsPrPsPIP¶CÍPIP°C,Pë C‰PsPSP°PNëPjPμPSC€Pμ 7 PrC-P±, PsPrPSP°Pe
C,CḡPëPIP°P»C-CÍC,CH C,PμCḡP°PíC— PjPsP¶PSP° PíPsPrPsPIP¶PëC,Pë PrPs 9 PrC-P±
PIC-PrPíPsPIC-PrPSPs PrPs C,CḡPëPIP°P»PscÍC,C- C...C-PjC-Psc,PμCḡP°PíC— C— C,P°
PeP»C-PSC-C±PSPsC— PsC†C-PSPePë.

PμP°C†C-C''PSC,Pë P»C-C,PSCHbPsPiPs PIC-PeCž

P''P»CÍ C†C-C''C— PeP°C,PμPiPsCḡC-C— PíP°C†C-C''PSC,C-PI PePsCḡPμPeC†C-CÍ PrPsP·Pë
PSPμ PíPsc,CḡC-P±PSP°.

PkPëCḡPePsPIP° PSPμPrPsCÍC,P°C,PSC-CÍC,CHb

Pj PíP°C†C-C''PSC,C-PI C-P· C,CÍP¶PePëPjPë PíPscḡCÍC€PμPSPSCÍPjPë C„CÍPSPeC†C-C—
PSPëCḡPsPe (PeP»C-CḡPμPSCÍ PeCḡPμP°C,PëPSC-PSCÍ <30 PjP»/C...PI)
PμC„PμPeC,PëPIPSC-CÍC,CH C,P° P±PμP·PíPμPeCÍ P·P°CÍC,PscÍCÍPIP°PSPSCÍ
P»C-PeP°CḡCÍCHbPePsPiPs P·P°CÍPsP±CÍ PIPëPIC±PμPSPs PSPμPrPsCÍC,P°C,PSCHbPs.
PμP°C†C-C''PSC,P°Pj C-P· PíPscḡCÍC€PμPSPSCÍPjPë C„CÍPSPeC†C-C— PSPëCḡPsPe
P»PμPiPePsPiPs P°P±Ps PíPspjC-CḡPSPsPiPs CÍC,CÍPíPμPSCÍ C,CÍP¶PePsCÍC,C-
PePsCḡPμPeC†C-CÍ PrPsP·Pë PSPμ PíPsc,CḡC-P±PSP°.

PμPμC±C-PSPePsPIP° PSPμPrPsCÍC,P°C,PSC-CÍC,CHb

P''PscÍP»C-PrP¶PμPSPSCÍ PμC„PμPeC,PëPIPSPsCÍC,C- C,P° P±PμP·PíPμPePë
P·P°CÍC,PscÍCÍPIP°PSPSCÍ C„PμP±CÍPeCÍPsCÍC,P°C,CÍ CÍ PíP°C†C-C''PSC,C-PI P·
C,CÍP¶PePsCḡ PíPμC±C-PSPePsIPsCḡ PSPμPrPsCÍC,P°C,PSC-CÍC,Cḡ (PeP»P°CÍ PŸ P·P°
C€PeP°P»PsCḡ P§P°PNëP»PrP°bḡ“Pμbḡ™ Cḡ) PSPμ PíCḡPsIPsPrPëP»Pë.

PμPsPrP°PiCḡP°. PμCḡPë PíPscḡCÍC€PμPSPSC- C„CÍPSPeC†C-C— PíPμC±C-PSPePë
P»PμPiPePsPiPs CÍC,CÍPíPμPSCÍ CḡPμPePsPjPμPSPPrPsPIP°PSP° PrPsP·P°
CÍC,P°PSPsPIPëC,CHb

80 PjPi. P''PscÍPIC-Pr P·P°CÍC,PscÍCÍPIP°PSPSCÍ P»C-PeP°CḡCÍCHbPePsPiPs P·P°CÍPsP±CÍ
PíCḡPë PíPscḡCÍC€PμPSPSC- C„CÍPSPeC†C-C— PíPμC±C-PSPePë PíPspjC-CḡPSPsPiPs
CÍC,CÍPíPμPSCÍ PsP±PjPμP¶PμPSPëPNë.

PŸP·Pμ. P— PsPíPscḡPSPsPiPs PrPsCÍP»C-PrP¶PμPSPSCÍ C„P°P·Pë III (FLORENCE) P±CÍP»Pë
PIPëPeP»CḡC±PμPSC- C,C-P»CHbPePë CÍCÍP±bḡ™ C''PeC,Pë C-P· PíPμC±C-PSPePsIPsCḡ
PSPμPrPsCÍC,P°C,PSC-CÍC,Cḡ C,CÍP¶PePsPiPs CÍC,CÍPíPμPSCÍ. P''P»CÍ PíP°C†C-C''PSC,C-PI,
CÍPeC- P±CÍP»Pë PIPeP»CḡC±PμPSC- PI PrPsCÍP»C-PrP¶PμPSPSCÍ, PePsCḡPμPeC†C-CÍ
PrPsP·Pë CÍ P·PIbḡ™ CÍP·PeCÍ P·C- CÍC,P°PSPsPj C„CÍPSPeC†C-PNë PíPμC±C-PSPePë PSPμ
PíPsc,CḡC-P±PSP°.

PŸPíPscÍC-P± P·P°CÍC,PscÍCžPIP°PSPSCÍ

$P''P \gg C_{II} \text{ } \ddot{P}iP_{\mu}C_{\overline{H}}PsC_{\overline{H}}P^{\circ}P \gg CH_{\overline{H}}PSPsPiPs \text{ } P \cdot P^{\circ}C_{II}^{\prime}C, PsC_{II}^{\prime}C_{\overline{r}}PIP^{\circ}PSPSC_{II}$.

$C_{,,}P_{\mu}P \text{ } PhP_{\alpha}P \cdot P' \text{ } P \cdot P^{\circ}C_{II}^{\prime}C, PsC_{II}^{\prime}PsPIC_{\overline{r}}PIP^{\circ}C, P\ddot{e} \text{ } \ddot{P}iP_{\mu}C_{\overline{H}}PsC_{\overline{H}}P^{\circ}P \gg CH_{\overline{H}}PSPs, \text{ } PSP_{\mu}P \cdot P^{\circ}P \gg P_{\mu}P \text{ } \overline{P}PSPs$
 $PIC-Pr \text{ } \overline{P}IP \text{ } \overline{P}P\ddot{e}PIP^{\circ}PSPSC_{II} \text{ } C-P \text{ } \overline{P}C-$.

$P''C-C, P\ddot{e}$

$P'P_{\mu}P \cdot \ddot{P}iP_{\mu}PeP^{\circ} \text{ } C, P^{\circ} \text{ } P_{\mu}C_{,,}P_{\mu}PeC, P\ddot{e}PIPSC-C_{II}^{\prime}C, CH_{\overline{H}} \text{ } P \cdot P^{\circ}C_{II}^{\prime}C, PsC_{II}^{\prime}C_{\overline{r}}PIP^{\circ}PSPSC_{II}$
 $C_{,,}P_{\mu}P \pm C_{\overline{r}}PeC_{II}^{\prime}PsC_{II}^{\prime}C, P^{\circ}C, C_{\overline{r}} \text{ } PrC-C, C_{II}P_j \text{ } PIC-PePsP_j \text{ } PrPs \text{ } 18 \text{ } C_{\overline{H}}PsPeC-PI \text{ } PSP_{\mu}$
 $PIC_{II}^{\prime}C, P^{\circ}PSPsPIP \gg P_{\mu}PSC- \text{ } P''P^{\circ}PSC- \text{ } C\%PsPrPs \text{ } P \cdot P^{\circ}C_{II}^{\prime}C, PsC_{II}^{\prime}C_{\overline{r}}PIP^{\circ}PSPSC_{II} \text{ } PIC-PrC_{II}^{\prime}C_{\overline{r}}C, PSC-$.

$P_{\mu}P_{\mu}C_{\overline{H}}P_{\mu}PrPsP \cdot C \acute{z}PIP^{\circ}PSPSC_{II}$

$P_j \text{ } C_{\overline{H}}P^{\circ}P \cdot C- \text{ } \ddot{P}iP_{\mu}C_{\overline{H}}P_{\mu}PrPsP \cdot C_{\overline{r}}PIP^{\circ}PSPSC_{II} \text{ } \ddot{P}iPsPeP^{\circ}P \cdot P^{\circ}PSP^{\circ} \text{ } C_{II}^{\prime}P\ddot{e}P_j\ddot{P}iC, PsP_jP^{\circ}C, P\ddot{e}C \ddagger PSP^{\circ} \text{ } C, P^{\circ}$
 $\ddot{P}iC-PrC, C_{\overline{H}}P\ddot{e}P_jC_{\overline{r}}PIP^{\circ}P \gg CH_{\overline{H}}PSP^{\circ} \text{ } C, P_{\mu}C_{\overline{H}}P^{\circ}\ddot{P}iC-C_{II}$.

$P_{\mu}PsP \pm C-C \ddagger PSC- \text{ } C_{\overline{H}}P_{\mu}P^{\circ}PeC \ddagger C-C-$

$P \text{ } P_{\mu}P \cdot C_{\overline{H}}P_jP_{\mu} \text{ } \ddot{P}iC_{\overline{H}}PsC_{,,}C-P \gg C_{\overline{H}} \text{ } P \pm P_{\mu}P \cdot \ddot{P}iP_{\mu}PeP\ddot{e}$

$P\acute{K}P^{\circ}PN_{\circ}C \ddagger P^{\circ}C_{II}^{\prime}C, C-C\ddot{e}P\ddot{e}P_jP\ddot{e} \text{ } \ddot{P}iPsP \pm C-C \ddagger PSP\ddot{e}P_jP\ddot{e} \text{ } C_{\overline{H}}P_{\mu}P^{\circ}PeC \ddagger C-C_{II}P_jP\ddot{e} \text{ } C_{\overline{r}}$
 $PeP \gg C-PSC-C \ddagger PSP\ddot{e}C... \text{ } PrPsC_{II}^{\prime}P \gg C-PrP \text{ } \overline{P}P_{\mu}PSPSC_{II}C... \text{ } (4072 \text{ } \ddot{P}iP^{\circ}C \ddagger C-C''PSC, P\ddot{e}, \text{ } C_{II}PeC-$
 $P \cdot P^{\circ}C_{II}^{\prime}C, PsC_{II}^{\prime}PsPIC_{\overline{r}}PIP^{\circ}P \gg P\ddot{e} \text{ } PrPsP \cdot C_{\overline{r}} \text{ } PIC-Pr \text{ } 10 \text{ } P_j\ddot{P}i \text{ } PrPs \text{ } 300 \text{ } P_j\ddot{P}i),$
 $\ddot{P}iC-C_{II}^{\prime}P \gg C_{II}C_{\overline{H}}P_{\mu}C''C_{II}^{\prime}C, C_{\overline{H}}P^{\circ}C \ddagger C-PN_{\circ}PSP\ddot{e}C... \text{ } PrPsC_{II}^{\prime}P \gg C-PrP \text{ } \overline{P}P_{\mu}PSPSC_{II}C... \text{ } P \pm P_{\mu}P \cdot \ddot{P}iP_{\mu}PeP\ddot{e}$
 $(PrPsC_{II}^{\prime}P \gg C-PrP \text{ } \overline{P}P_{\mu}PSPSC_{II} \text{ } FAST: \text{ } 3001 \text{ } C_{II}^{\prime}C_{\overline{r}}P \pm 'C''PeC_{,,} \text{ } C_{II}PeP\ddot{e}PN_{\circ} \text{ } PsC, C_{\overline{H}}P\ddot{e}P_jC_{\overline{r}}PIP^{\circ}PI$
 $\ddot{P}iC_{\overline{H}}P\ddot{e}PSP^{\circ}PN_{\circ}P_jPSC- \text{ } PrPsP \cdot C_{\overline{r}} \text{ } PIC-Pr \text{ } 80 \text{ } P_j\ddot{P}i \text{ } PrPs \text{ } 120 \text{ } P_j\ddot{P}i) \text{ } C, P^{\circ} \text{ } \ddot{P}iC_{\overline{H}}PsC \ddagger P_{\mu}C_{II}^{\prime}C-$
 $\ddot{P}iPsC_{II}^{\prime}C, P_jP^{\circ}C_{\overline{H}}PeP_{\mu}C, P\ddot{e}PSPiPsPIPsPiPs \text{ } PSP^{\circ}\ddot{P}iP \gg C_{II}PrC_{\overline{r}} \text{ } C_{\overline{r}} \text{ } \ddot{P}iP^{\circ}C \ddagger C-C''PSC, C-PI \text{ } P \cdot$
 $\ddot{P}iPsPrP^{\circ}\ddot{P}iC_{\overline{H}}PsC_{\overline{H}} \text{ } P \pm C_{\overline{r}}P \gg P\ddot{e} \text{ } P \cdot P^{\circ}\ddot{P}iPsC_{II}^{\prime}C, C_{\overline{H}}P_{\mu}PSPSC_{II} \text{ } (PSP^{\circ}\ddot{P}iP^{\circ}PrP\ddot{e}) \text{ } \ddot{P}iPsPrP^{\circ}\ddot{P}iC_{\overline{H}}P\ddot{e},$
 $\ddot{P}iPsC_{\overline{H}}C_{\overline{r}}C\ddot{e}P_{\mu}PSPSC_{II} \text{ } C_{,,}C_{\overline{r}}PSPeC \ddagger C-C- \text{ } \ddot{P}iP_{\mu}C \ddagger C-PSPeP\ddot{e}, \text{ } PrC-P^{\circ}C_{\overline{H}}P_{\mu}C_{II}, \text{ } PSC_{\overline{r}}PrPsC, P^{\circ},$
 $\ddot{P}iPsP \gg PsPIPSP\ddot{e}PN_{\circ} \text{ } P \pm C-P \gg CH_{\overline{H}}, \text{ } \ddot{P}iP\ddot{e}C_{II}^{\prime}P\ddot{e}\ddot{P}iP^{\circ}PSPSC_{II} \text{ } C, P^{\circ} \text{ } PSP^{\circ}P \pm C_{\overline{H}}C_{II}PeP\ddot{e},$
 $P \cdot P^{\circ}\ddot{P}iP^{\circ}P_jPsC_{\overline{H}}PsC \ddagger P_{\mu}PSPSC_{II}, \text{ } P \cdot P^{\circ}PrP\ddot{e}C\ddot{e}PeP^{\circ}, \text{ } C_{II}PIP_{\mu}C_{\overline{H}}P \pm C-P \text{ } \overline{P}, \text{ } P \pm C-P \gg CH_{\overline{H}} \text{ } C_{\overline{r}}$
 $C_{II}^{\prime}C_{\overline{r}}\ddot{P}iP \gg PsP \pm P^{\circ}C..., \text{ } P \pm C-P \gg CH_{\overline{H}} \text{ } C_{\overline{r}} \text{ } P_j'C_{II}P \cdot P^{\circ}C..., \text{ } P \pm C-P \gg CH_{\overline{H}} \text{ } C_{\overline{r}} \text{ } PeC-PSC \ddagger C-PIPeP^{\circ}C...,$
 $PSP^{\circ}P \pm C_{\overline{H}}C_{II}PeP\ddot{e} \text{ } C, P^{\circ} \text{ } \ddot{P}iC-PrPIP\ddot{e}C\%P_{\mu}PSP^{\circ} \text{ } PIC, PsP_jP \gg C_{\overline{H}}PIP^{\circ}PSC-C_{II}^{\prime}C, CH_{\overline{H}}. \text{ } P_{II}C-$
 $\ddot{P}iPsP \pm C-C \ddagger PSC- \text{ } C_{\overline{H}}P_{\mu}P^{\circ}PeC \ddagger C-C- \text{ } P_jP^{\circ}P \gg P\ddot{e} \text{ } C_{\overline{r}} \text{ } P \pm C-P \gg CH_{\overline{H}}C\ddot{e}PsC_{II}^{\prime}C, C- \text{ } \ddot{P}iP\ddot{e}\ddot{P}iP^{\circ}PrPeC-PI$
 $P \gg P_{\mu}\ddot{P}iPeP\ddot{e}PN_{\circ} \text{ } P^{\circ}P \pm Ps \text{ } C_{II}^{\prime}P_{\mu}C_{\overline{H}}P_{\mu}PrPSC-PN_{\circ} \text{ } C_{II}^{\prime}C, C_{\overline{r}}\ddot{P}iC-PSC_{\overline{H}} \text{ } C, C_{II}P \text{ } \overline{P}PePsC_{II}^{\prime}C, C-. \text{ } P_{II}C-Pr$
 $C \ddagger P^{\circ}C_{II}^{\prime} \text{ } \ddot{P}iPsC_{II}^{\prime}C, P_jP^{\circ}C_{\overline{H}}PeP_{\mu}C, P\ddot{e}PSPiPsPIPsPiPs \text{ } PSP^{\circ}\ddot{P}iP \gg C_{II}PrC_{\overline{r}} \text{ } P \pm C_{\overline{r}}P \gg P\ddot{e}$
 $\ddot{P}iPsPIC-PrPsP_jP \gg P_{\mu}PSPSC_{II} \text{ } \ddot{P}iC_{\overline{H}}Ps \text{ } C_{\overline{H}}C-PrPeC-C_{II}^{\prime}PSC- \text{ } \ddot{P}iP\ddot{e}\ddot{P}iP^{\circ}PrPeP\ddot{e} \text{ } C_{II}^{\prime}P_{\mu}C_{\overline{H}}PN_{\circ}PsP \cdot PSP\ddot{e}C...$
 $C_{\overline{H}}P_{\mu}P^{\circ}PeC \ddagger C-PN_{\circ} \text{ } \ddot{P}iC-\ddot{P}iP_{\mu}C_{\overline{H}}C \ddagger C_{\overline{r}}C, P \gg P\ddot{e}PIPsC_{II}^{\prime}C, C- \text{ } PSP^{\circ} \text{ } C_{,,}P_{\mu}P \pm C_{\overline{r}}PeC_{II}^{\prime}PsC_{II}^{\prime}C, P^{\circ}C_{,,}$
 $PrP_{\mu}C_{II}PeC- \text{ } P \cdot \text{ } PSP\ddot{e}C... \text{ } C_{II}^{\prime}C_{\overline{r}}\ddot{P}iC_{\overline{H}}PsPIPsPrP \text{ } \overline{P}C_{II}^{\prime}PIP^{\circ}P \gg P\ddot{e}C_{II}^{\prime}C_{II} \text{ } C_{II}^{\prime}P\ddot{e}C_{II}^{\prime}C, P_{\mu}P_jPSP\ddot{e}P_jP\ddot{e}$
 $C_{\overline{H}}P_{\mu}P^{\circ}PeC \ddagger C-C_{II}P_jP\ddot{e}, \text{ } C, P^{\circ} \text{ } \ddot{P}iC_{\overline{H}}Ps \text{ } C_{\overline{H}}C-PrPeC-C_{II}^{\prime}PSC- \text{ } C_{II}PIP\ddot{e}C\%P^{\circ} \text{ } C_{\overline{H}}P^{\circ}\ddot{P}iC, PsPIPsC-$
 $C_{II}^{\prime}P_{\mu}C_{\overline{H}}C \ddagger P_{\mu}PIPsC- \text{ } C_{II}^{\prime}P_jP_{\mu}C_{\overline{H}}C, C-$.

$P_j \text{ } PSP\ddot{e}P \text{ } \overline{P}C \ddagger P_{\mu}PSP^{\circ}PIP_{\mu}PrP_{\mu}PSC-PN_{\circ} \text{ } C, P^{\circ}P \pm P \gg P\ddot{e}C \ddagger C- \text{ } P \cdot P^{\circ}P \cdot PSP^{\circ}C \ddagger P_{\mu}PSPs \text{ } \ddot{P}iPsP \pm C-C \ddagger PSC-$
 $C_{\overline{H}}P_{\mu}P^{\circ}PeC \ddagger C-C-, \text{ } C_{II}PeC- \text{ } \ddot{P}iP\ddot{e}PSP\ddot{e}PeP^{\circ}C_{\overline{H}}C, CH_{\overline{H}} \text{ } \ddot{P}iC_{\overline{H}}P\ddot{e} \text{ } P \cdot P^{\circ}C_{II}^{\prime}C, PsC_{II}^{\prime}C_{\overline{r}}PIP^{\circ}PSPSC-$
 $C_{,,}P_{\mu}P \pm C_{\overline{r}}PeC_{II}^{\prime}PsC_{II}^{\prime}C, P^{\circ}C, C_{\overline{r}} \text{ } \ddot{P}iP^{\circ}C \ddagger C-C''PSC, P^{\circ}P_jP\ddot{e} \text{ } C, P^{\circ} \text{ } PeP \gg P^{\circ}C_{II}^{\prime}P\ddot{e}C_{,,}C-PePsPIP^{\circ}PSC-$
 $C, P^{\circ}PeP\ddot{e}P_j \text{ } C \ddagger P\ddot{e}PSPsP_j: \text{ } C \ddagger P^{\circ}C_{II}^{\prime}C, Ps \text{ } (PIC-Pr \geq 1/100 \text{ } PrPs < 1/10), \text{ } PSP_{\mu}C \ddagger P^{\circ}C_{II}^{\prime}C, Ps$
 $(PIC-Pr \geq 1/1000 \text{ } PrPs < 1/100) \text{ } C, P^{\circ} \text{ } C_{\overline{H}}C-PrPePs \text{ } (PIC-Pr \geq 1/10000 \text{ } PrPs < 1/1000).$

PŞP°CÍ'C,PsC,P° CĤPsP·PIPëC,PeCř T'CĤCřPSC,CřC"C,CHCÍ'CĬ PSP°
PrPsCÍ'P»C-PrP¶PµPSPSCĬC... C,P° PİPsCÍ'C,PjP°CĤPePµC,PëPSPiPsPIPsPjCř
PrPsCÍ'PIC-PrC- C%oPsPrPs PİP°C†C-C"PSC,C-PI C-P· PİPsPrP°PiCĤPsCĤ.

Pj PePsP¶PSC-PNë PiCĤCřPiC- P·P° C‡P°CÍ'C,PsC,PsCĤ CĤPsP·PIPëC,PeCř PİPsP±C-C‡PSC-
CĤPµP°PeC†C-C— PiCĤPµPrCÍ'C,P°PIP»PµPSPs Cř PİPsCĤCĬPrPeCř P·PjPµPSC€PµPSPSCĬ
CÍ'C,CřPiPµPSCĬ C,CĬP¶PePsCÍ'C,C-.

PŷP°P±P»PëC†CĬ 2

PµPsP±C-C‡PSC- CĤPµP°PeC†C-C—, C%oPs CÍ'PİPsCÍ'C,PµCĤC-PiP°P»PëCÍ'CĬ Cž C„P°P·C- 3
PePsPjP±C-PSPsPIP°PSPëC... CĤPsP·C€PëCĤPµPSPëC... PrPsPIPiPsCÍ'C,CĤPsPePsPIPëC...
PrPsCÍ'P»C-PrP¶PµPSCĤ, PiC-CÍ'P»CĬCĤPµC"CÍ'C,CĤP°C†C-PNëPSPëC...
PrPsCÍ'P»C-PrP¶PµPSPSCĬC... P±PµP·PiPµPePë C,P° Cž PiPµCĤC-PsPr
PİPsCÍ'C,PjP°CĤPePµC,PëPSPiPsPIPsPiPs CÍ'PİPsCÍ'C,PµCĤPµP¶PµPSPSCĬ PİP°C†C-C"PSC,C-PI
C-P· PİPsPrP°PiCĤPsCĤ

P— P±PsPeCř PeCĤPsPIC- C,P° P»C-PjC„P°C,PëC‡PSPsC— CÍ'PëCÍ'C,PµPjPë	<u>P C-PrPePs</u> PµP°PSC†PëC,PsPİPµPSC-CĬ, C,CĤPsPjP±PsC†PëC,PsPİPµPSC-CĬ, P°PiCĤP°PSCřP»PsC†PëC,PsP·*, P°PSPµPjC-CĬ [#]
P— P±PsPeCř C-PjCřPSPSPsC— CÍ'PëCÍ'C,PµPjPë	<u>P C-PrPePs</u> PĥPSP°C„C-P»P°PeC,PëC‡PSC- CĤPµP°PeC†C-C—*, PiC-PiPµCĤC‡CřC,P»PëPIC-CÍ'C,CH PrPs PiCĤPµPiP°CĤP°C,Cř*
P— P±PsPeCř PµPSPPrPsPeCĤPëPSPSPsC— CÍ'PëCÍ'C,PµPjPë	<u>PkPµC‡P°CÍ'C,Ps</u> PµC-PrPIPëC%oPµPSPSCĬ CĤC-PIPSCĬ C,PëCĤPµPsCÍ'C,PëPjCřP»CĤPIP°P»CHPSPsPiPs PiPsCĤPjPsPSCř PeCĤPsPIC-, PiC-PİPsC,PëCĤPµPsP. [#]
P— P±PsPeCř PsCĤPiP°PSC-PI P·PsCĤCř	<u>PkPµC‡P°CÍ'C,Ps</u> P—P°C,CřPjP°PSPµPSPëPNë P·C-CĤ <u>P C-PrPePs</u> PĥPeP»CĤP·C-CĬ P°CĤC,PµCĤC-C— CÍ'C-C,PeC-PIPePë [#]
P— P±PsPeCř C...P°CĤC‡CřPIP°PSPSCĬ C,P° PsP±PjC-PSCř CĤPµC‡PsPIPëPS	<u>PŞP°CÍ'C,Ps***</u> P—P°PiPsCÍ'C,CĤPµPSPSCĬ (PSP°PİP°PrPë) PİPsPrP°PiCĤPë <u>PkPµC‡P°CÍ'C,Ps</u> P CřPeCĤPsPIPëPNë PrC-P°P±PµC,, PiC-PiPµCĤP»C-PiC-PrPµPjC-CĬ, P·PSPëP¶PµPSPSCĬ P°PİPµC,PëC,Cř, P·P±C-P»CHC€PµPSPSCĬ PjP°CÍ'Pë C,C-P»P° <u>P C-PrPePs</u> P—PSPëP¶PµPSPSCĬ PjP°CÍ'Pë C,C-P»P°, PiC-PrPIPëC%oPµPSPSCĬ P°PİPµC,PëC,Cř, P°PSPsCĤPµPeCÍ'C-CĬ
P— P±PsPeCř PİCÍ'PëC...C-PePë	<u>PkPµC‡P°CÍ'C,Ps</u> P—PSPëP¶PµPSPSCĬ P»C-P±C-PrPs, P±PµP·CÍ'PsPSPSCĬ <u>P C-PrPePs</u> PkPµCĤPIPsP·PSC-CÍ'C,CH, PiCĤPëPiPSC-C‡PµPSPëPNë PSP°CÍ'C,CĤC-PNë [#] , CĤPsP·P»P°Pr CÍ'PSCř [#]

P— P±PsPeCf PSPμCḡPIPsPIPsC— CfPëCfC,PμPjPë	<u>PSP°CfC,Ps</u> P“PsP»PsPIPsPëPNë P±C-P»CHb, P·P°PïP°PjPsCḡPsC†PμPSPSCḡ <u>PkPμC†P°CfC,Ps</u> PμP°CḡPμCfC,PμP·C-C—, PiPμPjC-PïP°CḡPμP·, CfPsPSP»PëPIC-CfC,CHb, P»PμC,P°CḡPiC-Cḡ#, P·PjC-PSP° CfPjP°PePsPIPsPiPs CfPiCḡPëPNëPSCḡC,C,Cḡ, PiC-PïPμCfC,PμP·C-Cḡ, PiPsCfP»P°P±P»PμPSPSCḡ PSCḡC...Cf <u>P C-PrPePs</u> PḡPiPμPIP·C-Cḡ#, PIC-PrC†CfC,C,Cḡ PiPμC†C-PSPSCḡ#
P— P±PsPeCf PsCḡPiP°PSC-PI CfP»CfC...Cf C,P° P»P°P±C-CḡPëPSC,Cf	<u>PkPμC†P°CfC,Ps</u> PëCfPj Cf PICfC...P°C... <u>P C-PrPePs</u> P’PμCḡC,PëPiPs#
P— P±PsPeCf CfPμCḡC†PμPIPsC— CfPëCfC,PμPjPëB B B B	<u>PkPμC†P°CfC,Ps</u> PαC-P±CḡPëP»CḡC†C-Cḡ PiPμCḡPμPrCfPμCḡPrCHb, PIC-PrC†CfC,C,Cḡ CfPμCḡC†PμP±PëC,C,Cḡ, PIC-PrC...PëP»PμPSPSCḡ PIC-Pr PSPsCḡPjPë PSP° P·PḡP“, P±P»PsPeP°PrP° P»C-PIPsC— PSC-PḡPePë PiCfC†PeP° P“C-CfP° (PrPëPI. CḡPsP·PrC-P» B«PŸPëPSPrCḡPsPj P»C-P·PëCfCf PiCfC...P»PëPSPëB»), CfPëPSCfCfPsPIP° C,P°C...C-PeP°CḡPrC-Cḡ (PrPëPI. CḡPsP·PrC-P» B«PŸPëPSPrCḡPsPj P»C-P·PëCfCf PiCfC...P»PëPSPëB»),_P°CḡPëC,PjC-Cḡ# <u>P C-PrPePs</u> P P°PiC,PsPIP° CfPμCḡC†PμPIP° CfPjPμCḡC,CHb*
P— P±PsPeCf CfCfPrPëPSPSPSc— CfPëCfC,PμPjPëB B B B	— — <u>PkPμC†P°CfC,Ps</u> PḡCḡC,PμCḡC-P°P»CHbPSP° PiC-PïPμCḡC,PμPSP·C-Cḡ, PiCḡPëPiP»PëPIPë, PiCḡPëPiP»PëPIPë P· PIC-PrC†CfC,C,CḡPj PḡP°CḡCf, PeCḡPsPIPsC,PμC†C- (PrPëPI. CḡPsP·PrC-P» B«PŸPëPSPrCḡPsPj P»C-P·PëCfCf PiCfC...P»PëPSPëB»)) <u>P C-PrPePs</u> PiPëCḡPeCfP»CḡC,PsCḡPSPëPNë PePsP»P°PiCf#
P— P±PsPeCf PrPëC...P°P»CHbPSPSc— CfPëCfC,PμPjPë	<u>PSP°CfC,Ps</u> P—P°PrPëC€PeP° <u>PkPμC†P°CfC,Ps</u> P’CḡPsPSC...C-C,, C-PSC,,PμPeC†C-C— PIPμCḡC...PSC-C... PrPëC...P°P»CHbPSPëC... C€P»CḡC...C-PI, C-PSC,,PμPeC†C-Cḡ PSPëPḡPSC-C... PrPëC...P°P»CHbPSPëC... C€P»CḡC...C-PI#, PeP°C€PμP»CHb, CḡPëPSPsCḡPμCḡ# <u>P C-PrPePs</u> PμPSPμPIPjPsPSC-Cḡ#

P— P±PsPeCf C€P»CfPSPePsPIPs- PePëC€PePsPIPsPiPs C,CḡP°PeC,Cf	<u>P§P°CfC,Ps</u> P" C-P°CḡPμCf**, PSCfPrPsC,P° <u>PkPμC†P°CfC,Ps</u> P' C-P»CH Cf P¶PëPIPsC,C-, P·PrCfC,C,Cf P¶PëPIPsC,P°, PiP°CfC,CḡPsPμP·PsC,,P°PiPμP°P»CHPSP° CḡPμC,,P»CḡPeCfPSP° C...PIPsCḡPsP±P°, P±P»CḡPIP°PSPSCf, CfCfC...C-CfC,CH Cf CḡPsC,C-, PrPëCfPiPμPiCfC-Cf, P·P°PiPsCḡ, C†P°CfC,C- PIPëPiPsCḡPsP¶PSPμPSPSCf, PjPμC,PμPsCḡPëP·Pj, PrPëCfPePsPjC,,PsCḡC, Cf C€P»CfPSPeCf P°P±Ps PePëC€PμC†PSPëPeCf, P±C-P»CH Cf PIPμCḡC...PSC-C... PIC-PrPrC-P»P°C... P¶PëPIPsC,P° #, PIPëCḡP°P·PePë PI PrC-P»CfPSC†C- CḡPsC,C-, PSP°P±CḡCfPe PiCfP±#, PiP°PSPeCḡPμP°C,PëC, <u>P C-PrPePs</u> PμPμCḡC,,PsCḡP°C†C-Cf C€P»CfPSPePsPIPs- PePëC€PePsPIPsPiPs C,CḡP°PeC,Cf#, CfC,PsPjP°C,PëC,#
P— P±PsPeCf PïPμC†C-PSPePë C,P° P¶PsPIC†PsPIPëPIC-PrPSPëC... C€P»CfC...C-PI	<u>P§P°CfC,Ps</u> PμPsCḡCfC€PμPSPSCf C,,CfPSPeC†C-C— PiPμC†C-PSPePë** <u>PkPμC†P°CfC,Ps</u> P-PsPIC†PsPeP°Pjḡ™ CfPSP° C...PIPsCḡPsP±P° <u>P C-PrPePs</u> P" PμPiP°C,PëC,, P¶PsPIC,CfPSPëC†Cf*, PiPμC†C-PSPePsPIP° PSPμPrPsCfC,P°C,PSC-CfC,CH*, C...PsP»PμC†PëCfC,PëC,#

P— P±PsPeCf C€PeC-CHPë C,P° PïC-PrC€PeC-CHPSPs-P¶PëCHPsPIPsC— C,PeP°PSPëPSPë	<u>PSP°CfC,Ps</u> P'PëCfPëPïP°PSPSCf (Cf C,PsPjCf C±PëCfP»C- PIPëCfPëPïP°PSPSCf P· P±C-P»CHC€ PSPëP·CHPePsCH C±P°CfC,PsC,PsCH PIPëPSPëPePSPµPSPSCf, PrPëPI. PSPëP¶(C±Pµ), CfPIPµCHP±C-P¶ <u>PkPµC±P°CfC,Ps</u> P''PµCHPjP°C,PëC,, PeCHPsPïPëPIb™ C¶PSPeP°, P·PjC-PSP° P·P°P±P°CHPIP»PµPSPSCf C€PeC-CHPë, PïPsC€PePsPrP¶PµPSPSCf C€PeC-CHPë, PïPµC,PµC...C-C—, Pib™ C¶C,PSPëCfC,C- PIPëCfPëPïP°PSPSCf, PjP°PeCfP»PsPïP°PïCfP»CHPsP·PSC- PIPëCfPëPïP°PSPSCf, PïP°PïCfP»CHPsP·PSC- PIPëCfPëPïP°PSPSCf, PïC-PrPIPëC%PµPSP° PïC-C,P»PëPIC-CfC,CH, P°P»PsPïPµC†C-C¶, PµPeP·PµPjP°#, PµCHPëC,PµPjP°, PSC-C±PSP° PïC-C,P»PëPIC-CfC,CH#, PïCfPsCHC-P°P·#, CfPIPµCHP±P»C¶C±C- PIPëCfPëPïPë# <u>P C-PrPePs</u> PÿPsPeCfPëC±PSPëPNë PµPïC-PrPµCHPjP°P»CHPSPëPNë PSPµPeCHPsP»C-P·*, CfPëPSPrCHPsPj PÿC,C-PIPµPSCfP°b™“P”P¶PsPSCfPsPSP°*, P°PSPiC-PsPSP°P±CHC¶Pe*, CHPµP°PeC†C-C— PSP° PïCHPµPïP°CHP°C,, C%Ps CfCfPïCHPsPIPsPrP¶CfCHC,CHCfC¶ PµPsP·PëPSPsC,,C-P»C-C”CH C,P° CfPëCfC,PµPjPSPëPjPë CfPëPjPïC,PsPjP°PjPë*, PïPµPSPµCHP°P»C-P·PsPIP°PSC- PIPëCfPëPïP°PSPSCf (CfPµCHPNëPsP·PSC-)*, PµPeCfC,,PsP»C-P°C,PëPIPSC- PIPëCfPëPïP°PSPSCf, C,,PsP»C-PeCfP»C¶CHPSC- PIPëCfPëPïP°PSPSCf, PIPµP·PëPeCfP»CHPsP·PSC- PIPëCfPëPïP°PSPSCf, PïCfCfC,CfP»CHPsP·PSC- PIPëCfPëPïP°PSPSCf, PµCHPëC,PµPjP°C,PsP·PSC- PIPëCfPëPïP°PSPSCf, PePsCHPsPïPsPrC-P±PSC- PIPëCfPëPïP°PSPSCf
P— P±PsPeCf PsPïPsCHPSPs- CHCfC...PsPIPsPïPs P°PïP°CHP°C,Cf C,P° CfPïPsP»CfC±PSPsC— C,PeP°PSPëPSPë	<u>PSP°CfC,Ps</u> P'C-P»CH Cf CfCfPiP»PsP±P°C..., P±C-P»CH Cf Pjb™ C¶P·P°C..., P±C-P»CH Cf PeC-PSC†C-PIPeP°C...# <u>PkPµC±P°CfC,Ps</u> PhCHC,CHPëC,, CfPePµP»PµC,PSPs- Pjb™ C¶P·PsPIPëPNë P±C-P»CH, CfP»P°P±PeC-CfC,CH Cf Pjb™ C¶P·P°C..., CfCfPrPsPjPë Pjb™ C¶P·C-PI, CfPeCfC,C-CfC,CH Pjb™ C¶P·C-PI, P±CfCHCfPëC,, PSP°P±CHC¶Pe CfCfPiP»PsP±C-PI#, P±C-P»CH Cf CfPïPëPSC-#, CfPePµP»PµC,PSPs-Pjb™ C¶P·PsPIP° CfPeCfC,C-CfC,CH#, CfPeCfC,C-CfC,CH CfCfPiP»PsP±C-PI <u>P C-PrPePs</u> P P°P±PrPsPjC-PsP»C-P·*, CfPëPSPrCHPsPj P·PrP°PIP»PµPSPSCf CHPsC,P°C,PsCHP° PïP»PµC±P°#, CHPµPIPjP°C,PëC±PSP° PïPsP»C-PjC-P°P»PïC-C¶#.

P— P±PsPeCf PSpëCjPsPe C,P° CfPµC‡PsPIPëPIC-PrPSPëC... C€P»CjC...C-PI	<u>PkPµC‡P°CfC,Ps</u> PkPëCjPePsPIP° PSPµPrPsCfC,P°C,PSC-CfC,CH, CfPµC‡PsPeP°PjBj™ CjPSP° C...PIPsCjPsP±P°, PiPµPjP°C,CfCjC-Cj, PiPsP»P°PeC-CfCjC-Cj, PiCjPsC,PµC—PSCfCjC-Cj, PSPµCfC,CjPëPjPSC- PiPsP·PëPIPë PrPs CfPµC‡PsPIPëPiCfCfPeP°PSPSCj, C-PSC,,PµPeC†C-Cj CfPµC‡PsPIPëPIC-PrPSPëC... C€P»CjC...C-PI[#] <u>P C-PrPePs</u> PÿCfP±CfP»PsC-PSC,PµCjCfC,PëC†C-P°P»CHPSPëPN₂ PSPµC,,CjPëC,*.
P— P±PsPeCf CjPµPiCjPsPrCfPeC,PëPIPSPsC— CfPëCfC,PµPjPë C,P° PjPsP»PsC‡PSPëC... P·P°P»PsP·	<u>PkPµC‡P°CfC,Ps</u> P·CjPµPeC,PëP»CHPSP° PrPëCfC,,CfPSPeC†C-Cj
P— P±PsPeCf PsCjPiP°PSC-P·PjCf P·P°PiP°P»PsPj	<u>PSP°CfC,Ps</u> PkP°P±CjCjPePë, PiC-PrPIPëC%₀₀PµPSP° PIC,PsPjP»CjPIP°PSC-CfC,CH <u>PkPµC‡P°CfC,Ps</u> P'C-P»CH Cf PiCjCfPrCjC..., PIC-PrC‡CfC,C,Cj PrPëCfPePsPjC,,PsCjC,Cf Cf PiCjCfPrCjC..., P±C-P»CH [#], PSPµP·PrCfP¶P°PSPSCj[#] <u>P C-PrPePs</u> PÿPiCjP°PiP°, PIC-PrC‡CfC,C,Cj P¶P°CjCf[#]

P"PsPrP°C,PePsPIC- PjPμC,PsPrPë PrPsCÍP»C-PrP¶PμPSCĤ	<u>PḰPμC‡P°CÍC,Ps</u> PμC-PrPIPëC%PμPSPSCı ÇĤC-PIPSCı P°PjC-P»P°P·Pë CÍ PeCĤPsPIC-, P·PjPμPSC€PμPSPSCı PeC-P»CHPePsCÍC,C- C,ÇĤPsPjP±PsC†PëC,C-PI, P·PjPμPSC€PμPSPSCı PeC-P»CHPePsCÍC,C- P»PμPNëPePsC†PëC,C-PI CÍ PeCĤPsPIC-, P·PjPμPSC€PμPSPSCı PeC-P»CHPePsCÍC,C- P»C-PjC,,PsC†PëC,C-PI CÍ PeCĤPsPIC-, PïC-PrPIPëC%PμPSPSCı ÇĤC-PIPSCı PeCĤPμP°C,PëPSCÍ PI PeCĤPsPIC-, PïC-PrPIPëC%PμPSPSCı ÇĤC-PIPSCı PeCĤPμP°C,PëPSC-PSCÍ CÍ PeCĤPsPIC-, P·PSPëP¶PμPSPSCı ÇĤC-PIPSCı PiPμPjPsPiP»PsP±C-PSCÍ PeCĤPsPIC-, PïC-PrPIPëC%PμPSPSCı ÇĤC-PIPSCı CÍPμC‡PsPIPëPSPë PI PeCĤPsPIC-, PïC-PrPIPëC%PμPSPSCı ÇĤC-PIPSCı C,ÇĤPëPiP»C-C†PμCĤPëPrC-PI CÍ PeCĤPsPIC-, PïC-PrPIPëC%PμPSPSCı ÇĤC-PIPSCı C...PsP»PμCÍC,PμCĤPëPSCÍ PI PeCĤPsPIC-, P·PSPëP¶PμPSPSCı PiPμPjP°C,PsPeCĤPëC,CÍ, PïC-PrPIPëC%PμPSPSCı ÇĤC-PIPSCı P»P°PeC,P°C,PrPμPiC-PrCĤPsPiPμPSP°P·Pë (P>P" P") CÍ PeCĤPsPIC-, PïC-PrPIPëC%PμPSPSCı ÇĤC-PIPSCı PeP°P»C-CĤ CÍ PeCĤPsPIC-, PïC-PrPIPëC%PμPSPSCı ÇĤC-PIPSCı PjC-P¶PSP°CĤPsPrPSPsPiPs PSPsCĤPjP°P»C-P·PsPIP°PSPsPiPs PIC-PrPSPsC€PμPSPSCı (PḤPḰP')# <u>P C-PrPePs</u> PμC-PrPIPëC%PμPSPSCı ÇĤC-PIPSCı PiP»CĤPePsP·Pë CÍ PeCĤPsPIC-, PiPsPrPsPIP¶PμPSPSCı P°PeC,PëPIPsPIP°PSPsPiPs C‡P°CÍC,PePsPIPsPiPs C,ÇĤPsPjP±PsPiP»P°CÍC,PëPSPsPIPsPiPs C‡P°CÍCÍ, P·PSPëP¶PμPSPSCı PeC-P»CHPePsCÍC,C- PμCĤPëC,ÇĤPsC†PëC,C-PI CÍ PeCĤPsPIC-, PïC-PrPIPëC%PμPSPSCı ÇĤC-PIPSCı P»CÍP¶PSPsC— C,,PsCÍC,,P°C,P°P·Pë CÍ PeCĤPsPIC-, PïC-PrPIPëC%PμPSPSCı ÇĤC-PIPSCı PeCĤPμP°C,PëPSC,,PsCÍC,,PsPeC-PSP°P·Pë CÍ PeCĤPsPIC-*
PÿCĤP°PIPjPë, C-PSC,PsPeCÍPëPeP°C†C-C— C,P° CÍCÍPeP»P°PrPSPμPSPSCı PïCĤPsC†PμPrCÍCĤ	<u>PḰPμC‡P°CÍC,Ps</u> P—P°P±PëC,C,Cı#

* PμPsP±C-C‡PSC- ÇĤPμP°PeC†C-C—, C%Ps CÍPiPsCÍC,PμCĤC-PiP°P»PëCÍCı CÍ PjPμP¶P°C...
PiPsCÍC,PjP°CĤPePμC,PëPSPiPsPIPsPiPs CÍPiPsCÍC,PμCĤPμP¶PμPSPSCı.

** P"C-P°CĤPμCı C,P° PIC-PrC...PëP»PμPSPSCı ÇĤPμP·CÍP»CHC,P°C,C-PI
C,,CÍPSPeC†C-PsPSP°P»CHPSPëC... PiCĤPsP± PiPμC‡C-PSPePë PIC-Pr PSPsCĤPjPë, CıPeC-
PIPëPjP°PiP°P»Pë C,PμCĤP°PiC-C—, C%Ps CÍPiPsCÍC,PμCĤC-PiP°P»PëCÍCı PI
PrPsCÍP»C-PrP¶PμPSPSCıC... C,,P°P·Pë 3, ÇĤPsP·PIPëPIP°P»PëCÍCı C‡P°CÍC,C-C€Pμ CÍ
PiP°C†C-C"PSC,C-PI, CıPeC- PsC,ÇĤPëPjCÍPIP°P»Pë CÍCÍPiCÍC,PSCĤ C,PμCĤP°PiC-CĤ
PePsP»C...C-C†PëPSPsPj.

*** P"PePI. CḡPsP·PrC-P» B«PḡP°CḡPjP°PePsPrPēPSP°PjC-PeP°B» C%PsPrPs C‡P°CḡC,PsC,Pē
P·P°PiPsCḡC,CḡPμPSCḡ (PSP°PīP°PrC-PI) PīPsPrP°PiCḡPē, C%Ps
CḡPiPsCḡC,PμCḡC-PiP°P»PēCḡCḡ Cḡ C,,P°P·C- 3 C-PSPrPēPIC-PrCḡP°P»CḡPSPēC...
CḡP°PSPrPsPjC-P·PsPIP°PSPēC... PePsPSC,CḡPsP»CḡPsPIP°PSPēC... PrPsCḡP»C-PrP¶PμPSCḡ.

PμPsP±C-C‡PSC- CḡPμP°PeC‡C-C—, PīCḡPs CḡPeC- PīPsPIC-PrPsPjP»CḡC"C,CḡCḡCḡ
PI C...PsPrC- PīC-CḡP»CḡCḡPμC"CḡC,CḡP°C‡C-PNḡPSPēC... PrPsCḡP»C-PrP¶PμPSCḡ
P±PμP·PīPμPePē.

PhPiPēCḡ PsPeCḡPμPjPēC... PīPsP±C-C‡PSPēC... CḡPμP°PeC‡C-PNḡ

PJ PjPμP¶P°C... PīPsCḡC,PjP°CḡPePμC,PēPSPiPsPiPsPSP°PiP»CḡPrCḡ P±CḡP»Pē
PīPsPIC-PrPsPjP»PμPSPSCḡ PīCḡPs CḡC-PrPeC-CḡPSC- PIPēPīP°PrPePē CḡPμCḡPNḡPsP·PSPēC...
CḡPμP°PeC‡C-PNḡ PiC-PiPμCḡC‡CḡC,P»PēPIPsCḡC,C- PSP° C,,PμP±CḡPeCḡPsCḡC,P°C,, Cḡ
C,PsPjCḡ C‡PēCḡP»C- CḡPēPSPrCḡPsPj PḡC,C-PIPμPSCḡP°ḡḡ"P"¶PsPSCḡPsPSP°,
C,PsPeCḡPēC‡PSPēPNḡ PμPiC-PrPμCḡPjP°P»CḡPSPēPNḡ PSPμPeCḡPsP»C-P· C,P°
P°PSP°C,,C-P»P°PeC,PēC‡PSC- CḡPμP°PeC‡C-C—/CḡPsPe. PḡPēPSPrCḡPsPj
PḡC,C-PIPμPSCḡP°ḡḡ"P"¶PsPSCḡPsPSP° C,P° C,PsPeCḡPēC‡PSPēPNḡ
PμPiC-PrPμCḡPjP°P»CḡPSPēPNḡ PSPμPeCḡPsP»C-P· C...P°CḡP°PeC,PμCḡPēP·CḡC"C,CḡCḡCḡ
PīCḡPsPiCḡPμCḡCḡCḡCḡPēPj CḡPeC-CḡPSPēPj PIPēCḡPēPīP°PSPSCḡPj P· P±CḡP»CḡPsP·PSPēPj
CḡCḡP°P¶PμPSPSCḡPj CḡPeC-CḡPē P°P±Ps CḡP»PēP·PsPIPēC... PsP±PsP»PsPSPsPe C,P°
PīPsPrCḡP°P·PSPμPSPSCḡPj CḡP»PēP·PsPiPsC— PsP±PsP»PsPSPePē PsC‡PμPNḡ. P PμP°PeC‡C-C—
PiC-PiPμCḡC‡CḡC,P»PēPIPsCḡC,C- PSP° C,,PμP±CḡPeCḡPsCḡC,P°C, PjPsP¶CḡC,Cḡ
PīCḡPsCḡPIP»CḡC,PēCḡCḡ C,P°PePēPjPē CḡPēPjPiC,PsPjP°PjPē: CḡPeC-CḡPSPēPjPē
CḡPμP°PeC‡C-CḡPjPē, C%Ps C...P°CḡP°PeC,PμCḡPēP·CḡCḡC,CḡCḡCḡ
C-PSC,,C-P»CḡC,CḡPsPIP°PSPēPjPē PjP°PeCḡP»PsPīP°PiCḡP»CḡPsP·PSPēPjPē
PIPēCḡPēPīP°PSPSCḡPjPē, PiPμPSPμCḡP°P»C-P·PsPIP°PSPēPjPē P°P±Ps
PμPeCḡC,,PsP»C-P°C,PēPIPsPēPjPē PIPēCḡPēPīP°PSPSCḡPjPē, P° C,P°PePsP¶
CḡCḡP°P¶PμPSPSCḡPjPē CḡPeC-CḡPē, PSP°P±CḡCḡPePsPj PsP±P»PēC‡CḡCḡ,
PiP°CḡCḡCḡPēPsCḡ, PiPμPjP°C,PsP»PsPiC-C‡PSPēPjPē PīPsCḡCḡCḡPμPSPSCḡPjPē, C,P°PePēPjPē
CḡPe C,CḡPsPjP±PsC‡PēC,PsPiPμPSC-Cḡ C,P° PμPsP·PēPSPsC,,C-P»C-Cḡ, C,P°
CḡCḡP°P¶PμPSPSCḡPj PsPeCḡPμPjPēC... PsCḡPiP°PSC-PI P°P±Ps PeC-P»CḡPePsC...
PsCḡPiP°PSC-PI (PiPμC‡C-PSPeP° C,P° PSPēCḡPePē, Cḡ C,PsPjCḡ C‡PēCḡP»C-
C,CḡP±CḡP»PsC-PSC,PμCḡCḡC,PēC‡C-P°P»CḡPSPēPNḡ PSPμC,,CḡPēC,).

P—P°PiPsCḡC,CḡPμPSPSCḡ (PSP°PīP°PrPē) PīPsPrP°PiCḡPē P·P°P·PIPēC‡P°PNḡ
CḡPiPsCḡC,PμCḡC-PiP°P»PēCḡCḡ PSPμPIPrPsPIP·C- PīC-CḡP»Cḡ PīPsC‡P°C,PeCḡ
P»C-PeCḡPIP°PSPSCḡ C,P° PīCḡPsC,CḡPiPsPj PīPμCḡCḡPēC... PjC-CḡCḡCḡCḡ-PI
P»C-PeCḡPIP°PSPSCḡ. PḡP°CḡC,PsC,P° PSP°PīP°PrC-PI PīPsPrP°PiCḡPē
P·PSPēP¶CḡPIP°P»P°CḡCḡ P· C‡P°CḡPsPj. PμCḡPē P·P°CḡC,PsCḡCḡPIP°PSPSC-
C,,PμP±CḡPeCḡPsCḡC,P°C,Cḡ CḡPμPePsPjPμPSPrCḡC"C,CḡCḡCḡ PīCḡPsC,,C-P»P°PeC,PēPeP°
PiPsCḡC,CḡPēC... PSP°PīP°PrC-PI PīPsPrP°PiCḡPē.

PḡPēPSPrCḡPsPj P»C-P·PēCḡCḡ PīCḡC...P»PēPS (PḡP·Pμ)

P PμP·CḡPjPμ PīCḡPsC,,C-P»Cḡ P±PμP·PīPμPePē

PJ PīCḡPsCḡPμCḡC- CḡP°PSPrPsPjC-P·PsPIP°PSPsPiPs PīPsPrPIC-PNḡPSPsPiPs CḡP»C-PiPsPiPs
PsPīPsCḡPSPsPiPs PrPsCḡP»C-PrP¶PμPSPSCḡ C,,P°P·Pē 3 FLORENCE (FLO-01), Cḡ CḡPePsPjCḡ
PīPsCḡC-PIPsCḡPIP°P»Pē C,,PμP±CḡPeCḡPsCḡC,P°C, C,P° P°P»PsPīCḡCḡPēPSPsP» (346

РіР°С†С-С"РSC,С-РІ, СІРРсС- РіС-РrРrР°СґС,СґСІСІСІ С...С-РjС-РsС,РµСґР°РіС-С— Р·
РіСґРёРІРsРrСr РіРµРјРјР°С,РsР»РsРіС-С†РSPёС... Р·Р»РsСІРРсС-СІРSPёС...
РSPsРІРsСrС,РІРsСґРµРsСґС Р· РіРsРјС-СґРSPёРј Р°Р±Рs РІРёСІРsРёРёРј СґРёР·РёРёРёРsРј
РŸР·Рµ), С,С-Р»СґРёРё Сr 22 (6,4 %) РіР°С†С-С"РSC,С-РІ СІРіРіСІСІС,РµСґС-РіР°Р»Р»РёСІСІ
РіРsР±С-С†РSC- СґРµР°Р°РёС†С-С—, Р° СІР°РјРµ - Сr 11 (6,4 %) РіР°С†С-С"РSC,С-РІ Сr
РёРsР¶РІSC-Р№ РіСґСrРіС- Р»С-РёСrРІР°РSPSCІ. Р'С-Р»СґСІС-СІС,Сґ РіРsР±С-С†РSPёС...
СґРµР°Р°РёС†С-Р№ Р±СrР»Рё Р»РµРіРёРsРіРs Р°Р±Рs РіРsРјС-СґРSPsРіРs СІС,СrРіРµРsСІС.

Рј С†С-Р»РsРјСr РІ РіСґРsС†РµРіС- РrРsСІР»С-РrР¶РµРSPSCІ FLORENCE Р±СrРrСґС-
СІРРёС... РrРsРrР°С,РёРsРІРёС... РіС-РrРsР·Сґ С°РsРrРs Р±РµР·РіРёРёРё
Р·Р°СІС,РsСІСrРІР°РSPSCІ С,,РµР±СrРёСІСІС,Р°С,Сr РіР°С†С-С"РSC,Р°Рј С-Р·
РіРsРrР°РіСґРsСґ РSPµ Р±СrР»Рs, Р·Р° РІРёРSPSCІС,РёРsРј РSPёР¶СРµР·Р°РµР°РSP°С†РµРSPёС...
С,СґСґРsС... РіРsР±С-С†РSPёС... СґРµР°Р°РёС†С-Р№ (РrРёРІ. С,Р°Р±Р». 2).

РµРsСґСrСІСРµРµРSPSCІ Р· Р±РsРёСr СІРµСґС†РµРІРІРsС— СІРёСІС,РµРјРё.

РќРµР°Р°Р°СІС,Рs: Р±Р»РsРёР°РrР° Р»С-РІРsС— РSC-Р¶РёРё РіСrС†РёР° Р"С-СІР°,
СІРёРSPCІСІРsРІР° С,Р°С...С-РёР°СґРrС-СІС.

РµРsСґСrСІСРµРµРSPSCІ Р· Р±РsРёСr СІСrРrРёРSPSPС— СІРёСІС,РµРјРё.

РќРµР°Р°Р°СІС,Рs: РёСґРsРІРsС,РµР±С-

*РµРsРІС-РrРsРјР»РµРSPSCІ РіСґРs РіС-РrРsР·СґРІР°РSC- РіРsР±С-С†РSC-
СґРµР°Р°РёС†С—*

РµРsРІС-РrРsРјР»РµРSPSCІ РіСґРs РіРsР±С-С†РSC- СґРµР°Р°РёС†С-С— РіС-СІР»СІС
СґРµР°С"СІС,СґР°С†С-С— Р»С-РёР°СґСІСґРёРsРіРs Р·Р°СІРsР±Сr РјР°С" РІР°Р¶Р»Р»РёРµРІ
Р·РSP°С†РµРSPSCІ. РіРµ РrР°С" Р·РјРsРіСr РіСґРsРІРsРrРёС,Рё РјРsРSC-С,РsСґРёРSPi
СІРіРіС-РІРІС-РrРSPScРµРµРSPSCІ РёРsСґРёСІС,Сґ/СґРёР·Р·Рё РіСґРё
Р·Р°СІС,РsСІСrРІР°РSPSC- С†СґРsРіРs Р»С-РёР°СґСІСґРёРsРіРs Р·Р°СІРsР±Сr.
РґРµРrРёС†РSPёРј С,Р° С,,Р°СґРјР°С†РµРІС,РёС†РSPёРј РіСґР°С†С-РІSPёРёР°Рј, Р°
С,Р°РёРsР¶ РіР°С†С-С"РSC,Р°Рј Р°Р±Рs С—С... Р·Р°РёРsРSPSPёРј РіСґРµРrСІС,Р°РІSPёРёР°Рј
СІР»С-Рr РіРsРІС-РrРsРјР»СІС,Рё РіСґРs СrСІС- РІРёРіР°РrРёРё РіС-РrРsР·СґРІР°РSPёС...
РіРsР±С-С†РSPёС... СґРµР°Р°РёС†С-Р№ С,Р° РІС-РrСІСrС,РSPScІС,С-
РµС,,РµРёС,РёРІSPScІС,С- Р»С-РёР°СґСІСґРёРsРіРs Р·Р°СІРsР±Сr С†РµРґРµРµР·
Р°РІС,РsРјР°С,РёР·РІРsРІР°С-РSC,,РsСґРјР°С†С-Р№РSCr СІРёСІС,РµРјСr Р·
С,,Р°СґРјР°РёРsРSP°РіР»СІРrСr Р·Р° РіРsСІРёР»Р°РSPSCІРј: <https://aisf.dec.gov.ua>

РŸРµСґРјС-РS РіСґРёРrР°С,РSPScІС,С-. 3 СґРsРёРё.

РјРјРsРІРё Р·Р±РµСґС-РіР°РSPSCІ. РŸРіРµС†С-Р°Р»СґРSC- СrРјРsРІРё
Р·Р±РµСґС-РіР°РSPSCІ РSPµ РІРёРјР°РіР°СґС,СґСІСІ. Р—Р±РµСґС-РіР°С,Рё Сr
РSPµРrРsСІС,СrРіРSPsРјСr РrР»СІ РrС-С,РµР№ РјС-СІС†С-.

РјРіР°РёРsРІРё. РµРs 14 С,Р°Р±Р»С,РsРё Сr Р±Р»С-СІС,РµСґС-; РіРs 2
Р±Р»С-СІС,РµСґРё Сr РёР°СґС,РsРSPSC-Р№ РёРsСґРsР±С†С-.

$$\mathbf{P} \mathbf{L} \mathbf{P}^{\circ} \mathbf{C}, \mathbf{P} \mathbf{u} \mathbf{P} \mathbf{i} \mathbf{P} \mathbf{s} \mathbf{C} \mathbf{H} \mathbf{C} - \mathbf{C} \mathbf{H} \mathbf{P} \mathbf{I} \mathbf{C} - \mathbf{P} \mathbf{r} \mathbf{P} \mathbf{i} \mathbf{C} \mathbf{r} \mathbf{C} \mathbf{I} \mathbf{P} \mathbf{e} \mathbf{C} \mathbf{r}. \mathbf{P} - \mathbf{P}^{\circ} \mathbf{C} \mathbf{H} \mathbf{P} \mathbf{u} \mathbf{C} \mathbf{I} \mathbf{P} \mathbf{u} \mathbf{P} \mathbf{i} \mathbf{C}, \mathbf{P} \mathbf{s} \mathbf{P} \mathbf{j}.$$

P'PëCḤPsP±PSPëPε. P"PμPSPμC,,P°CḤPj PŸPḥ.

**РнС-СГС†РмР·PSP°С...PsPrP¶РмPSPSC¶ PIPëCЪPsP±PSPëPeP° C,P° P°PrCЪРмСГР°
PjC-СГС†С¶ PïCЪPsPIP°PrP¶РмPSPSC¶ PNøPsPiPs PrC-С¶Р»СнPSPsСГС,C-.**

[illegible]