

**PrP»CЦ PjPμPrPëC‡PSPsPiPs P•P°CíC,PsCíCíPIP°PSPSCЦ P»C-PeP°CĤCíCĤPePsPiPs  
P•P°CíPsP±Cí**

## Irinotecan Amaxa

P†CḡPēPSPsC,PμPeP°PS PḡPjP°PeC†P° C” PSP°PīC-PIC†PēPSC,PμC,PēC†PSPsCḡ  
 CḡPμC†PsPIPēPSPsCḡ, PīPsC...C-PrPSPsCḡ PeP°PjPīC,PsC,PμC†PēPSC†. P|Pμ  
 PīCḡPsC,PēPīC†C...P»PēPSPSPēPNē PīCḡPμPīP°CḡP°C,, C%Ps PIPēC†C,C†PīP°C”  
 C†PīPμC†PēC,,C-C†PSPēPj C-PSPiC-P±C-C,PsCḡPsPj P”P†Pḡ-  
 C,PsPīPsC-P·PsPjPμCḡP°P·Pē P†. PμC-Pr PrC-C”Cḡ  
 PeP°CḡP±PsPeC†PēP»PμC†C,PμCḡP°P·Pē C† P±C-P»CHC€PsC†C,C- C,PeP°PSPēPS  
 PīCḡPμPīP°CḡP°C, PjPμC,P°P±PsP»C-P·C†C”C,CHC†C† PrPs C†PīPsP»C†PePē SN-38,  
 C†PeP° PīPsCḡC-PIPSC†PSPs P· C-CḡPēPSPsC,PμPeP°PSPsPj C” P±C-P»CHC€  
 P°PeC,PēPIPSPsCḡ C%PsPrPs PsC†PēC%PuPSPsC— C,PsPīPsC-P·PsPjPμCḡP°P·Pē P†

C,P° P±C-P»CHC€ C†PëC,PsC,PsPeC†PëC‡PSPsCĤ PIC-PrPSPsC†PSPs CĤC‡PrCř  
P»C-PSC-PNë PiCřC...P»PëPSPSPëC... PeP»C-C,PëPS P»CĤPrPëPSPë C,P° PjPëC€PμPNë.  
PμCĤPëPiPSC-C‡PμPSPSC‡ P”PќPљ-C,PsPiPsC-P·PsPjPμCĤP°P·Pë P† PiC-Pr PrC-C”CĤ  
C-CĤPëPSPsC,PμPeP°PSCř C‡Pë SN-38 PiCĤPëP·PIPsPrPëC,CH PrPs  
PiPsC€PePsPrP¶PμPSCĤ PsPrPSPsP»P°PSC†CĤPiPsPIPsC— P”PќPљ, C‡PeC-  
P±P»PsPeCřCĤC,CH CĤPμPiP»C-PeP°C,PëPIPSCř PIPëP»PeCř P”PќPљ C,P°  
PiCĤPëP·PIPsPrC‡C,CH PrPs C†PëC,PsC,PsPeC†PëC‡PSPsC— PrC-C—. P’CřP»Ps  
PIC†C,P°PSPsPIP»PμPSPs, C°Ps C,P°PePëPNë C†PëC,PsC,PsPeC†PëC‡PSPëPNë  
PμC,,PμPeC, C” P·P°P»PμP¶PSPëPj PIC-Pr C‡P°C†Cř C,P° C†PiPμC†PëC,,C-C‡PSPëPj  
PrP»C‡ S-C,,P°P·Pë PeP»C-C,PëPSPSPsPiPs C†PëPeP»Cř.

PљCĤC-Pj PiCĤPsC,PëPiCřC...P»PëPSPSPsC— P°PeC,PëPIPSPsC†C,C-, PSP°PNëP±C-P»CHC€  
P·PSP°C‡Cř°PsCĤ C,,P°CĤPjP°PePsP»PsPiC-C‡PSPsCĤ PrC-C”CĤ C-CĤPëPSPsC,PμPeP°PSCř  
C” PiCĤPëPiPSC-C‡PμPSPSC‡ P°PeC,PëPIPSPsC†C,C-  
P°C†PμC,PëP»C...PsP»C-PSPμC†C,PμCĤP°P·Pë.

*PμP°C†C-C”PSC,Pë P·C- P·PSPëP¶PμPSPsCĤ P°PeC,PëPIPSC-C†C,CĤ UGT1A1.*

PjCĤPëPrPëPSPPrPëC,,PsC†C,,P°C,-PiP»CĤPeCřCĤPsPSC-P»C,CĤP°PSC†C,,PμCĤP°P·P° 1Pĥ1  
(UGT1A1) P±PμCĤPμ CřC‡P°C†C,CH Cř PjPμC,P°P±PsP»C-C‡PSC-PNë C-PSP°PeC,PëPIP°C†C-C—  
SN-38, P°PeC,PëPIPSPsPiPs PjPμC,P°P±PsP»C-C,Cř C-CĤPëPSPsC,PμPeP°PSCř, P·  
CřC,PIPsCĤPμPSPSC‡Pj PSPμP°PeC,PëPIPSPsPiPs SN-38-PiP»CĤPeCřCĤPsPSC-PrCř (SN-38G).  
P”PμPS UGT1A1 C...P°CĤP°PeC,PμCĤPëP·CřC”C,CHC†C‡ PIPëC†PsPePëPj  
PiPsP»C-PjPsCĤC,,C-P·PjPsPj, C°Ps P·P°P±PμP·PiPμC‡CřC” PSP°C‡PIPSC-C†C,CH  
CĤC-P·PSPsPjP°PSC-C,PSPëC... PIP°CĤC-P°PSC,C-PI C-PSC,PμPSC†PëPIPSPsC†C,C-  
PjPμC,P°P±PsP»C-P·PjCř Cř PiCĤCřPiC-. 1 PsC†PsP±P»PëPIPëPNë PIP°CĤC-P°PSC, PiPμPSP°  
UGT1A1 PjC-C†C,PëC,CH PiPsP»C-PjPsCĤC,,PSCř PrC-P»C‡PSPeCř PI PrC-P»C‡PSC†C-  
PiCĤPsPjPsC,PsCĤP°, C†PμPNë PIP°CĤC-P°PSC, PSPsC†PëC,CH PSP°P·PICř UGT1A1\*28.  
PŸP°PePëPNë PIP°CĤC-P°PSC,, P° C,P°PePsP¶ C-PSC€C- C†PiP°PrPePsPIC- PiPsCĤCřC€PμPSPSC‡  
PμPeC†PiCĤPμC†C-C— UGT1A1 (C,P°PeC- C‡Pe C†PëPSPrCĤPsPj P-PëP»CHP±PμCĤP° P°P±Ps  
C†PëPSPrCĤPsPj PљCĤPëPiP»PμCĤP°-Pќ°PNëC‡CĤP°) PiPsPIbĤ™ C‡P·CřCĤC,CH P·C-  
P·PSPëP¶PμPSPsCĤ P°PeC,PëPIPSC-C†C,CĤ C†CHPsPiPs C,,PμCĤPjPμPSC,Cř.  
P PμP·CřP»CHC,P°C,Pë PjPμC,P°P°PSP°P»C-P·Cř C†PIC-PrC‡P°C,CH, C°Ps PiP°C†C-C”PSC,Pë  
C-P· C†PëPSPrCĤPsPjPsPj PљCĤPëPiP»PμCĤP°-Pќ°PNëC‡CĤP° (C,PëPi 1 C,P° 2) P°P±Ps  
PiPsPjPsP·PëPiPsC,Pë P·P° P°P»PμP»PμPj UGT1A1\*28 (C†PëPSPrCĤPsPj P-PëP»CHP±PμCĤP°)  
PIC...PsPrC‡C,CH PrPs PiCĤCřPiPë PiC-PrPIPëC°PμPSPsPiPs CĤPëP·PëPeCř  
PIPëPSPëPePSPμPSPSC‡ PiPμPjP°C,PsP»PsPiC-C‡PSPsC— C,PsPeC†PëC‡PSPsC†C,C- (III C,P° IV  
C†C,CřPiPμPSC-PI) PiC-C†P»C‡ PIPiPμPrPμPSPSC‡ C†PμCĤPμPrPSC-C... P°P±Ps  
PIPëC†PsPePëC... PrPsP· C-CĤPëPSPsC,PμPeP°PSCř (>150 PjPi/Pj²).  
P’P·P°C”PjPsP·PIbĤ™ C‡P·PsPe PjC-P¶ PiPμPSPsC,PëPiPsPj UGT1A1 C,P°  
PIPëPSPëPePSPμPSPSC‡Pj PrC-P°CĤPμC— PIPSP°C†P»C-PrPsPe PrC-C—  
C-CĤPëPSPsC,PμPeP°PSCř PSPμ PIC†C,P°PSPsPIP»PμPSPs.

PμP°C†C-C”PSC,P°Pj P· B PIC-PrPsPjPëPjPë PiPsPjPsP·PëPiPsC,P°PjPë P·P° P°P»PμP»PμPj  
UGT1A1\*28 C†P»C-Pr P·P°C†C,PsC†PsPICřPIP°C,Pë P·PIPëC‡P°PNëPSCř PiPsC‡P°C,PePsPICř  
PrPsP·Cř C-CĤPëPSPsC,PμPeP°PSCř. P’PsPrPSPsC‡P°C† P·P° C,P°PePëPjPë PiP°C†C-C”PSC,P°PjPë  
C†P»C-Pr C†PiPsC†C,PμCĤC-PiP°C,Pë C°PsPrPs PiCĤPsC‡PIC-PI  
PiPμPjP°C,PsP»PsPiC-C‡PSPsC— C,PsPeC†PëC‡PSPsC†C,C-. P”P»C‡ PiP°C†C-C”PSC,C-PI, Cř  
C‡PePëC... PiC-Pr C‡P°C† PiPsPiPμCĤPμPrPSC-C... PeCřCĤC†C-PI P»C-PeCřPIP°PSPSC‡ PIP¶Pμ  
PIPëPSPëPeP°P»Pë PiCĤPsC‡PIPë PiPμPjP°C,PsP»PsPiC-C‡PSPsC— C,PsPeC†PëC‡PSPsC†C,C-,  
C†P»C-Pr CĤPsP·PiP»C‡PSCřC,Pë PjPsP¶P»PëPIC-C†C,CH P·PSPëP¶PμPSPSC‡

PiPsC†P°C,PePsPIPsC— PrPsP·Pë C-CĤPëPSPsC,PμPeP°PSCr. PŷPsC†PSCr PIPμP»PëC†PëPSCr P·PSPëP¶PμPSPSCĬ PİPsC†P°C,PePsPIPsC— PrPsP·Pë PrP»CĬ C†C-C°C— PiCĤCrPİPë PİP°C†C-C°PSC,C-PI PSPμ PICrC,P°PSPsPIP»CĤPIP°P»Pë. P'CrPrCH-CĬPeC- PİPsPrP°P»CHC€C- P·PjC-PSPë PrPsP·CrPIP°PSPSCĬ CĬP»C-Pr PİCĤPsPIPsPrPëC,Pë, PIPëC...PsPrCĬC†Pë P· C,PsPiPs, CĬPe PİP°C†C-C°PSC, PİPμCĤPμPSPsCĬPëC,CH P»C-PeCrPIP°PSPSCĬ (PrPëPI. CĤPsP·PrC-P»Pë B«PhCĬPsP±P»PëPIPsCĬC,C- P·P°CĬC,PsCĬCrPIP°PSPSCĬB» C,P° B«PŷPİPsCĬC-P± P·P°CĬC,PsCĬCrPIP°PSPSCĬ C,P° PrPsP·PëB»). PkP° CĬCHPsPiPsPrPSC- PSPμPrPsCĬC,P°C,PSCHPs PeP»C-PSC-C†PSPëC... PrP°PSPëC... PrP»CĬ PIPëCĬPSPsPIPeCr C°%PsPrPs PrPsC†C-P»CHPSPsCĬC,C- PiPμPSPsC,PëPİCrPIP°PSPSCĬ PİP°C†C-C°PSC,C-PI P·P° P°P»PμP»CĬPjPë UGT1A1.

*PαP°CĤPjP°PePsPeC-PSPμC,PëPeP°.*

PμC-CĬP»CĬ PIPIPμPrPμPSPSCĬ C-CĤPëPSPsC,PμPeP°PSCr PI PrPsP·C- 100-750 PjPi/Pj<sup>2</sup> C€P»CĬC...PsPj 30-C...PIPëP»PëPSPSPsC— PIPSCrC,CĤC-C€PSCHPsPIPμPSPSPsC— C-PSC,,CrP·C-C— PePsP¶PSC- 3 C,PëP¶PSC- CĬPİPsCĬC,PμCĤC-PİP°C°C,CHCĬCĬ PrPIPs- P°P±Ps C,CĤPëC,,P°P·PsPIP° PİP»P°P·PjPsPIP° PμP»C-PjC-PSP°C†C-CĬ C-CĤPëPSPsC,PμPeP°PSCr. PŷPμCĤPμPrPSC-PNë PİP»P°P·PjPsPIPëPNë PeP»C-CĤPμPSCĬ - 15 P»/PiPsPr/Pj<sup>2</sup>, PsP±BĤ™ C°Pj CĤPsP·PİPsPrC-P»Cr PI CĤC-PIPSPsPIP°P¶PSPsPjCr CĬC,P°PSC- (Vss) - 157 P»/Pj<sup>2</sup> PİPsPIPμCĤC...PSC- C,C-P»P°. PŷPμCĤPμPrPSC-PNë PİPμCĤC-PsPr PSP°PİC-PIPIPëPIPμPrPμPSPSCĬ P· PİP»P°P·PjPë PeCĤPsPIC- PİC-Pr C†P°CĬ PİPμCĤC€PsC— C,,P°P·Pë C,CĤPëC,,P°P·PsPIPsC— PjPsPrPμP»C- CĬC,P°PSPsPIPëPI 12 C...PI, PİC-Pr C†P°CĬ PrCĤCrPiPsC— C,,P°P·Pë BĤ" 2,5 PiPsPrPëPSPë, PİC-Pr C†P°CĬ C,CĤPμC,CHPsC— C,,P°P·Pë BĤ" 14,2 PiPsPrPëPSPë. PμP»P°P·PjPsPIP° PμP»C-PjC-PSP°C†C-CĬ SN-38 P±CrP»P° PrPIPsC,,P°P·PsPIP° P·C- CĬPμCĤPμPrPSC-Pj PeC-PSC†PμPIPëPj PİPμCĤC-PsPrPsPj PSP°PİC-PIPIPëPIPμPrPμPSPSCĬ 13,8 PiPsPrPëPSPë.

P—PIBĤ™ CĬP·CrPIP°PSPSCĬ P· P±C-P»PeP°PjPë PİP»P°P·PjPë PeCĤPsPIC- Cr PrPsCĬP»C-PrP¶PμPSPSC- *in vitro* CĬC,P°PSPsPIPëC,CH PİCĤPëP±P»PëP·PSPs 65 % PrP»CĬ C-CĤPëPSPsC,PμPeP°PSCr C- 95 % PrP»CĬ PjPμC,P°P±PsP»C-C,Cr SN-38.

P'C-P»CHC€Pμ 50 % PrPsP·Pë C-CĤPëPSPsC,PμPeP°PSCr, PIPIPμPrPμPSPsPiPs PIPSCrC,CĤC-C€PSCHPsPIPμPSPSPs, PIPëPrC-P»CĬC°C,CHCĬCĬ Cr PSPμP·PjC-PSPμPSPsPjCr PIPëPiP»CĬPrC-, 33 % PIPëPrC-P»CĬC°C,CHCĬCĬ P· PeP°P»PsPj, PI PsCĬPSPsPIPsPjCr C†PμCĤPμP· P¶PsPIC±, C,P° 22 % BĤ" C-P· CĬPμC†PμCĤ.

PμP»C-CĤPμPSCĬ C-CĤPëPSPsC,PμPeP°PSCr P·PjPμPSC€CrC°C,CHCĬCĬ PjP°PNëP¶Pμ PSP° 40 % Cr PİP°C†C-C°PSC,C-PI P· P±C-P»C-CĤCrP±C-PSPμPjC-C°CĤ (PePsPSC†PμPSC,CĤP°C†C-CĬ P·P°PiP°P»CHPSPsPiPs P±C-P»C-CĤCrP±C-PSCr PI CĬPëCĤPsPIP°C,C†C- PeCĤPsPIC- Cr 1,5-3 CĤP°P·Pë PIPëC°%P° P·P° PIPμCĤC...PSCĤ PjPμP¶Cr PSPsCĤPjPë). Pj C†PëC... PİP°C†C-C°PSC,C-PI PrPsP·P° C-CĤPëPSPsC,PμPeP°PSCr 200 PjPi/Pj<sup>2</sup> PİCĤPëP·PIPsPrPëC,CH PrPs PμPeCĬPİPsP·PëC†C-C— PİCĤPμPİP°CĤP°C,Cr PI PİP»P°P·PjC- PeCĤPsPIC-, CĬPeP° PİPsCĤC-PIPSCĬPSPSP° P· C,P°PePsCĤ PİCĤPë PrPsP·C- 350 PjPi/Pj<sup>2</sup> Cr C...PIPsCĤPëC... PSP° CĤP°Pe P· PSPsCĤPjP°P»CHPSPëPjPë PİPsPeP°P·PSPëPeP°PjPë C,,CrPSPeC†C-C— PİPμC†C-PSPePë.

P†PSC,PμPSCĬPëPIPSC-CĬC,CH PSP°PNëP±C-P»CHC€ PIPëCĤP°P¶PμPSPëC... C,PsPeCĬPëC†PSPëC... PμC,,PμPeC,C-PI C-CĤPëPSPsC,PμPeP°PSCr (PSP°PİCĤPëPeP»P°Pr, P»PμPNëPePsPSPμPNëC,CĤPsPİPμPSC-C— C- PrC-P°CĤPμC—) PİPsPIBĤ™ CĬP·P°PSP° C-P· PIPİP»PëPIPsPj (PİP»PsC°%P° PİC-Pr PeCĤPëPIPsCĤ B«PePsPSC†PμPSC,CĤP°C†C-CĬ-C†P°CĬB» (AUC)) PSPμP·PjC-PSPμPSPsPiPs C-CĤPëPSPsC,PμPeP°PSCr C,P° PNëPsPiPs PjPμC,P°P±PsP»C-C,Cr SN-38. P†CĬC,PsC,PSPëPNë PIP·P°C°PjPsP·PIBĤ™ CĬP·PsPe

СГРiPsCГC, PμCГC-PiP°PICГCПjC-P¶ PiPμPjP°C, PsP»PsPiC-C‡PSPsCГ  
C, PsPeCГP€C‡PSC-CГC, CГ (P·PjPμPSC€PμPSPSCПj PeC-P»CГPePsCГC, C-  
P»PμPNεPePsC‡P€C, C-PI C- PSPμPNεC, CГPsC„C-P»C-PI PrPs PjC-PSC-PjCГPjCГ) P°P±Ps  
C-PSC, PμPSCГP€PIPSC-CГC, CГ PrC-P°CГPμC— PNε AUC C-CГP€PSPsC, PμPeP°PSCГ C, P°  
PNεPsPiPs PjPμC, P°P±PsP»C-C, CГ SN-38 PiCГP€ PjPsPSPsC, PμCГP°PiC-C—.

**PљP»C-PSC-C‡PSC- C...P°CГP°PeC, PμCГP€CГC, P€PeP€.**

**PμPsPeP°P·P°PSPSCП.**

P>C-PeCГPIP°PSPSCП PiP°C‡C-C”PSC, C-PI C-P· PiPsC€P€CГPμPSP€Pj  
PePsP»PsCГPμPeC, P°P»CГPSP€Pj CГP°PePsPj:

B· CГ PePsPjP±C-PSP°C‡C-C— P· 5-C„C, PsCГCГCГP°C‡P€P»PsPj (5-PαPJ) C, P°  
C„PsP»C-PSC-C”PIPsCГ PeP€CГP»PsC, PsCГ (PαPљ), CПPeC%Ps PiP°C‡C-C”PSC, P€ PSPμ  
PsC, CГP€PjCГPIP°P»P€ PiPsPiPμCГPμPrPSCГPsC— C...C-PjC-PsC, PμCГP°PiC-C— PrP»CП  
P»C-PeCГPIP°PSPSCП PiPsC€P€CГPμPSPsPiPs P·P°C...PIPsCГCГPIP°PSPSCП;

B· CПPe PjPsPSPsC, PμCГP°PiC-CП, CПPeC%Ps PICГC, P°PSPsPIP»PμPSP€PNε CГPμP¶P€Pj  
P»C-PeCГPIP°PSPSCП C-P· P·P°CГC, PsCГCГPIP°PSPSCПj 5-PαPJ PiP€CПPIP€PICГCП  
PSPμPμC„PμPeC, P€PIPSP€Pj.

P‡CГP€PSPsC, PμPeP°PS PђPjP°PeCГP° CГ PePsPjP±C-PSP°C‡C-C— P·  
C‡PμC, CГPeCГP€PjP°P±PsPj PiPsPeP°P·P°PSP€PNε PrP»CП P»C-PeCГPIP°PSPSCП  
PiP°C‡C-C”PSC, C-PI C-P· PjPμC, P°CГC, P°C, P€C‡PSP€Pj  
PePsP»PsCГPμPeC, P°P»CГPSP€Pj CГP°PePsPj P· PrP€PeP€Pj C, P€PiPsPj PiPμPSP° KRAS,  
C%Ps CГCГPiCГPsPIPsPrP¶CГC”C, CГCГCП PiPsCГP€P»PμPSPsCГ PμPeCГPiCГPμCГC-C”CГ  
CГPμC‡PμPiC, PsCГP° PμPiC-PrPμCГPjP°P»CГPSPsPiPs C„P°PeC, PsCГP° CГPsCГC, CГ (P P·PαP ),  
CПPeC- CГP°PSC-C€Pμ PSPμ PsC, CГP€PjCГPIP°P»P€ C...C-PjC-PsC, PμCГP°PiC-CГ, P°P±Ps  
PiC-CГP»CП PSPμPμC„PμPeC, P€PIPSPsC— C‡P€C, PsC, PsPeCГP€C‡PSPsC— C, PμCГP°PiC-C—,  
CПPeP° PiPeP»CГC‡P°P»P° C-CГP€PSPsC, PμPeP°PS.

Pj PePsPjP±C-PSP°C‡C-C— P· 5-PαPJ, PαPљ C, P° P±PμPIP°C‡P€P·CГPjP°P±PsPj  
P‡CГP€PSPsC, PμPeP°PS PђPjP°PeCГP° P·P°CГC, PsCГPsPICГCГC, CГ CПPe  
C, PμCГP°PiC-CГ PiPμCГC€PsC— P»C-PSC-C— PiP°C‡C-C”PSC, P°Pj C-P·  
PjPμC, P°CГC, P°C, P€C‡PSP€PjP€ PeP°CГC‡P€PSPsPjP°PjP€ C, PsPICГC, PsC— P°P±Ps  
PiCГCПjPsC— PeP€C€PeP€.

Pj PePsPjP±C-PSP°C‡C-C— P· PeP°PiPμC‡P€C, P°P±C-PSPsPj (P· PrPsPrP°PIP°PSPSCПj  
P±PμPIP°C‡P€P·CГPjP°P±CГ P°P±Ps P±PμP· PSCHPsPiPs) P‡CГP€PSPsC, PμPeP°PS PђPjP°PeCГP°  
P·P°CГC, PsCГPsPICГCГC, CГ CПPe C, PμCГP°PiC-CГ PiPμCГC€PsC— P»C-PSC-C—  
PiP°C‡C-C”PSC, P°Pj C-P· PjPμC, P°CГC, P°C, P€C‡PSP€Pj PePsP»PsCГPμPeC, P°P»CГPSP€Pj  
CГP°PePsPj.

**PμCГPsC, P€PiPsPeP°P·P°PSPSCП.**

P-PëPIC- P°C,PμPSCrPNεPsPIP°PSC- PIP°PeC†PëPSPë (PSP°PïCḡPëPeP»P°Pr, PIP°PeC†PëPSP°PïCḡPsC,Pë P¶PsPIC,PsC— PiP°CḡCḡC†PePë) вḡ“ CḡPëP·PëPe PIPëPSPëPePSPμPSPSCḡCḡPëCḡC,PμPjPSPëC... P·P°C...PIPScḡCḡPIP°PSCḡ P· PjPsP¶P»PëPIPëPj P»PμC,P°P»CḡPSPëPj PSP°CḡP»C-PrPePsPj (PSP°PïCḡPëPeP»P°Pr, C-PSC,,PμPeC†C-C—). P¡PμPNε CḡPëP·PëPe P·P±C-P»CḡCḡCrC”C,CḡCḡCḡ, CḡPeC%oPs Cr PïP°C†C-C”PSC,C-PI CrP¶Pu

PiC7PëPiPSC-C#PµPSP° C-PjCfPSPSP° C7PëC7C,PµPjP° PIPSP°C7P»C-PrPsPe  
PsC7PSPsPIPSPsPiPs P·P°C...PIPsC7C7PIP°PSPSC7. PhPrPSPsC#P°C7PSPµ  
P·P°C7C,PsC7C7PIP°PSPSC7 P¶PëPIPëC... P°C,PµPSC7PNsPsPIP°PSPëC... PIP°PeC7PëPS  
PiC7PsC,PëPiPsPeP°P·P°PSPs PiC-Pr C#P°C7 P»C-PeC7PIP°PSPSC7 C-C7PëPSPsC,PµPeP°PSPsPj  
C,P° PiC7PsC,C7PiPsPj CëPµC7C,Pë PjC-C7C7C7C-PI PiC-C7P»C7 P·P°PeC-PSC#PµPSPSC7  
C...C-PjC-PsC,PµC7P°PiC-C—. PÿP»C-Pr P·P°C7C,PsC7PsPIC7PIP°C,Pë  
C-PSP°PeC,PëPIPsPIP°PSC- PIP°PeC7PëPSPë, C7PeC%Ps PIPsPSPë C-C7PSC7C7C,CH  
(PiPsP»C-PsPjC-C”P»C-C,), P°P»Pµ PIC-PrPiPsPIC-PrCH PSP° C,P°PeC- PIP°PeC7PëPSPë  
PjPsP¶Pµ P±C7C,Pë P·PSPëP¶PµPSP°.

P»C-PeP°C7C7CHPeC- P·P°C7PsP±Pë, PsPrPSPsC#P°C7PSPµ PiC7PëP·PSP°C#PµPSPSC7  
C7PePëC... C-P· PiC7PµPiP°C7P°C,PsPj P7C7PëPSPsC,PµPeP°PS PhPjP°PeC7P° PSPµ  
C7PµPePsPjPµPSPPrPsPIP°PSPs (PrPëPI. C7PsP·PrC-P» B«PhC7PsP±P»PëPIPsC7C,C-  
P·P°C7C,PsC7C7PIP°PSPSC7B»):

PÿP»C-Pr C7PSPëPeP°C,Pë PsPrPSPsC#P°C7PSPsPiPs P·P°C7C,PsC7C7PIP°PSPSC7  
C-C7PëPSPsC,PµPeP°PSC7 C,P° C7PëP»CHPSPëC...  
C-PSP7C7PeC,PsC7C-PI/C-PSPiC-P±C-C,PsC7C-PI C7PëC,PsC...C7PsPjC7 P450 3A4  
(CYP3A4), PsC7PeC-P»CHPePë C7Pµ PjPsP¶Pµ PiC7PëP·PIPsPrPëC,Pë PrPs P·PjC-PS  
PjPµC,P°P±PsP»C-P·PjC7 C-C7PëPSPsC,PµPeP°PSC7 (PrPëPI. C7PsP·PrC-P»  
B«PhC7PsP±P»PëPIPsC7C,C- P·P°C7C,PsC7C7PIP°PSPSC7B»).

PÿPëP»CHPSC- C-PSP7C7PeC,PsC7Pë CYP3A4 C,P°/P°P±Ps UGT1A1  
(PSP°PiC7PëPeP»P°Pr, C7PëC,,P°PjPiC-C7PëPS, PeP°C7P±P°PjP°P·PµPiC-PS,  
C,,PµPSPsP±P°C7P±C-C,P°P», C,,PµPSC-C,PsC—PS P°P±Ps P°PiP°P»C7C,P°PjC-Pr) B7“  
C7PµP·C7P»CHC,P°C,Pë PrPµPeC-P»CHPePsC... PrPsC7P»C-PrP¶PµPSC7  
PiC7PsPrPµPjPsPSC7C,C7C7PIP°P»Pë, C%Ps PsPrPSPsC#P°C7PSPµ  
P·P°C7C,PsC7C7PIP°PSPSC7 PiC7PsC,PëC7C7PrPsPjPSPëC... PiC7PµPiP°C7P°C,C-PI,  
C-PSP7C7PeC,PsC7C-PI CYP3A4 (PeP°C7P±P°PjP°P·PµPiC-PS,  
C,,PµPSPsP±P°C7P±C-C,P°P» P°P±Ps C,,PµPSC-C,PsC—PS), PiC7PëP·PIPsPrPëC,CH PrPs  
P·PjPµPSCëPµPSPSC7 PµC,,PµPeC,PëPIPsPSC7C,C- C-C7PëPSPsC,PµPeP°PSC7, SN-38  
C,P° SN-38-PiP»CHPeC7C7PsPSC-PrC7, C%Ps, C7 C7PIPsC7 C#PµC7PiC7,  
PiC7PëP·PIPsPrPëC,CH PrPs P·PjPµPSCëPµPSPSC7  
C,,P°C7PjP°PePsPrPëPSP°PjC-C#PSPsPiPs PµC,,PµPeC,C7. P”C-C7 C,P°PePëC...  
PiC7PsC,PëC7C7PrPsPjPSPëC... PiC7PµPiP°C7P°C,C-PI PiPsP»C7PiP°P»P° C7  
P·PSPëP¶PµPSPSC- AUC PrP»C7 SN-38 C,P° SN-38-PiP»CHPeC7C7PsPSC-PrC7 PSP° 50 %  
C#Pë PSP°PIC-C,CH P±C-P»CHCëPµ. P7C7C-Pj C-PSP7C7PeC7C-C—  
C7PëC,PsC...C7PsPjC7 P450 3A4, P·PSPëP¶PµPSPSC7 C7C-PIPsC7  
PµPeC7PiPsP·PëC7C-C— C-C7PëPSPsC,PµPeP°PSC7 C,P° PNsPiPs  
PjPµC,P°P±PsP»C-C,C-PI PjPsP¶Pµ P±C7C,Pë PsP±C7PjPsPIP»PµPSPµ C,P°PePsP¶  
PiPsC7PëP»PµPSPsC7 PiP»CHPeC7C7PsPSC-P·P°C7C-C”C7 C,P° P±C-P»CHCë  
C-PSC,PµPSC7PëPIPsPëPj PIPëPIPµPrPµPSPSC7Pj C-P· P¶PsPIC7C7.

P»PµPSC-C,PsC—PS B7“ C7PëP·PëPe P·P°PiPsC7C,C7PµPSPSC7 C7C7PrPsPj  
PIPSP°C7P»C-PrPsPe P·PSPëP¶PµPSPSC7 C-PSC,PµPSC7PëPIPsPSC7C,C-  
PiPsPiP»PëPSP°PSPSC7 C,,PµPSC-C,PsC—PSC7 C7 C,C7P°PIPsPjC7 C,C7P°PeC,C- PiC-Pr  
PIPiP»PëPIPsPj C7PëC,PsC,PsPeC7PëC#PSPsPiPs PiC7PµPiP°C7P°C,C7.

PÿPëP»CHPSC- C-PSPiC-P±C-C,PsC7Pë CYP3A4 (PSP°PiC7PëPeP»P°Pr,

PePμC,PsPePsPSP°P·PsP», C-C,CTHP°PePsPSP°P·PsP», PIPsCTHPëPePsPSP°P·PsP»,  
PïPsP·P°PePsPSP°P·PsP», C-PSPiC-P±C-C,PsCTHPë PïCTHPsC,PμP°P·Pë,  
PeP»P°CTHPëC,CTHPsPjC-C†PëPS, PμCTHPëC,CTHPsPjC-C†PëPS, C,PμP»C-C,CTHPsPjC-C†PëPS)  
вҒ“ Cр CTHPμP·CрP»CHC,P°C,C- PrPsCрP»C-PrP¶PμPSPSC¶ P±CрP»Ps  
PICрC,P°PSPsPIP»PμPSPs, C%Ps PsPrPSPsC†P°CрPSPμ P·P°CрC,PsCрCрPIP°PSPSC¶  
PePμC,PsPePsPSP°P·PsP»Cр PïCTHPëP·PIPPrPëP»Ps PrPs P·PSPëP¶PμPSPSC¶ AUC  
PjPμC,P°P±PsP»C-C,Cр APC PSP° 87 %, P° AUC PjPμC,P°P±PsP»C-C,Cр SN-38  
P·PSPëP¶CрPIP°P»P°CрCH PSP° 109 % PïPsCTHC-PIPSCTHPSPs C-P·  
P·P°CрC,PsCрCрPIP°PSPSC¶Pj C-CTHPëPSPsC,PμPeP°PSCр C¶Pe  
PjPsPSPsC,PμCTHP°PïC-C—.

P†PSPiC-P±C-C,PsCTHPë UGT1A1 (PSP°PïCTHPëPeP»P°Pr, P°C,P°P·P°PSP°PIC-CTH,  
PePμC,PsPePsPSP°P·PsP», CTHPμPiPsCTHP°C„PμPSC-P±) вҒ“ CTHPëP·PëPe  
PïC-PrPIPëC%PμPSPSC¶ CрPëCрC,PμPjPSPsC— PμPeCрPïPsP·PëC†C-C—  
P°PeC,PëPIPSsPiPs PjPμC,P°P±PsP»C-C,Cр C-CTHPëPSPsC,PμPeP°PSCр вҒ“ SN-38.  
P>C-PeP°CTHC¶Pj CрP»C-Pr PICHP°C...PsPICрPIP°C,Pë C†CH PjPsP¶P»PëPIC-CрC,CH  
PïCTHPë PsPrPSPsC†P°CрPSPsPjCр PïCTHPëP·PSP°C†PμPSPSC- C†PëC... PrPIPsC...  
PïCTHPμPïP°CTHP°C,C-PI.

P†PSC€C- C-PSPiC-P±C-C,PsCTHPë CYP3A4 (PSP°PïCTHPëPeP»P°Pr, PeCTHPëP·PsC,PëPSC-P±,  
C-PrPμP»P°P»C-P·PëP±) вҒ“ CTHPëP·PëPe PïC-PrPIPëC%PμPSPSC¶ C,PsPeCрPëC†PSPsCрC,C-  
C-CTHPëPSPsC,PμPeP°PSCр PIPSP°CрP»C-PrPsPe P·PSPëP¶PμPSPSC¶ PN₂PsPiPs  
PjPμC,P°P±PsP»C-P·PjCр PïCTHPë PsPrPSPsC†P°CрPSPsPjCр P·P°CрC,PsCрCрPIP°PSPSC- P·  
PeCTHPëP·PsC,PëPSC-P±PsPj P°P±Ps C-PrPμP°P»C-P·PëP±PsPj.

P>C-PeP°CTHCрCHPeC- P·P°CрPsP±Pë, C¶PeC- CTHP°P·PsPj C-P· PïCTHPμPïP°CTHP°C,PsPj  
P†CTHPëPSPsC,PμPeP°PS PhPjP°PeCрP° CрP»C-Pr P·P°CрC,PsCрPsPICрPIP°C,Pë P·  
PsP±PμCTHPμP¶PSC-CрC,CH:

PhPSC,P°PiPsPSC-CрC,Pë PIC-C,P°PjC-PSCр Pᄡ вҒ“ PïC-PrPIPëC%PμPSPëPN₂  
CTHPëP·PëPe PIPëPSPëPePSPμPSPSC¶ PeCTHPsPiPsC,PμC† C- C,CTHPsPjP±PsP·C-PI Cр  
PïP°C†C-C”PSC,C-PI C-P· PïCрC...P»PëPSPSPëPjPë P·P°C...PIPsCTHCPIP°PSPSC¶PjPë.  
P—P° PSP°C¶PIPSsCрC,C- PïPsPeP°P·P°PSCᄡ PrPs P·P°CрC,PsCрCрPIP°PSPSC¶  
P°PSC,P°PiPsPSC-CрC,C-PI PIC-C,P°PjC-PSCр Pᄡ PSPμPsP±C...C-PrPSPs  
C†P°CрC,C-C€Pμ, PSC-P¶ P·P°P·PIPëC†P°PN₂, PePsPSC,CTHPsP»CTHIP°C,Pë  
PïPsPeP°P·PSPëPe PhC-P¶PSP°CTHPsPrPSPsPiPs PSPsCTHPjP°P»C-P·PsPIP°PSPsPiPs  
PIC-PrPSPsC€PμPSPSC¶ (PᄡPᄡP’).

P†PjCрPSPsCрCрPïCTHPμCрP°PSC,Pë (PSP°PïCTHPëPeP»P°Pr, C†PëPeP»PsCрPïPsCTHPëPS,  
C,P°PeCTHPsP»C-PjCрCр) вҒ“ CTHPëP·PëPe PSP°PrPjC-CTHPSPsPiPs PïCTHPëPiPSC-C†PμPSPSC¶  
C-PjCрPSPSPsC— CрPëCрC,PμPjPë P· CTHPëP·PëPePsPj CTHPsP·PIPëC,PeCр  
PïCTHPsP»C-C„PμCTHP°C†C-C— P»C-PjC„PsC†PëC,C-PI.

P’P»PsPeP°C,PsCTHPë PSPμPN₂CTHPsPjвҒ™ C¶P·PsPIPsC— PIP·P°C”PjPsPrC-C— вҒ“  
PSPμPjPsP¶P»PëPIPs PIPëPeP»CTHC†PëC,Pë PIP·P°C”PjPsPrC-CTH PjC-P¶  
C-CTHPëPSPsC,PμPeP°PSPsPj C,P° P±P»PsPeP°C,PsCTHP°PjPë PSPμPN₂CTHPsPjвҒ™ C¶P·PsPIPsC—  
PIP·P°C”PjPsPrC-C—. PhCрPeC-P»CHPePë C-CTHPëPSPsC,PμPeP°PS C†PëPSPëC,CH  
P°PSC,PëC...PsP»C-PSPμCрC,PμCTHP°P·PSCр PrC-CTH, PïCTHPμPïP°CTHP°C,Pë, C%Ps C,P°PePsP¶  
C†PëPSC¶C,CH P°PSC,PëC...PsP»C-PSPμCрC,PμCTHP°P·PSCр PrC-CTH, PjPsP¶CрC,CH  
P·P±C-P»CHC€CрPIP°C,Pë C,CTHPëPIP°P»C-CрC,CH PSPμPN₂CTHPsPjвҒ™ C¶P·PsPIPsPiPs

P±P»PsPeCíPíP°PSPSCİ CíCíPeCíP°PjPµC,PsPSC-Cİ C,P° PíCİPSc,PëPrC-CİC,Pë  
PSPµPNëCİPScPjPb™ CİP·PsPíPScPjCí P±P»PsPeCíPíP°PSPSCİ  
PSPµPrPµPíPScP»CİCİPëP·CíCİC±PëC... PíCİPµPíP°CİP°C,C-PI.

P†PSC€C- PePsPjP±C-PSP°C†C-C—.

5-PαPJ/PαPљ **БҘ**“ PsPrPSPSc±P°CíPSPµ P·P°CíC,PsCíCíPíP°PSPSCİ 5-PαPJ/PαPљ Cí  
CíPeP»P°PrC- PePsPjP±C-PSPsPíP°PSPSc— C,PµCİP°PíC-C— PSPµ P·PjC-PSCHC”  
C„P°CİPjP°PePsPeC-PSPµC,PëPeCí C-CİPëPSPSc,PµPeP°PSCí.

P·PµPíP°C†PëP·CíPjP°P± **БҘ**“ CİPµP·CíP»CHC,P°C,Pë CíPíPµC†PëC„C-C†PSPsPíPs  
PrPsCíP»C-PrP¶PµPSPSCİ PíP·P°C”PjPsPrC-C— PjC-P¶ P»C-PeP°CİCíCHPePëPjPë  
P·P°CíPScP±P°PjPë PSPµ PíCİPScPrPµPjPsPSCíC,CİCíPíP°P»Pë P·PSP°C†PSPsPíPs  
PíPíP»PëPíCí P±PµPíP°C†PëP·CíPjP°P±Cí PSP° C„P°CİPjP°PePsPeC-PSPµC,PëPeCí  
C-CİPëPSPSc,PµPeP°PSCí C,P° PNëPsPíPs P°PeC,PëPíPSPsPíPs PjPµC,P°P±PsP»C-C,Cí  
SN-38. PhPrPSP°Pe C†Pµ PSPµ PíPëPeP»CHC±P°C” P±CíPrCH-CİPePsPíPs  
PíC-PrPíPëC%PµPSPSCİ C,PsPeCíPëC†PSPScíC,C- PíPSP°CíP»C-PrPsPe  
C—C...PSC-C... C„P°CİPjP°PePsP»PsPíC-C†PSPëC... PíP»P°CíC,PëPíPScíC,PµPNë.

PíPµC,CíPeCíPëPjP°P± **БҘ**“ C-PSC„PsCİPjP°C†C-Cİ C%PsPrPs PíPíP»PëPíCí  
C†PµC,CíPeCíPëPjP°P±Cí PSP° PíCİPSc„C-P»CH P±PµP·PíPµC†PSPScíC,C-  
C-CİPëPSPSc,PµPeP°PSCí P°P±Ps PíCİPSc P°PSP°P»PsPíC-C†PSPëPNë PíPíP»PëPí  
C-CİPëPSPSc,PµPeP°PSCí PSP° C†PµC,CíPeCíPëPjP°P± PíC-PrCíCíC,PSCİ.

PhPSC,PëPSPµPsPíP»P°CíC,PëC†PSC- P·P°CíPScP±Pë (PíPeP»CHC±P°CHC±Pë  
C„P»CíC†PëC,PsP·PëPS CİPe PíCİPScP»C-PePë 5-C„C,PsCİCíCİP°C†PëP»Cí) **БҘ**“  
PíPsP±C-C†PSC- PµC„PµPeC,Pë C-CİPëPSPSc,PµPeP°PSCí, C,P°PeC- CİPe  
PjC-C”P»PsCíCíPíCİPµCíC-Cİ, PjPsP¶CíC,CH PíPScíPëP»CHPíP°C,PëCíCİ C-PSC€PëPjPë  
PíCİPSc,PëPíCíC...P»PëPSPSPëPjPë PíCİPµPíP°CİP°C,P°PjPë, C%Ps PjP°CHC,CH  
PíPsPrC-P±PSPëPNë PíCİPSc„C-P»CH PíPsP±C-C†PSPëC... PµC„PµPeC,C-PI.

**PhCíPScP±P»PëPíPScíC,C- P·P°CíC,PsCíCíPíP°PSPSCİ.**

P—P°CíC,PsCíPScPíCíPíP°C,Pë PíCİPµPíP°CİP°C, P†CİPëPSPSc,PµPeP°PS PhPjP°PeCíP°  
CíP»C-Pr PíPëPeP»CHC†PSPs Cí PíC-PrPrC-P»PµPSPSC-, C%Ps  
CíPíPµC†C-P°P»C-P·CíC”C,CHCíCİ PSP° PíCİPScPíPµPrPµPSPSC-  
C†PëC,PsC,PsPeCíPëC†PSPSc— C...C-PjC-PsC,PµCİP°PíC-C—. PµCİPµPíP°CİP°C, CíP»C-Pr  
P·P°CíC,PsCíPScPíCíPíP°C,Pë PíPëPeP»CHC†PSPs PíC-Pr PePsPSC,CİPScP»PµPj  
PePíP°P»C-C„C-PePsPíP°PSPsPíPs P»C-PeP°CİCİ, CİPePëPNë  
CíPíPµC†C-P°P»C-P·CíC”C,CHCíCİ PSP° PíCİPScPíPµPrPµPSPSC- PíCİPSc,PëCİP°PePsPíPScPíPs  
C...C-PjC-PsC,PµCİP°PíPµPíC,PëC†PSPsPíPs P»C-PeCíPíP°PSPSCİ.

P·CİP°C...PsPíCíCHC±Pë C...P°CİP°PeC,PµCİ C,P° C†P°CíC,PsC,Cí CİPScP·PíPëC,PeCí  
PíPsP±C-C†PSPëC... CİPµP°PeC†C-PNë, Cí PSPëP¶C†PµP·P°P·PSP°C†PµPSPëC...  
PíPëPíP°PrPeP°C... P†CİPëPSPSc,PµPeP°PS PhPjP°PeCíP° PSPµPsP±C...C-PrPSPs  
P·P°CíC,PsCíPScPíCíPíP°C,Pë P»PëC€Pµ PíC-CíP»Cİ PsC†C-PSPëPë  
CíPíC-PíPíC-PrPSPSc€PµPSPSCİ PsC†C-PeCíPíP°PSPSc— PePsCİPëCíC,C- C,P°

PjPsP¶P»PëPIPëC... C¶PëP·PëPeC-PI PIC-Pr P»C-PeCíPIP°PSPSC¶:

- PrP»C¶ P»C-PeCíPIP°PSPSC¶ PïP°C†C-C"°PSC,C-PI C-P· C„P°PeC,PsC¶P°PjPë C¶PëP·PëPeCí, P·PsPeC¶PµPjP° PïP°C†C-C"°PSC,C-PI C-P· PïPsPeP°P·PSPëPePsPj P·P°PiP°P»CHßPSPsPiPs C¶C,P°PSCí P·P° C-PSPrPµPeC¶PsPj P'PhPhP—, C%Ps PrPsC¶C-PIPSC¶C" 2;

- Cí PsPeC¶PµPjPëC... C¶C-PrPeC-C¶PSPëC... PIPëPïP°PrPeP°C..., PePsP»Pë PIPIP°P¶P°C,CßC¶C¶, C%Ps PïP°C†C-C"°PSC,Pë PSP°PIC¶C¶Pr C±Pë P±CíPrCíC,CH PrPsC,C¶PëPjCíPIP°C,PëC¶Cß C¶PµPePsPjPµPSPPr°C†C-PNë C%PsPrPs P»C-PeCíPIP°PSPSC¶ PïPsP±C-C±PSPëC... C¶PµP°PeC†C-PNë (PSPµPsP±C...C-PrPSC-C¶C,CHß PSPµPiP°PNëPSPsPiPs C,P° PrPsPIPiPsC,C¶PëPIP°P»PsPiPs P»C-PeCíPIP°PSPSC¶ PrC-P°C¶PµC— Cí PïPsC"PrPSP°PSPSC- P· PIP¶PëPIP°PSPSC¶Pj PIPµP»PëPePsC— PeC-P»CHßPePsC¶C,C- C¶C-PrPëPSPë PSP° PïPsC±P°C,PeCí PIC-PrC¶C,C¶PsC±PµPSPsC— PrC-P°C¶PµC—); C,P°PePëPj PïP°C†C-C"°PSC,P°Pj C¶PµPePsPjPµPSPPrCíC"°C,CßC¶C¶ C¶PµC,PµP»CHßPSPµ C¶PïPsC¶C,PµC¶PµP¶PµPSPSC¶ PI CíPjPsPIP°C... C¶C,P°C†C-PsPSP°C¶Cí.

PµC¶Pë P·P°C¶C,PsC¶CíPIP°PSPSC- C-C¶PëPSPsC,PµPeP°PSCí C¶Pe PjPsPSPsC,PµC¶P°PïC-C— PNëPsPiPs P·P°P·PIPëC±P°PNë PïC¶PëP·PSP°C±P°C¶C,CHß P·P° PïC¶P°C„C-PePsPj PrPsP·CíPIP°PSCß PePsP¶PSC- 3 C,PëP¶PSC-. PhPrPSP°Pe C¶C...PµPjCí PrPsP·CíPIP°PSPSC¶ 1 C¶P°P· PSP° C,PëP¶PrPµPSCß PjPsP¶PSP° PIPëPePsC¶PëC¶C,PsPICíPIP°C,Pë PïP°C†C-C"°PSC,P°Pj, C¶PePëPj PjPsP¶Pµ P·PSP°PrPsP±PëC,PëC¶C¶ P±C-P»CHßC¶ C¶PµC,PµP»CHßPSPµ C¶PïPsC¶C,PµC¶PµP¶PµPSPSC¶ P°P±Ps C¶PePëPj P·P°PïC¶PsP¶CíC" PsC¶PsP±P»PëPIP° PSPµP±PµP·PïPµPeP° PSPµPNëC,C¶PsPïPµPSC-C—.

P'C-PrC¶C,C¶PsC±PµPSP° PrC-P°C¶PµC¶.

PµP°C†C-C"°PSC,C-PI C¶P»C-Pr PïPsPIC-PrPsPjPëC,Pë PïC¶Ps C¶PëP·PëPe C¶PsP·PIPëC,PeCí PIC-PrC¶C,C¶PsC±PµPSPsC— PrC-P°C¶PµC—, C%Ps PIPëPSPëPeP°C" P±C-P»CHßC¶ PSC-P¶ C±PµC¶PµP· 24 PïPsPrPëPSPë PïC-C¶P»C¶ P·P°C¶C,PsC¶CíPIP°PSPSC¶ PïC¶PµPïP°C¶P°C,Cí P†C¶PëPSPsC,PµPeP°PS PhPjP°PeC¶P° C,P° Cí P±CíPrCß-C¶PePëPNë C±P°Cí PïPµC¶PµPr PSP°C¶C,CíPïPSPëPj PeCíC¶C¶PsPj P»C-PeCíPIP°PSPSC¶. PµC¶Pë PjPsPSPsC,PµC¶P°PïC-C— PjPµPrC-P°PSP° C¶PsP·PIPëC,PeCí PïPµC¶C¶PsPiPs PµPïC-P·PsPrCí C¶C-PrPePëC... PIPëPïPsC¶PsP¶PSPµPSCß C¶C,P°PSPsPIPëP»P° 5 PrPSC-PI P· PjPsPjPµPSC,Cí PIPIPµPrPµPSPSC¶ PïC¶PµPïP°C¶P°C,Cí P†C¶PëPSPsC,PµPeP°PS PhPjP°PeC¶P°. PµP°C†C-C"°PSC,Pë PïPsPIPëPSPSC- PSPµ P·PIPsP»C-PeP°C¶C±Pë PïPsPIC-PrPsPjPëC,Pë P»C-PeP°C¶Cß PïC¶Ps C¶PsP·PIPëC,PsPe PrC-P°C¶PµC— C,P° PSPµPiP°PNëPSPs C¶PsP·PïPsC±P°C,Pë PIC-PrPïPsPIC-PrPSCí C,PµC¶P°PïC-Cß.

P"Ps PïC¶CíPïPë PïC-PrPIPëC%PµPSPsPiPs C¶PëP·PëPeCí C¶PsP·PIPëC,PeCí PrC-P°C¶PµC— PSP°P»PµP¶P°C,CHß PïP°C†C-C"°PSC,Pë, C¶PeC- C¶P°PSC-C¶Pµ PsC,C¶PëPjCíPIP°P»Pë PïC¶PsPjPµPSPµPICí C,PµC¶P°PïC-Cß P·PsPSPë P¶PëPIPsC,P° P°P±Ps C,P°P·P°, PïP°C†C-C"°PSC,Pë, Cí C¶PePëC... PSP° PIPëC...C-PrPSPsPjCí C¶C-PIPSC- PSP°C¶IPSPëPNë PïC-PïPµC¶P»PµPNëPePsC†PëC,PsP·, PïP°C†C-C"°PSC,Pë P·

C-PSPPrPμPeCfPsPj CfC,P°PSCr P·PrPsCfPsPIBf™ Cμ P·P° C€PeP°P»PsCf P'PhPhP— ≥ 2  
C,P° P¶C-PSPePë. P—P° PIC-PrCfCrC,PSpScfC,C- PSp°P»PμP¶PSPsPiPs P»C-PeCfPIP°PSPSCμ  
PrC-P°CfPμCμ PjPsP¶Pμ CfC,P°PSPsPiPëC,Pë P·P°PiCfPsP·Cr PrP»Cμ P¶PëC,C,Cμ,  
PsCfPsP±P»PëPIPs CμPeC%Ps PIPsPSP° CfCrPiCfPsPIPsPrP¶CfC"C,ChCfCμ  
PSPμPNëC,CfPsPiPμPSC-C"Cf.

PμC-CfP»Cμ PiPμCfC€PsPiPs PμPiC-P·PsPrCr CfC-PrPePëC...  
PIPëPiPsCfPsP¶PSPμPSCf PiP°C†C-C"PSC,Cr CfP»C-Pr PSPμPiP°PNëPSPs  
CfPsP·PiPsC†PëPSP°C,Pë PiCfPëPNëPsPj PIPμP»PëPePsC— PeC-P»ChPePsCfC,C-  
CfC-PrPëPSPë, C%Ps PjC-CfC,PëC,Ch PμP»PμPeC,CfPsP»C-C,Pë, C,P°  
PiCfPsPIPsPrPëC,Pë PIC-PrPiPsPIC-PrPSPμ PiCfPsC,PëPrC-P°CfPμPNëPSPμ  
P»C-PeCfPIP°PSPSCμ. PμCfPsPIPsPrPëC,Pë PiCfPsC,PëPrC-P°CfPμPNëPSPμ  
P»C-PeCfPIP°PSPSCμ PSPμPsP±C...C-PrPSPs Cr PIC-PrPrC-P»PμPSPSC-, PrPμ  
PiP°C†C-C"PSC,Cr PIPsPrPëP»Pë P†CfPëPSPsC,PμPeP°PS PhPjP°PeCfP°. PμC-CfP»Cμ  
PIPëPiPëCfPePë P· P»C-PeP°CfPSC- PiP°C†C-C"PSC,Cr CfP»C-Pr PsC,CfPëPjP°C,Pë  
PiCfPëP·PSP°C†PμPSC- PiCfPμPiP°CfP°C,Pë, C%PsP± PjP°C,Pë PjPsP¶P»PëPIC-CfC,Ch  
PiPsC†P°C,Pë P»C-PeCfPIP°PSPSCμ PrC-P°CfPμC— PsPrCfP°P·Cr PiC-CfP»Cμ C—C—  
PIPëPSPëPePSPμPSPSCμ. PμCfC-Pj C,PsPiPs, PiP°C†C-C"PSC, PiPsPiPëPSPμPS  
PiPsPIC-PrPsPjPëC,Pë PiCfPs PIPëPSPëPePSPμPSPSCμ PrC-P°CfPμC— CfPIPsC"PjCr  
P»C-PeP°CfCf P°P±Ps P»C-PeP°CfCf PIC-PrPrC-P»PμPSPSCμ, PI CμPePsPjCr  
PiP°C†C-C"PSC,Cr PIPsPrPëP»Pë P†CfPëPSPsC,PμPeP°PS PhPjP°PeCfP°.

P PμPePsPjPμPSPPrPsPIP°PSPμ PSP° CfChPsPiPsPrPSC- PiCfPsC,PëPrC-P°CfPμPNëPSPμ  
P»C-PeCfPIP°PSPSCμ PiPsP»CμPiP°C" Cr P·P°CfC,PsCfCrPIP°PSPSC- PIPμP»PëPePëC...  
PrPsP· P»PsPiPμCfP°PjC-PrCr (4 PjPi PSP° PiPμCfC€Pμ P·P°CfC,PsCfCrPIP°PSPSCμ,  
PiPsC,C-Pj PiPs 2 PjPi C†PμCfPμP· PePsP¶PSC- 2 PiPsPrPëPSPë). P»C-PeCfPIP°PSPSCμ  
CfP»C-Pr PiCfPsPIPsPrPëC,Pë PiCfPsC,CμPiPsPj 12 PiPsPrPëPS PiC-CfP»Cμ  
PsCfC,P°PSPSCHPsPiPs PμPiC-P·PsPrCr CfC-PrPePëC... PIPëPiPsCfPsP¶PSPμPSCf.  
PŸC...PμPjP° P»C-PeCfPIP°PSPSCμ PSPμ PiC-PrP»CμPiP°C" PjPsPrPëC,,C-PeP°C†C-CμPj.  
P»PsPiPμCfP°PjC-Pr Cr C,P°PePëC... PrPsP·P°C... PSC- PI CμPePsPjCr CfP°P·C- PSPμ  
CfP»C-Pr P·P°CfC,PsCfPsPICrPIP°C,Pë PrPsPIC€Pμ PSC-P¶ 48 PiPsPrPëPS Cr  
P·PIBf™ CμP·PeCf P· CfPëP·PëPePsPj CfPsP·PIPëC,PeCf PiP°CfP°P»C-C,PëC†PSPsC—  
PePëC€PePsPIPsC— PSPμPiCfPsC...C-PrPSPsCfC,C-; PIPsPrPSPsC†P°Cf  
P»C-PeCfPIP°PSPSCμ PSPμ PiPsPiPëPSPSPs C,CfPëPiP°C,Pë PjPμPSC€Pμ PSC-P¶ 12  
PiPsPrPëPS.

Pj CfP°P·C-, PePsP»Pë PrC-P°CfPμCμ CfCrPiCfPsPIPsPrP¶CfC"C,ChCfCμ  
C,CμP¶PePsCf PSPμPNëC,CfPsPiPμPSC-C"Cf (PeC-P»ChPeC-CfC,Ch  
PSPμPNëC,CfPsC,,C-P»C-PI PSPëP¶C†Pμ B B B B B B B B B B 500  
PeP»C-C,PëPS/PjPj³), PrPsPrP°C,PePsPIPs PrPs PiCfPsC,PëPrC-P°CfPμPNëPSPsPiPs  
P»C-PeCfPIP°PSPSCμ CfP»C-Pr P· PiCfPsC,,C-P»P°PeC,PëC†PSPsCf PjPμC,PsCf  
P·P°CfC,PsCfPsPICrPIP°C,Pë P°PSC,PëP±C-PsC,PëPePë C€PëCfPsPePsPiPs  
CfPiPμPeC,CfP° PrC-C—.

P"PsPrP°C,PePsPIPs PrPs P·P°CfC,PsCfCrPIP°PSPSCμ P°PSC,PëP±C-PsC,PëPeC-PI  
PrP»Cμ P»C-PeCfPIP°PSPSCμ PrC-P°CfPμC— CfPμPePsPjPμPSPPrPsPIP°PSPs  
PiPsCfPiC-C,P°P»C-P·CfPIP°C,Pë PiP°C†C-C"PSC,C-PI Cr C,P°PePëC...  
PIPëPiP°PrPeP°C...:

РѹСѢСсС,СІІРІсРј Р»С-РєСрРІР°РSPSCІІ РїСѢРѹРїР°СѢР°С,РсРј Р†СѢРѢSPsС,РѹРєР°РSP  
РђРјР°Р°Р°СІР°СѢРѹРєРсРјРѹРSPР°РсРІР°РSPs С%РсС,РѢР¶РSPSCІІ РєРсРSPC,СѢРсР»СѢРІР°С,РѢ  
РїРсРєР°Р°РSPѢРєРѢ РєР»С-РSC-С†РSPsРїРс Р°РSP°Р»С-Р°Ср РєСѢРсРІС-. РѹР°С†С-С"РSC,С-РІ  
СІР°С»С-Рр РїРсРїРѹСѢРѹРрР¶Р°С,РѢ РїСѢРс СѢРѢР°РѢРє СѢРсР°РІѢС,РєСр  
РSPРѹР№С,СѢРсРїРѹРSPC-С— С,Р° РїСѢРс Р°РSP°С†СрС%С-СІС,Сђ РїР°СѢСІС†РєРѢ.  
РќРѹРсР±С...С-РрSPs РSPРїР°РР№РSPs СѢРсР°РїРсС†РѢРSP°С,РѢ Р»С-РєСрРІР°РSPSCІІ  
С,,РѹР±СѢРѢР»СђРSPs— РSPРѹР№С,СѢРсРїРѹРSPC-С— (С,РѹРјРјРїРѹСѢР°С,СрСѢР° >38 В°С С,Р°  
РєС-Р»СђРєС-СІС,Сђ РSPРѹР№С,СѢРсС,,С-Р»С-РІ ≤1000 РєР»С-С,РѢРSP/РјРј<sup>3</sup>) РІ СрРјРсРІР°С...  
СІС,Р°С†С-РсРSP°СѢСр Р° РІРSCрС,СѢС-СєРSCђРсРІРѹРSPSPѢРј РІРІРѹРрРѹРSPSCІІРј  
Р°РSPC,РѢР±С-РсС,РѢРєС-РІ СєРѢСѢРсРєРсРїРс СІРїРѹРєС,СѢР° РрС-С—. РѹР°С†С-С"РSC,Р°Рј  
Р° СрСІРєР»Р°Р°Р°Р°Р°Р°РSPРSPSCІІРјРѢ С,СІІР¶РєРсРїРс СІС,СрРїРѹРSPCІІ Р° Р±РсРєСр  
СІРѢСІС,РѹРјРѢ РєСѢРсРІС- СѢРѹРєРсРјРѹРSPР°РсРІР°РSPs Р°РSPѢР°РѢС,РѢ РрРсР°Ср РІ  
РїРсРрР°Р»СђСєРѢС... С†РѢРєР»Р°Р°С... Р»С-РєСрРІР°РSPSCІІ (РрРѢРІ. СѢРсР°РрС-Р»  
В«РЎРїРсСІС-Р± Р°СІС,РсСІСрРІР°РSPSCІІ С,Р° РрРсР°РѢВ»). Рј РїР°С†С-С"РSC,С-РІ  
Р° РрС-Р°СѢРѹС"Сђ С,СІІР¶РєРсРїРс СІС,СрРїРѹРSPCІІ РїС-РрРІѢС%СрС"С,СђСІСІІ

$\text{P}_{\mu}\text{P}^{\circ}\text{C}^{\dagger}\text{C}-\text{C}^{\prime\prime}\text{PSC}, \text{P}^{\circ}\text{P}_{\text{j}} \text{C}-\text{P} \cdot \text{C}\overline{\text{H}}\text{C}-\text{PIPSP}_{\mu}\text{P}_{\text{j}} \text{P}^{\pm}\text{C}-\text{P} \gg \text{C}-\text{C}\overline{\text{H}}\text{C}^{\dagger}\text{P}^{\pm}\text{C}-\text{PSC}^{\dagger} \text{PIP}\ddot{\text{C}}\%_{\text{P}_{\mu}}$   
 $\text{PIP}_{\mu}\text{C}\overline{\text{H}}\text{C} \dots \text{PSC}\overline{\text{H}}\text{PsC}-\text{P}_{\text{j}}\text{P}_{\mu}\text{P}^{\dagger}\text{C}-\text{PSPsC}\overline{\text{H}}\text{P}_{\text{j}}\text{P}\ddot{\text{C}} \text{C}^{\dagger} 1,5\text{B}\overline{\text{H}}^{\circ} 3 \text{C}\overline{\text{H}}\text{P}^{\circ}\text{P} \cdot \text{P}\ddot{\text{C}} \text{C}^{\dagger}\text{P} \gg \text{C}-\text{Pr}$   
 $\text{C}\%_{\text{PsC}}, \text{P}\ddot{\text{C}}\text{P}^{\dagger}\text{PSC}\overline{\text{H}} \text{PePsPSC}, \text{C}\overline{\text{H}}\text{PsP} \gg \text{C}\overline{\text{H}}\text{PIP}^{\circ}\text{C}, \text{P}\ddot{\text{C}} \text{P}\ddot{\text{C}}\text{PsPeP}^{\circ}\text{P} \cdot \text{PSP}\ddot{\text{C}}\text{PeP}\ddot{\text{C}} \text{PeP} \gg \text{C}-\text{PSC}-\text{C}\ddagger\text{PSPsPiPs}$   
 $\text{P}^{\circ}\text{PSP}^{\circ}\text{P} \gg \text{C}-\text{P} \cdot \text{C}^{\dagger} \text{PeC}\overline{\text{H}}\text{PsPIC}-\text{C}^{\dagger} \text{P} \cdot \text{P}\overline{\text{I}}\text{B}\overline{\text{H}}^{\text{TM}} \text{C}\overline{\text{H}}\text{P} \cdot \text{PeC}^{\dagger} \text{P} \cdot \text{C}-\text{P} \cdot \text{PSP}\ddot{\text{C}}\text{P}^{\dagger}\text{P}_{\mu}\text{PSPSC}\overline{\text{H}}\text{P}_{\text{j}}$   
 $\text{PeP} \gg \text{C}-\text{C}\overline{\text{H}}\text{P}_{\mu}\text{PSC}^{\dagger}\text{C}^{\dagger} \text{C}-\text{C}\overline{\text{H}}\text{P}\ddot{\text{C}}\text{PSPsC}, \text{P}_{\mu}\text{PeP}^{\circ}\text{PSC}^{\dagger} (\text{PrP}\ddot{\text{C}}\text{PI}, \text{C}\overline{\text{H}}\text{PsP} \cdot \text{PrC}-\text{P} \gg$   
 $\text{B} \ll \text{P}\overline{\alpha}\text{P}^{\circ}\text{C}\overline{\text{H}}\text{P}_{\text{j}}\text{P}^{\circ}\text{PePsPeC}-\text{PSP}_{\mu}\text{C}, \text{P}\ddot{\text{C}}\text{PeP}^{\circ}\text{B} \gg), \text{C}\%_{\text{Ps}} \text{P}\ddot{\text{C}}-\text{PrPIP}\ddot{\text{C}}\%_{\text{C}^{\dagger}}\text{C}^{\prime\prime} \text{C}\overline{\text{H}}\text{P}\ddot{\text{C}}\text{P} \cdot \text{P}\ddot{\text{C}}\text{Pe}$

PiPμPjP°C,PsC,PsPeCíPëC±PSPsCíC,C-. PkPμ CíP»C-Pr PIPiPsPrPëC,Pë P†CĤPëPSPsC,PμPeP°PS PĥPjP°PeCíP° PíP°C†C-C”PSC,P°Pj C-P· CĤC-PIPSpμPj P±C-P»C-CĤCíP±C-PSCí PIPëC%Pμ PIPμCĤC...PSCĤPsC— PjPμP¶C- PSPsCĤPjPë P±C-P»CHC€ PSC-P¶ Cí 3 CĤP°P·Pë (PrPëPI. CĤPsP·PrC-P» B«PμCĤPsC,PëPíPsPeP°P·P°PSPSCİB»).

PkCzPrPsC,P° C,P° P±P»CĤPIP°PSPSCİ.

PμPμCĤPμPr PePsP¶PSPëPj PIPiPμPrPμPSPSCİPj P»C-PeP°CĤCíCĤPePsPiPs P·P°CíPsP±Cí P†CĤPëPSPsC,PμPeP°PS PĥPjP°PeCíP° CĤPμPePsPjPμPSPPrCíC”C,CHCíCİ P· PíCĤPsC,,C-P»P°PeC,PëC±PSPsCĤ PjPμC,PsCĤ P·P°CíC,PsCíPsPICíPIP°C,Pë PíCĤPsC,PëP±P»CĤPIP°P»CHPSC- PíCĤPμPíP°CĤP°C,Pë. PμCĤPë P·P°CíC,PsCíCíPIP°PSPSC- PíCĤPμPíP°CĤP°C,Cí C±P°CíC,Ps PíPsPIC-PrPsPjP»CİP»PsCíCİ PíCĤPs PIPëPSPëPePSPμPSPSCİ PSCíPrPsC,Pë C,P° P±P»CĤPIP°PSPSCİ. PμP°C†C-C”PSC,Pë P· P±P»CĤPIP°PSPSCİPj, C%Ps CíCíPíCĤPsPiPsPrP¶CíC”C,CHCíCİ PIC-PrCíC,CĤPsC±PμPSPsCĤ PrC-P°CĤPμC”CĤ, PíPsC,CĤPμP±CíCĤC,CH PiPsCíPíC-C,P°P»C-P·P°C†C-C— Cí PSP°PNPePsCĤPsC,C€PëPN C,PμCĤPjC-PS PrP»Cİ PíCĤPsPiPμPrPμPSPSCİ PSP°P»PμP¶PSPsPiPs P»C-PeCíPIP°PSPSCİ.

P”PsCíC,CĤPëPN C...PsP»C-PSPμCĤPiC-C±PSPëPN CíPëPSPPrCĤPsPj.

P—P° PIC-PrCíCíC,PSPsCíC,C- PeP»C-PSC-C±PSPëC... PíCĤPsC,PëPíPsPeP°P·P°PSCĤ (PrPëPI. CĤPsP·PrC-P» B«PμPsP±C-C±PSC- CĤPμP°PeC†C-C—B») Cí CĤP°P·C- CĤPsP·PIPëC,PeCí PiPsCíC,CĤPsPiPs C...PsP»C-PSPμCĤPiC-C±PSPsPiPs CíPëPSPPrCĤPsPjCí (CĤP°PSPSCİ PrC-P°CĤPμCİ Cí PePsPjP±C-PSP°C†C-C— P· CĤC-P·PSPsPjP°PSC-C,PSPëPjPë C-PSC€PëPjPë PsP·PSP°PeP°PjPë C,P° CíPëPjPíC,PsPjP°PjPë, C,P°PePëPjPë CİPe PíC-PrPIPëC%PμPSP° PíC-C,P»PëPIC-CíC,CH, CíPíP°P·PjPë Cí P¶PëPIPsC,C-, PjC-PsP· C,P° PíC-PrPIPëC%PμPSPμ CíP»PëPSPsPiPëPrC-P»PμPSPSCİ) CíP»C-Pr PIPiPsPrPëC,Pë 0,25 PjPi P°C,CĤPsPiC-PSCí CíCíP»CHC,,P°C,Cí PíC-PrC€PeC-CĤPSPs. PμPsCİPICí C†PëC... CíPëPjPíC,PsPjC-PI, CİPeC- PjPsP¶CíC,CH CíPíPsCíC,PμCĤC-PiP°C,PëCíCİ PíCĤPsC,CİPiPsPj P°P±Ps PsPrCĤP°P·Cí PíC-CíP»Cİ C-PSC,,CíP·C-C— C-CĤPëPSPsC,PμPeP°PSCí, PíPsPIbĤ™ CİP·CíCĤC,CH P· P°PSC,PëC...PsP»C-PSPμCíC,PμCĤP°P·PSPsCĤ P°PeC,PëPIPSC-CíC,CĤ PíPsC±P°C,PePsPiPsC— CíPíPsP»CíPePë C-CĤPëPSPsC,PμPeP°PSCí. PμPμCĤPμPrP±P°C±P°C”C,CHCíCİ, C%Ps PíCĤPë P·P°CíC,PsCíCíPIP°PSPSC- P±C-P»CHC€ PIPëCíPsPePëC... PrPsP· C-CĤPëPSPsC,PμPeP°PSCí C±P°CíC,PsC,P° C—C... PIPëPSPëPePSPμPSPSCİ P·CĤPsCíC,P°C,PëPjPμ.

P>C-PeCíPIP°C,Pë PíP°C†C-C”PSC,C-PI P· P°CíC,PjPsCĤ CíP»C-Pr P· PsP±PμCĤPμP¶PSC-CíC,CĤ. PμP°C†C-C”PSC,P°Pj C-P· PiPsCíC,CĤPëPj C...PsP»C-PSPμCĤPiC-C±PSPëPj CíPëPSPPrCĤPsPjPj C,CİP¶PePsPiPs CíC,CíPíPμPSCİ PíPμCĤPμPr PePsP¶PSPëPj PSP°CíC,CíPíPSPëPj P·P°CíC,PsCíCíPIP°PSPSCİPj PíCĤPμPíP°CĤP°C,Cí P†CĤPëPSPsC,PμPeP°PS PĥPjP°PeCíP° CĤPμPePsPjPμPSPPrPsPIP°PSPs PíCĤPsPiPsPrPëC,Pë PíCĤPsC,,C-P»P°PeC,PëC±PSPμ P»C-PeCíPIP°PSPSCİ P°C,CĤPsPíC-PSCí CíCíP»CHC,,P°C,PsPj.

P PsP·P»P°PrPë P· P±PsPeCz PrPëC...P°P»CHPSPsC— CíPëCíC,PμPjPë.

PμC-Pr C±P°Cí P»C-PeCíPIP°PSPSCİ PrP°PSPëPj PíCĤPμPíP°CĤP°C,PsPj PjPsP¶P»PëPIC- PSPμC±P°CíC,C- PIPëPíP°PrPePë CĤPsP·PIPëC,PeCí C-PSC,PμCĤCíC,PëC†C-P°P»CHPSPsC— C...PIPsCĤPsP±Pë P»PμPiPμPSC-PI, C%Ps PíCĤPsCİPIP»CİC”C,CHCíCİ Cí PIPëPiP»CİPrC- CíC,PIPsCĤPμPSPSCİ C-PSC,,C-P»CHC,CĤP°C,C-PI Cí P»PμPiPμPSCİC..., P°P»Pμ P·P°C...PIPsCĤCĤPIP°PSPSCİ PjPsP¶Pμ PíCĤPëP·PIPsPrPëC,Pë PrPs P»PμC,P°P»CHPSPsPiPs PSP°CíP»C-PrPeCí. P”Ps C,,P°PeC,PsCĤC-PI CĤPëP·PëPeCí, PjPsP¶P»PëPIPs PíPsPIbĤ™ CİP·P°PSPëC... C-P· CĤPsP·PIPëC,PePsPj C-PSC,PμCĤCíC,PëC†C-P°P»CHPSPsC—

C...PIPsCḡPsP±Pë P»PµPiPµPSC-PI, PIC-PrPSPsCíCḡC,CH P·P°CíC,PsCíCíPIP°PSPSCḡ  
PíCḡPµPíP°CḡP°C,C-PI, C,PsPeCíPëC±PSPëC... C%PsPrPs P»PµPiPµPSC-PI, PíCḡPsPjPµPSPµPICí  
C,PµCḡP°PíC-Cḡ C,P° PePsP»PsPSC-C"íC,PëPjCíP»CḡCḡC±C- C,,P°PeC,PsCḡPë. P—P°  
PíP°CíC-C"PS C,P°PjPë P·PSP°CḡPIPSPëPjPë C,,P°PeC,PsCḡP°PjPë CḡPëP·PëPeCí PrPs  
PíPsC±P°C,PeCí C,P° PíC-Pr C±P°Cí P»C-PeCíPIP°PSPSCḡ CíP»C-Pr CḡPµC,PµP»CHPSPs  
CíPíPsCíC,PµCḡC-PíP°C,Pë C%PsPrPs PIPëPSPëPePSPµPSPSCḡ CíPëPjPíC,PsPjC-PI P·  
P±PsPeCí PrPëC...P°P»CHPSPsC— CíPëCíC,PµPjPë.

P·PeCíC,CḡP°PIP°P·P°CíC-Cḡ.

PíPsC±P° C-CḡPëPSPsC,PµPeP°PS PSPµ PSP°P»PµPḡPëC,CH PrPs  
PíCḡPµPíP°CḡP°C,C-PI, C%Ps PíCḡPëP·PIPsPrCḡC,CH PrPs CíC,PIPsCḡPµPSPSCḡ  
PSPµPeCḡPsP·Cí C,PeP°PSPëPS, PíCḡPµPíP°CḡP°C, CíP»C-Pr PIPsPrPëC,Pë P·  
PsP±PµCḡPµPḡPSC-CíC,Cḡ C,P° PePsPSC,CḡPsP»CḡPIP°C,Pë CíC,P°PS PjC-CíCíCḡ  
C-PSC,,CíP·C-C— C%PsPrPs PsP·PSP°Pe P·P°PíP°P»PµPSPSCḡ. Pj PIPëPíP°PrPeCí  
PíPsC,CḡP°PíP»CḡPSPSCḡ PíCḡPµPíP°CḡP°C,Cí P·P° PjPµPḡC- CíCíPrPëPSPë  
CḡPµPePsPjPµPSPPrPsPIP°PSPs PíCḡPsPjPëC,Pë PjC-CíCíPµ C-PSC,,CíP·C-C— C,P°  
PíCḡPëPeP»P°CíC,Pë P»C-Pr.

PµP°CíC-C"PS C,Pë P»C-C,PSCHPsPiPs PIC-PeCé.

Pj P·PIBḡ™ CḡP·PeCí P· P±C-P»CHCéPsCḡ C±P°CíC,PsC,PsCḡ P·PSPëPḡPµPSPSCḡ  
P±C-PsP»PsPíC-C±PSPëC... C,,CíPSPeCíC-PNḡ, P·PsPeCḡPµPjP° C,,CíPSPeCíC-C—  
PíPµC±C-PSPePë, PíP°CíC-C"PS C,P°Pj P»C-C,PSCHPsPiPs PIC-PeCí PrPsP·Cí  
PíCḡPµPíP°CḡP°C,Cí PíCḡPëPSPsC,PµPeP°PS PḡPjP°PeCíP° CíP»C-Pr PíC-PrP±PëCḡP°C,Pë P·  
PsP±PµCḡPµPḡPSC-CíC,Cḡ (PrPëPI. CḡPsP·PrC-P» B«PḡPíPsCíC-P±  
P·P°CíC,PsCíCíPIP°PSPSCḡ C,P° PrPsP·PëB»).

PíCḡPsPSC-C±PSC- P·P°PíP°P»CHPSC- P·P°C...PIPsCḡCḡPIP°PSPSCḡ PePëCéPµC±PSPëPeCé  
C,P°/P°P±Ps PsP±CíC,CḡCéPeCíC-Cḡ PePëCéPµC±PSPëPeCé.

PµP°CíC-C"PS C,P°Pj PSPµ CíP»C-Pr P·P°CíC,PsCíCíPIP°C,Pë PíCḡPëPSPsC,PµPeP°PS  
PḡPjP°PeCíP° PrPsPePë PSP°CḡPIPSP° PsP±CíC,CḡCíPeCíC-Cḡ PePëCéPµC±PSPëPeCí (PrPëPI.  
CḡPsP·PrC-P» B«PµCḡPsC,PëPíPsPeP°P·P°PSPSCḡB»).

PµP°CíC-C"PS C,Pë P· PíPsCḡCéCéPµPSPSCḡPjPë C,,CéPSPeCíC-C— PSPëCḡPsPe.

PḡPíPsCíC,PµCḡC-PíP°P»PsCíCḡ PíC-PrPIPëC%PµPSPSCḡ CḡC-PIPSḡ  
CíPëCḡPsPIP°C,PePsPIPsPiPs PeCḡPµP°C,PëPSC-PSCí P°P±Ps P°P·PsC,Cí CíPµC±PsPIPëPSPë  
PeCḡPsPIC-. P' CíP»Pë PIPëPíP°PrPePë PíPsCíC,CḡPsC— PSPëCḡPePsPIPsC—  
PSPµPrPsCíC,P°C,PSPsCíC,C-. PíC- CḡPIPëC%P° P·P°P·PIPëC±P°PNḡ P±CíP»Pë  
PíPsPIBḡ™ CḡP·P°PSC- P· CíCíPeP»P°PrPSPµPSPSCḡPjPë C-PSC,,PµPeCíC-PNḡ P°P±Ps  
P·PSPµPIPsPrPSPµPSPSCḡPj PsCḡPíP°PSC-P·PjCí PIPSP°CíP»C-PrPsPe PSCíPrPsC,Pë,  
P±P»CḡPIP°PSPSCḡ C±Pë PrC-P°CḡPµC—. PḡCḡC-Pj C,PsPiPs, PSP°PrC...PsPrPëP»Pë  
PíPsPIC-PrPsPjP»PµPSPSCḡ PíCḡPs PíPsPsPrPëPSPsPeC- PIPëPíP°PrPePë PíPsCḡCíCéPµPSPSCḡ  
C,,CíPSPeCíC-C— PSPëCḡPsPe PIPSP°CíP»C-PrPsPe CíPëPSPPrCḡPsPjCí P»C-P·PëCíCí  
PíCíC...P»PëPSPë.

P PsP·P»P°PrPë P· P±PsPeCé CíPµCḡCíCḡ.

PµC-CíP»Cḡ P·P°CíC,PsCíCíPIP°PSPSCḡ C-CḡPëPSPsC,PµPeP°PSCí  
CíPíPsCíC,PµCḡC-PíP°P»PëCíCḡ PIPëPíP°PrPePë CḡPsP·PIPëC,PeCí C-CéPµPjC-C—

PjC-PsPeP°CḡPrP°, PiPμCḡPμPIP°P¶PSPs Cr PiP°C†C-C''PSC,C-PI C-P· PSP°C¶PIPSpPjPjPë  
P·P°C...PIPsCḡCḡPIP°PSPSC¶PjPë CḡPμCḡC†C¶, C-PSC€PëPjPë PIC-PrPsPjPëPjPë  
C,,P°PeC,PsCḡP°PjPë CḡPëP·PëPeCr CḡPsP·PIPëC,PeCr P·P°C...PIPsCḡCḡPIP°PSCḡ  
CḡPμCḡC†C¶ C,P° Cr PiP°C†C-C''PSC,C-PI, C¶PeC- CḡP°PSC-C€Pμ PsC,CḡPëPjC†PIP°P»Pë  
C†PëC,PsC,PsPeCḡPëC†PSCr C...C-PjC-PsC,PμCḡP°PiC-Cḡ (PrPëPI. CḡPsP·PrC-P»  
B«PμPsP±C-C†PSC- CḡPμP°PeC†C-C-B»). P'C-PrPiPsPIC-PrPSPs, PiP°C†C-C''PSC,Pë P·  
PIC-PrPsPjPëPjPë C,,P°PeC,PsCḡP°PjPë CḡPëP·PëPeCr PiPsC,CḡPμP±CrCḡC,CH  
CḡPμC,PμP»CHPSPsPiPs PSP°PiP»C¶PIPrCr. PŸP»C-Pr PIP¶PëC,Pë P·P°C...PsPrC-PI PrP»C¶  
P·PIPμPrPμPSPSC¶ PrPs PjC-PSC-PjC†PjC† PIC†C-C... C,,P°PeC,PsCḡC-PI CḡPëP·PëPeCr, C%Ps  
PiC-PrPrP°CḡC,CHCḡC¶ CḡPμPiC†P»CḡPIP°PSPSCḡ (PSP°PiCḡPëPeP»P°Pr, PiP°P»C-PSPSC¶,  
P°CḡC,PμCḡC-P°P»CHPSP° PiC-PiPμCḡC,PμPSP·C-C¶ C,P° PiC-PiPμCḡP»C-PiC-PrPμPjC-C¶).

P PsP·P»P°PrPë P· P±PsPeCé CḡCéPrPëPS.

PJ PiP°C†C-C''PSC,C-PI, C¶PeC- PjP°P»Pë PjPSPsP¶PëPSPSC- C,,P°PeC,PsCḡPë CḡPëP·PëPeCr  
PSP° PrPsPrP°C,PsPe PrPs PsCḡPSPsPIPSPsPiPs PSPsPIPSCrC,PIPsCḡPμPSPSC¶,  
P·P°CḡC,PsCḡC†PIP°PSPSC¶ C-CḡPëPSPsC,PμPeP°PSCr PI CḡC-PrPeC-CḡPSPëC...  
PIPëPiP°PrPeP°C... PiPsPiBḡ™ C¶P·CrPIP°P»Pë P· PIPëPSPëPePSPμPSPSC¶Pj  
C,CḡPsPjP±PsPμPjP±PsP»C-C†PSPëC... CrCḡPeP»P°PrPSPμPSCḡ (P»PμPiPμPSPμPIP°  
PμPjP±PsP»C-C¶, PIPμPSPsP·PSPëPμ C,CḡPsPjP±PsP· C,P° P°CḡC,PμCḡC-P°P»CHPSP°  
C,CḡPsPjP±PsPμPjP±PsP»C-C¶).

PμCḡPsPjPμPSPμPIP° C,PμCḡP°PiC-C¶.

PμP°C†C-C''PSC,Pë, C¶PeC- CḡP°PSC-C€Pμ PsC,CḡPëPjC†PIP°P»Pë PsPiCḡPsPjC-PSPμPSPSC¶  
PsCḡPIP°PSC-PI PjP°P»PsPiPs C,P°P·P° P°P±Ps C†PμCḡPμPIPSPsC— PiPsCḡPsP¶PSPëPSPë,  
PIC...PsPrC¶C,CH PrPs PiCḡC†PiPë PiC-PrPIPëC%PμPSPsPiPs CḡPëP·PëPeCr CḡPsP·PIPëC,PeCr  
PjC-C''P»PsCḡC†PiCḡPμCḡC-C— PSP° C,P»C- P»C-PeCrPIP°PSPSC¶ C-CḡPëPSPsC,PμPeP°PSPsPj.  
P>C-PeP°CḡC- PjP°CḡC,CH P· PsP±PμCḡPμP¶PSC-CḡC,Cḡ P·P°CḡC,PsCḡPsPIC†PIP°C,Pë  
PrP°PSPëPμ P»C-PeP°CḡCḡCHPePëPμ P·P°CḡC-P± PiP°C†C-C''PSC,P°Pj, C¶PeC- PI  
PjPëPSCrP»PsPjC† PsC,CḡPëPjC†PIP°P»Pë PμPeCḡC,PμPSCḡPëPIPSCr PiCḡPsPjPμPSPμPICr  
C,PμCḡP°PiC-Cḡ (PSP°PiCḡPëPeP»P°Pr, PsPiCḡPsPjC-PSPμPSPSC¶ > 25 %  
PeC-CḡC,PePsPIPsPiPs PjPsP·PeCr PiCḡPsC,C¶PiPsPj 6 C,PëP¶PSC-PI PrPs PiPsC†P°C,PeCr  
P»C-PeCrPIP°PSPSC¶ C-CḡPëPSPsC,PμPeP°PSPsPj). P|C-Pμ PiCḡC†PiC- PiP°C†C-C''PSC,C-PI  
PjPsP¶Pμ P·PSP°PrPsP±PëC,PëCḡC¶ PePsCḡPëPiC†PIP°PSPSC¶ PrPsP·Pë PiCḡPμPiP°CḡP°C,Cr  
(PrPëPI. CḡPsP·PrC-P» B«PŸPiPsCḡC-P± P·P°CḡC,PsCḡC†PIP°PSPSC¶ C,P° PrPsP·PëB»).

PμPμCḡC-PsPr PiPsPrCéPIP°PSPSC¶ PiCḡCéPrPrCḡ.

PJ P·PiBḡ™ C¶P·PeCr P· PjPsP¶P»PëPIC-CḡC,Cḡ PIPëPSPëPePSPμPSPSC¶ PiPsP±C-C†PSPëC...  
CḡPμP°PeC†C-Pμ Cr PiCḡC†PrPSPëC... PrC-C,PμPμ PiPsPrC†PIP°PSPSC¶ PiCḡC†PrPrCḡ  
CḡP»C-Pr PiCḡPëPiPëPSPëC,Pë PSP° C†P°Cḡ P»C-PeCrPIP°PSPSC¶ PiCḡPμPiP°CḡP°C,PsPj  
(PrPëPI. CḡPsP·PrC-P»Pë B«PμCḡPsC,PëPiPsPeP°P·P°PSPSC¶B» C,P°  
B«P—P°CḡC,PsCḡC†PIP°PSPSC¶ Cr PiPμCḡC-PsPr PIP°PiC-C,PSPsCḡC,C- P°P±Ps  
PiPsPrC†PIP°PSPSC¶ PiCḡC†PrPrCḡB»).

PJ P·PiBḡ™ C¶P·PeCr P· PjPsP¶P»PëPIC-CḡC,Cḡ PiPμPSPsC,PsPeCḡPëC†PSPsCḡC,C-  
P¶C-PSPeP°Pj CḡPμPiCḡPsPrC†PeC,PëPIPSPsPiPs PIC-PeCr CḡPμPePsPjPμPSPPrPsPIP°PSPs  
PIPëPePsCḡPëCḡC,PsPIC†PIP°C,Pë PIPëCḡPsPePsPμC,,PμPeC,PëPIPSC- P·P°CḡPsP±Pë  
PePsPSC,CḡP°C†PμPiC†C-C— PiC-Pr C†P°Cḡ P»C-PeCrPIP°PSPSC¶ C,P° PiCḡPsC,C¶PiPsPj 6  
PjC-CḡC¶C†C-PI PiC-CḡP»C¶ P·P°CḡC,PsCḡC†PIP°PSPSC¶ PsCḡC,P°PSPSCHPsC— PrPsP·Pë  
C-CḡPëPSPsC,PμPeP°PSCr.

PJ P·PIB<sup>™</sup> CΠP·PeC<sub>r</sub> P· PjPsPΠP»PëPIC-C<sub>r</sub>C, C<sub>h</sub> PiPμPSPsC, PsPeC<sub>r</sub>PëC±PSPsC<sub>r</sub>C, C- C<sub>r</sub>P»C-Pr C<sub>h</sub>PμPePsPjPμPSPPrC<sub>r</sub>PIP° C, Pë PiP°C<sub>r</sub>C-C" PSC, P°Pj-C±PsP»PsPIC-PeP°Pj C-P· PiP°C<sub>h</sub>C, PSPμC<sub>h</sub>PeP°PjPë-PΠC-PSPeP°PjPë P· C<sub>h</sub>PμPiC<sub>h</sub>PsPrC<sub>r</sub>PeC, PëPIPSPëPj PiPsC, PμPSC<sub>r</sub>C-P°P»PsPj PIPëPePsC<sub>h</sub>PëC<sub>r</sub>C, PsPIC<sub>r</sub>PIP° C, Pë PμC, PμPeC, PëPIPSC- P·P°C<sub>r</sub>PsP±Pë PePsPSC, C<sub>h</sub>P°C<sub>r</sub>PμPiC<sub>r</sub>C-C— PiC-Pr C±P°C<sub>r</sub> P»C-PeC<sub>r</sub>PIP°PSPSCΠ C, P° PiC<sub>h</sub>PsC, CΠPiPsPj 3 PjC-C<sub>r</sub>CΠC<sub>r</sub>C-PI PiC-C<sub>r</sub>P»CΠ P·P°C<sub>r</sub>C, PsC<sub>r</sub>C<sub>r</sub>PIP°PSPSCΠ PsC<sub>r</sub>C, P°PSPSCHbPsC— PrPsP·Pë C-C<sub>h</sub>PëPSPsC, PμPeP°PSC<sub>r</sub> (PrPëPI. C<sub>h</sub>PsP·PrC-P» B«P-P°C<sub>r</sub>C, PsC<sub>r</sub>C<sub>r</sub>PIP°PSPSCΠ C<sub>r</sub> PiPμC<sub>h</sub>C-PsPr PIP°PiC-C, PSPsC<sub>r</sub>C, C- P°P±Ps PiPsPrC<sub>r</sub>PIP°PSPSCΠ PiC<sub>h</sub>C<sub>r</sub>PrPrC<sub>h</sub>B»).

P†PSC€C- C, P°PeC, PsC<sub>h</sub>Pë.

P<sub>h</sub>C<sub>r</sub>PeC-P»C<sub>h</sub>PePë PiC<sub>h</sub>PμPiP°C<sub>h</sub>P° C, PjC-C<sub>r</sub>C, PëC, C<sub>h</sub> D-C<sub>r</sub>PsC<sub>h</sub>P±C-C,, CΠPePëPN<sub>2</sub> C" PrPΠPμC<sub>h</sub>PμP»PsPj C,, C<sub>h</sub>C<sub>r</sub>PeC, PsP·Pë, PN<sub>2</sub>PsPiPs PSPμ PjPsPΠPSP° P·P°C<sub>r</sub>C, PsC<sub>r</sub>PsPIC<sub>r</sub>PIP° C, Pë PrP»CΠ P»C-PeC<sub>r</sub>PIP°PSPSCΠ PiP°C<sub>r</sub>C-C" PSC, C-PI P·C- C<sub>r</sub>PiP°PrPePsPIPsC<sub>h</sub> PSPμPiPμC<sub>h</sub>PμPSPsC<sub>r</sub>PëPjC-C<sub>r</sub>C, C<sub>h</sub> C,, C<sub>h</sub>C<sub>r</sub>PeC, PsP·Pë (PŸP<sub>k</sub>P<sub>α</sub>). PJ PSPμPjPsPIP»CΠC, C, P° PjP°P»PμPSC<sub>h</sub>PePëC... PrC-C, PμPN<sub>2</sub> PIC-PePsPj PrPs 2 C<sub>h</sub>PsPeC-PI PjPsPΠPμ C%Pμ PSPμ P±C<sub>r</sub>C, Pë PrC-P°PiPSPsC<sub>r</sub>C, PsPIP°PSPs PŸP<sub>k</sub>P<sub>α</sub>. P>C-PeP°C<sub>h</sub>C<sub>r</sub>CHbPeC- P·P°C<sub>r</sub>PsP±Pë, CΠPeC- PjC-C<sub>r</sub>C, CΠC, C<sub>h</sub> C,, C<sub>h</sub>C<sub>r</sub>PeC, PsP·C<sub>r</sub> C, P° PIPIPsPrCΠC, C<sub>h</sub>C<sub>r</sub>CΠ PIPSC<sub>r</sub>C, C<sub>h</sub>C-C€PSC<sub>h</sub>PsPIPμPSPSPs, PjPsPΠC<sub>r</sub>C, C<sub>h</sub> PjP° C, Pë PSPμP±PμP·PiPμC±PSC- PrP»CΠ PΠPëC, C, CΠ PμC, PμPeC, Pë C<sub>r</sub> P»C<sub>h</sub>PrPμPN<sub>2</sub> P·C- PŸP<sub>k</sub>P<sub>α</sub>, C, PsPjC<sub>r</sub> C—C... PSPμ C<sub>r</sub>P»C-Pr PIPIPsPrPëC, Pë C, P°PePëPj PiP°C<sub>r</sub>C-C" PSC, P°Pj, CΠPeC%Ps PSPμPjP°C" PiPsC<sub>r</sub>C, C<sub>h</sub>PsC— PeP»C-PSC-C±PSPsC— PSPμPsP±C...C-PrPSPsC<sub>r</sub>C, C- P°P±Ps PSPμPjP°C" P°P»C<sub>h</sub>C, PμC<sub>h</sub>PSP° C, PëPIPë.

PμPμC<sub>h</sub>PμPr P·P°C<sub>r</sub>C, PsC<sub>r</sub>C<sub>r</sub>PIP°PSPSCΠPj C<sub>r</sub>CHbPsPiPs P»C-PeP°C<sub>h</sub>C<sub>r</sub>CHbPePsPiPs P·P°C<sub>r</sub>PsP±C<sub>r</sub> C<sub>r</sub> PePsPΠPSPsPiPs PiP°C<sub>r</sub>C-C" PSC, P° C<sub>r</sub>P»C-Pr P·C-P±C<sub>h</sub>P° C, Pë P°PSP°PjPSPμP· C%PsPrPs C<sub>r</sub>PëPjPiC, PsPjC-PI PŸP<sub>k</sub>P<sub>α</sub>.

P<sub>h</sub>PrPSPsC±P°C<sub>r</sub>PSPμ PIPIPμPrPμPSPSCΠ C-C<sub>h</sub>PëPSPsC, PμPeP°PSC<sub>r</sub> P· C<sub>r</sub>PëP»C<sub>h</sub>PSPëPj C-PSPiC-P±C-C, PsC<sub>h</sub>PsPj (PSP°PiC<sub>h</sub>PëPeP»P°Pr, PePμC, PsPePsPSP°P·PsP»PsPj) P°P±Ps C-PSPPrC<sub>r</sub>PeC, PsC<sub>h</sub>PsPj (PSP°PiC<sub>h</sub>PëPeP»P°Pr, C<sub>h</sub>PëC,, P°PjPiC-C<sub>r</sub>PëPSPsPj, PeP°C<sub>h</sub>P±P°PjP°P·PμPiC-PSPsPj, C,, PμPSPsP±P°C<sub>h</sub>P±C-C, P°P»PsPj, C,, PμPSC-C, PsC—PSPsPj, P°PiP°P»C<sub>r</sub>C, PsPjC-PrPsPj) CYP3A4 PjPsPΠPμ P·PjC-PSPëC, Pë PjPμC, P°P±PsP»C-P·Pj C-C<sub>h</sub>PëPSPsC, PμPeP°PSC<sub>r</sub> C- PN<sub>2</sub>PsPiPs C<sub>r</sub>P»C-Pr C<sub>r</sub>PSPëPeP° C, Pë (PrPëPI. C<sub>h</sub>PsP·PrC-P» B«P·P·P°C" PjPsPrC-CΠ P· C-PSC€PëPjPë P»C-PeP°C<sub>h</sub>C<sub>r</sub>CHbPePëPjPë P·P°C<sub>r</sub>PsP±P°PjPë C, P° C-PSC€C- PIPëPrPë PIP·P°C" PjPsPrC-PN<sub>2</sub>B»).

P<sub>α</sub>P»P°PePsPSPë P†C<sub>h</sub>PëPSPsC, PμPeP°PS P<sub>h</sub>PjP°PeC<sub>r</sub>P° PsP±B<sup>™</sup>C" PjPsPj PSP°PiPsPIPSPμPSPSCΠ 2 PjP» C, P° 5 PjP» PjC-C<sub>r</sub>C, CΠC, C<sub>h</sub> PjPμPSC€Pμ 1 PjPjPsP»C<sub>h</sub> (23 PjPi)/PrPsP·C<sub>r</sub> PSP° C, C<sub>h</sub>C-C<sub>h</sub>, C, PsP±C, Ps PiC<sub>h</sub>P°PeC, PëC±PSPs PIC-P»C<sub>h</sub>PSC- PIC-Pr PSP° C, C<sub>h</sub>C-C<sub>h</sub>.

P<sub>α</sub>P»P°PePsPS P†C<sub>h</sub>PëPSPsC, PμPeP°PS P<sub>h</sub>PjP°PeC<sub>r</sub>P° PsP±B<sup>™</sup>C" PjPsPj PSP°PiPsPIPSPμPSPSCΠ 15 PjP» PjC-C<sub>r</sub>C, PëC, C<sub>h</sub> 36 PjPi/PrPsP·C<sub>r</sub> PSP° C, C<sub>h</sub>C-C<sub>h</sub>. PŸP»C-Pr P±C<sub>r</sub>C, Pë PsP±PμC<sub>h</sub>PμPΠPSPëPj PiC<sub>h</sub>Pë P·P°C<sub>r</sub>C, PsC<sub>r</sub>C<sub>r</sub>PIP°PSPSC- PiP°C<sub>r</sub>C-C" PSC, P°Pj, CΠPeC- P·P°C<sub>r</sub>C, PsC<sub>r</sub>PsPIC<sub>r</sub>C<sub>h</sub>C, C<sub>h</sub> PSP° C, C<sub>h</sub>C-PN<sub>2</sub>- PePsPSC, C<sub>h</sub>PsP»C<sub>h</sub>PsPIP°PSC<sub>r</sub> PrC-C" C, C<sub>r</sub>.

*P—P°CÍC,PsCÍCžPIP°PSPSCÍ Cž PiPµCĤC-PsPr PIP°PiC-C,PSPsCÍC,C- P°P±Ps  
PiPsPrCžPIP°PSPSCÍ PiCĤCžPrPrCĤ.*

*PµPsPSC,CĤP°C†PµPiC†C-CÍ.*

PJ P·PIBĤ™ CÍP·PeCÍ P· PjPsP¶P»PëPIC-CÍC,CĤ PiPµPSPsC,PsPeCÍPëC‡PSPsCÍC,C-  
P¶C-PSPeP°Pj CĤPµPiCĤPsPrCÍPeC,PëPIPSsPiPs PIC-PeCÍ  
CĤPµPePsPjPµPSPPrPsPIP°PSPs PIPëPePsCĤPëCÍC,PsPICÍPIP°C,Pë  
PIPëCÍPsPePsPµC,,PµPeC,PëPIPSC- P·P°CÍPsP±Pë PePsPSC,CĤP°C†PµPiC†C-C— PiC-Pr  
C‡P°CÍ P»C-PeCÍPIP°PSPSCÍ C,P° PiCĤPsC,CÍPiPsPj 6 PjC-CÍCÍC†C-PI PiC-CÍP»CÍ  
P·P°CÍC,PsCÍCÍPIP°PSPSCÍ PsCÍC,P°PSPSCHPsC— PrPsP·Pë  
C-CĤPëPSPsC,PµPeP°PSCÍ (PrPëPI. CĤPsP·PrC-P» B«PhCÍPsP±P»PëPIPsCÍC,C-  
P·P°CÍC,PsCÍCÍPIP°PSPSCÍB»).

PJ P·PIBĤ™ CÍP·PeCÍ P· PjPsP¶P»PëPIC-CÍC,CĤ PiPµPSPsC,PsPeCÍPëC‡PSPsCÍC,C-  
CÍP»C-Pr CĤPµPePsPjPµPSPPrCÍPIP°C,Pë PiP°C†C-C”PSC,P°Pj-C‡PsP»PsPIC-PeP°Pj C-P·  
PiP°CĤC,PSPµCĤPeP°PjPë-P¶C-PSPeP°PjPë P· CĤPµPiCĤPsPrCÍPeC,PëPIPSPëPj  
PiPsC,PµPSC†C-P°P»PsPj PIPëPePsCĤPëCÍC,PsPICÍPIP°C,Pë PµC,,PµPeC,PëPIPSC-  
P·P°CÍPsP±Pë PePsPSC,CĤP°C†PµPiC†C-C— PiC-Pr C‡P°CÍ P»C-PeCÍPIP°PSPSCÍ C,P°  
PiCĤPsC,CÍPiPsPj 3 PjC-CÍCÍC†C-PI PiC-CÍP»CÍ P·P°CÍC,PsCÍCÍPIP°PSPSCÍ  
PsCÍC,P°PSPSCHPsC— PrPsP·Pë C-CĤPëPSPsC,PµPeP°PSCÍ (PrPëPI. CĤPsP·PrC-P»  
B«PhCÍPsP±P»PëPIPsCÍC,C- P·P°CÍC,PsCÍCÍPIP°PSPSCÍB»).

*PµPµCĤC-PsPr PIP°PiC-C,PSPsCÍC,C-.*

P”P°PSC- C%PsPrPs P·P°CÍC,PsCÍCÍPIP°PSPSCÍ C-CĤPëPSPsC,PµPeP°PSCÍ  
PIP°PiC-C,PSPëPj P¶C-PSPeP°Pj PsP±PjPµP¶PµPSC-. PJ PrPsCÍP»C-PrP¶PµPSPSCÍC...  
PSP° C,PIP°CĤPëPSP°C... P±CÍP»Ps PiCĤPsPrPµPjPsPSCÍC,CĤPsPIP°PSPs, C%Ps  
C-CĤPëPSPsC,PµPeP°PS C‡PëPSPëC,Ch PµPjP±CĤC-PsC,PsPeCÍPëC‡PSCÍ C,P°  
C,PµCĤP°C,PsPiPµPSPSCÍ PrC-CĤ. P’PµCĤCÍC‡Pë PrPs CÍPIP°PiPë  
CĤPµP·CÍP»ChC,P°C,Pë PrPsCÍP»C-PrP¶PµPSCĤ PSP° C,PIP°CĤPëPSP°C... C,P°  
PjPµC...P°PSC-P·Pj PrC-C— C-CĤPëPSPsC,PµPeP°PSCÍ, PSPµ CÍP»C-Pr  
P·P°CÍC,PsCÍPsPICÍPIP°C,Pë PrP°PSPëPµ PiCĤPµPiP°CĤP°C, PiC-Pr C‡P°CÍ  
PIP°PiC-C,PSPsCÍC,C-, PsCÍPsP±P»PëPIPs CÍ PiPµCĤC€PsPjCÍ C,CĤPëPjPµCÍC,CĤC-,  
P·P° PIPëPSCÍC,PePsPj PSP°PiP°P»ChPSPsC— PiPsC,CĤPµP±Pë. P-C-PSPeP°Pj  
PrC-C,PsCĤPsPrPSPsPiPs PIC-PeCÍ PSPµ P·P°CÍC,PsCÍPsPICÍPIP°C,Pë  
C-CĤPëPSPsC,PµPeP°PS, PrPsPePë PSPµ P±CÍPrPµ PIPëPeP»ChC‡PµPSP°  
PIP°PiC-C,PSC-CÍC,Ch. PkPµPsP±C...C-PrPSPs CÍPSPëPeP°C,Pë PIP°PiC-C,PSPsCÍC,C-,  
CÍPeC%Ps C...C,PsCÍCh C-P· PiP°CĤC,PSPµCĤC-PI PsC,CĤPëPjCÍC”  
C-CĤPëPSPsC,PµPeP°PS.

*P’PiP»PëPI PSP° CĤPµPiCĤPsPrCžPeC,PëPIPSCž C,,CžPSPeC†C-CĤ.*

P†PSC,,PsCĤPjP°C†C-CÍ C%PsPrPs PIPiP»PëPICÍ C-CĤPëPSPsC,PµPeP°PSCÍ PSP°  
CĤPµPiCĤPsPrCÍPeC,PëPIPSCÍ C,,CÍPSPeC†C-CĤ P»ChPrPëPSPë PIC-PrCÍCÍC,PSCÍ. PJ  
PrPsCÍP»C-PrP¶PµPSPSCÍC... PSP° C,PIP°CĤPëPSP°C... P±CÍP»Pë  
PrPsPeCÍPjPµPSC,P°P»ChPSPs P·P°CĤPµC”CÍC,CĤPsPIP°PSC- PiPsP±C-C‡PSC-



$P''PsC, C\bar{H}P\bar{e}PjC\bar{r}C\bar{H}C\bar{+}P\bar{e}C\bar{I}'C\bar{H} PSPsC\bar{H}Pj P^{\circ}C\bar{I}'P_{\mu}P\bar{i}C, P\bar{e}P\bar{e}P\bar{e}, PIC-PrP\pm P\bar{e}C\bar{H}P^{\circ}C\bar{H}C, C\bar{H}$   
 $PeP^{\circ}P \gg C-P\pm C\bar{H}PsPIP^{\circ}PSP\bar{e}Pj C\bar{e}P\bar{i}C\bar{H}P\bar{e}C\bar{+}PsPj PSP_{\mu}PsP\pm C...C-PrPSC\bar{r}$   
 $PeC-P \gg C\bar{H}PeC-C\bar{I}'C, C\bar{H} C\bar{H}PsP\cdot C\bar{+}P\bar{e}PSC\bar{r} P\bar{i}C\bar{H}P_{\mu}P\bar{i}P^{\circ}C\bar{H}P^{\circ}C, C\bar{r} P\bar{+}C\bar{H}P\bar{e}PSPsC, P_{\mu}PeP^{\circ}PS$   
 $P\bar{h}PjP^{\circ}PeC\bar{I}'P^{\circ} P\cdot C,,P \gg P^{\circ}PePsPSP^{\circ} C, P^{\circ} PIPiPsPrC\bar{I}C, C\bar{H} PrPsP\cdot C\bar{r} PI P\bar{i}P^{\circ}PeP_{\mu}C, P^{\circ}P\pm Ps$   
 $P\bar{i}P \gg C\bar{I}C\bar{e}PeC\bar{r} PsP\pm B\bar{H}^{\text{TM}} C''PjPsPj 250 PjP \gg, C\%_{\text{oo}}Ps PjC-C\bar{I}'C, P\bar{e}C, C\bar{H} 0,9 \% C\bar{H}PsP\cdot C\bar{+}P\bar{e}PS$   
 $PSP^{\circ}C, C\bar{H}C-C\bar{H} C...P \gg PsC\bar{H}P\bar{e}PrC\bar{r} P^{\circ}P\pm Ps 5 \% C\bar{H}PsP\cdot C\bar{+}P\bar{e}PS P\bar{i}P \gg C\bar{H}PePsP\cdot P\bar{e}.$   
 $P P_{\mu}C, P_{\mu}P \gg C\bar{H}PSPs P\bar{i}P_{\mu}C\bar{H}P_{\mu}PjC-C\bar{e}C\bar{r}C\bar{H}C, C\bar{H} C\bar{H}PsP\cdot C\bar{+}P\bar{e}PS, PIC\bar{H}C\bar{r}C\bar{+}PSC\bar{r}$   
 $PsP\pm P_{\mu}C\bar{H}C, P^{\circ}C\bar{H}C\bar{+}P\bar{e} C''PjPSC-C\bar{I}'C, C\bar{H}.$

P<sub>μ</sub>C<sub>7</sub>P<sub>6</sub> PjPsPSPsC,P<sub>μ</sub>C<sub>7</sub>P°PiC-C— PiC<sub>7</sub>P<sub>μ</sub>PiP°C<sub>7</sub>P°C, P†C<sub>7</sub>P<sub>6</sub>PSPsC,P<sub>μ</sub>Pe°PS  
P<sub>6</sub>JpP°PeCΓP° P·P°P·PIPëC‡P°PN<sub>6</sub> PiC<sub>7</sub>P<sub>6</sub>P·PSP°C‡P°C<sub>H</sub>C,C<sub>H</sub> 1 C<sub>7</sub>P°P· PSP° 3  
C,PëP¶PSC-. P'PsPrPSPsC‡P°CΓ PiP°C†C-C''PSC,P°Pj, CΠPePëPj PjPsP¶P<sub>μ</sub>  
P·PSP°PrPsP±PëC,PëCΓCΠ P±C-P»CHC€ C<sub>7</sub>P<sub>μ</sub>C,P<sub>μ</sub>P»CHBPSPëPN<sub>6</sub> PSP°PiP»CΠPr P°P±Ps  
CΠPeC- P·PSP°C...PsPrCΠC,C<sub>H</sub>CΓCΠ Cr PiC<sub>7</sub>CrPiC- PiC-PrPIPëC‰P<sub>μ</sub>PSPsPiPs  
C<sub>7</sub>P<sub>6</sub>P·PëPeCr C<sub>7</sub>PsP·PIPëC,PeCr C,CΠP¶PePsC— PSP<sub>μ</sub>PN<sub>6</sub>C,C<sub>7</sub>PsPiP<sub>μ</sub>PSC-C—,  
PjPsP¶PSP° C<sub>7</sub>PsP·PiP»CΠPSCrC,Pë C‰PsC,PëP¶PSP<sub>μ</sub>PICr CΓC...P<sub>μ</sub>PjCr  
P·P°CΓC,PsCΓCΓPIP°PSPSCΠ PiC<sub>7</sub>P<sub>μ</sub>PiP°C<sub>7</sub>P°C,Cr (PrPëPI. C<sub>7</sub>PsP·PrC-P»  
B«PαP°C<sub>7</sub>PjP°PePsP»PsPiC-C‡PSC- PIP»P°CΓC,PëPIPsCΓC,C-B»).).

P P<sub>μ</sub>PePsPjP<sub>μ</sub>PSPrPsPIP°PSP° PrPsP·P° PīC<sub>7</sub>H<sub>2</sub>P<sub>μ</sub>PīP°C<sub>7</sub>H<sub>2</sub>P°C, C<sub>7</sub> P†C<sub>7</sub>H<sub>2</sub>PēPSPsC, P<sub>μ</sub>PeP°PS  
Ph<sub>2</sub>PjP°PeC<sub>7</sub>P° C<sub>7</sub>C, P°PSPsPIPēC, CH<sub>2</sub> 350 PjPi/Pj<sup>2</sup> PīPsPIP<sub>μ</sub>C<sub>7</sub>H<sub>2</sub>C...PSC- C, C-P»P°,  
PIPIP<sub>μ</sub>PrP<sub>μ</sub>PSPēC... CēP»C<sub>7</sub>C...PsPj PIPSc<sub>7</sub>C, C<sub>7</sub>H<sub>2</sub>-CēPSC<sub>7</sub>PsPIP<sub>μ</sub>PSPSPsC— C-PSC,, C<sub>7</sub>P·C-C—  
C, C<sub>7</sub>H<sub>2</sub>PēPIP°P»C-C<sub>7</sub>C, CH<sub>2</sub> 30B<sub>7</sub>°90 C...PI C†P<sub>μ</sub>C<sub>7</sub>H<sub>2</sub>P<sub>μ</sub>P· PePsP¶PSC- 3 C, PēP¶PSC- (PrPēPI.  
C<sub>7</sub>H<sub>2</sub>PsP·PrC-P» B«PhC<sub>7</sub>PsP±P»PēPIPsC<sub>7</sub>C, C- P·P°C<sub>7</sub>C, PsC<sub>7</sub>C<sub>7</sub>PIP°PSPSC<sub>7</sub>B»).

$P \cdot C_{\mu}, P_{\mu}PeC, P\ddot{e}PIPSC - C\acute{I}C, CH_3 C, P^{\circ} P \pm P_{\mu}P \cdot \ddot{P}iP_{\mu}PeC\acute{r} P \cdot P^{\circ}C\acute{I}C, PsC\acute{I}C\acute{r}PIP^{\circ}PSPSC\ddot{I}$   
 $C - C\grave{H}P\ddot{e}PSPsC, P_{\mu}PeP^{\circ}PSC\acute{r} C\acute{r} PePsPjP \pm C - PSP^{\circ}C\ddot{I}C - C - P \cdot 5 - P\alpha Pj C, P^{\circ} P\alpha P_{\mu}$   
 $PsC\ddot{I}C - PSC\grave{H}PIP^{\circ}P \gg P\ddot{e} P \cdot P^{\circ} PSP\ddot{e}P\grave{I}C\ddot{I}P_{\mu}P \cdot P^{\circ}P \cdot PSP^{\circ}C\ddot{I}P_{\mu}PSPsC\grave{H} C\acute{I}C \dots P_{\mu}PjPsC\grave{H}$   
 $PrPsP \cdot C\acute{r}PIP^{\circ}PSPSC\ddot{I} (PrP\ddot{e}Pi. C\grave{H}PsP \cdot PrC - P \gg B \langle P\alpha P^{\circ}C\grave{H}PjP^{\circ}PePsPrP\ddot{e}PSP^{\circ}PjC - PeP^{\circ}B \rangle).$   
 $P P_{\mu}PePsPjP_{\mu}PSPPrPsPIP^{\circ}PSP^{\circ} PrPsP \cdot P^{\circ} C - C\grave{H}P\ddot{e}PSPsC, P_{\mu}PeP^{\circ}PSC\acute{r} C\acute{I}C, P^{\circ}PSPsPIP\ddot{e}C, CH_3$   
 $180 PjPi/Pj^2 1 C\grave{H}P^{\circ}P \cdot PSP^{\circ} 2 C, P\ddot{e}P\grave{I}PSC - C\acute{r} PIP\ddot{e}PiP \gg C\ddot{I}PrC -$   
 $PIPSC\acute{r}C, C\grave{H}C - C\epsilon PSC\grave{H}PsPIP_{\mu}PSPSPsC - C - PSC_{\mu}, C\acute{r}P \cdot C - C - \ddot{P}iC\grave{H}PsC, C\ddot{I}PiPsPj 30B\grave{H} "90$   
 $C \dots PIP\ddot{e}P \gg P\ddot{e}PS, \ddot{P}iC - C\acute{I}P \gg C\ddot{I} C\ddot{I}PsPiPs PIPiPsPrC\ddot{I}C, CH_3 P\alpha P_{\mu} C - 5 - P\alpha Pj.$   
 $P\ddot{I}PSC_{\mu}, PsC\grave{H}PjP^{\circ}C\ddot{I}C - C\grave{H} \ddot{P}iC\grave{H}Ps PrPsP \cdot P\ddot{e} C - C\acute{I}\ddot{P}iPsC\acute{I}PsP \pm P\ddot{e} C\acute{I}C\acute{r}\ddot{P}iC\acute{r}C, PSC\grave{H}PsPiPs$   
 $PIPI_{\mu}PrP_{\mu}PSPSC\ddot{I} C\ddot{I}P_{\mu}C, C\acute{r}PeC\acute{I}P\ddot{e}PjP^{\circ}P \pm C\acute{r} PjPsP\grave{I}PSP^{\circ} P \cdot PSP^{\circ}PN_{\epsilon}C, P\ddot{e} Pi$   
 $PePsC\grave{H}PsC, PeC - PN_{\epsilon} C \dots P^{\circ}C\grave{H}P^{\circ}PeC, P_{\mu}C\grave{H}P\ddot{e}C\acute{I}C, P\ddot{e}C\ddot{I}C - PrP^{\circ}PSPsPiPs$

P»C-PeP°CḡCḡCHPePsPiPs P·P°CḡPsP±Cḡ. P—P°P·PIPëC±P°PNë  
 P·P°CḡC,PsCḡPsPICḡCḡC,CH C,P°PeCḡ Pḡ PrPsP·Cḡ C-CḡPëPSPsC,PμPeP°PSCḡ, CḡPe C-  
 PI PīPsPīPμCḡPμPrPSC-C... PeCḡCḡCḡP°C... P»C-PeCḡPIP°PSPSCḡ C-P·  
 P·P°CḡC,PsCḡCḡPIP°PSPSCḡPj CḡC...PμPj, C%Ps PIPeP»CḡC±P°CḡC,CH  
 C-CḡPëPSPsC,PμPeP°PS. P†CḡPëPSPsC,PμPeP°PS CḡP»C-Pr PIPsPrPëC,Pë PSPμ  
 CḡP°PSC-CḡPμ PSC-Pḡ C±PμCḡPμP· 1 PiPsPrPëPSCḡ PīC-CḡP»Cḡ  
 P·P°PeC-PSC±PμPSPSCḡ C-PSC,,CḡP·C-C— C†PμC,CḡPeCḡPëPjP°P±Cḡ. P”P»Cḡ  
 PsC,CḡPëPjP°PSPSCḡ C-PSC,,PsCḡPjP°C†C-C— PīCḡPs PrPsP·CḡPIP°PSPSCḡ C,P°  
 CḡPīPsCḡPsP±Pë P·P°CḡC,PsCḡCḡPIP°PSPSCḡ P±PμPIP°C†PëP·CḡPjP°P±Cḡ,  
 P·PIPμCḡPSC-C,CHCḡCḡ PrPs PePsCḡPsC,PePsC— C...P°CḡP°PeC,PμCḡPëCḡC,PëPePë  
 PrP°PSPsPiPs P»C-PeP°CḡCḡCHPePsPiPs P·P°CḡPsP±Cḡ. P†PSC,,PsCḡPjP°C†C-Cḡ  
 PīCḡPs PrPsP·CḡPIP°PSPSCḡ C,P° P·P°CḡC,PsCḡCḡPIP°PSPSCḡ  
 C-CḡPëPSPsC,PμPeP°PSCḡ PI PePsPjP±C-PSP°C†C-C— P· PeP°PīPμC†PëC,P°P±C-PSPsPj  
 PrPëPI. Cḡ CḡPsP·PrC-P»C- B«P»P°CḡPjP°PePsP»PsPiC-C±PSC- PIP»P°CḡC,PëPIPsCḡC,C-B»  
 C,P° Cḡ PIC-PrPīPsPIC-PrPSPëC... CḡPsP·PrC-P»P°C... PePsCḡPsC,PePsC—  
 C...P°CḡP°PeC,PμCḡPëCḡC,PëPePë PeP°PīPμC†PëC,P°P±C-PSCḡ.

PlPsCḡPμPeC†C-Cḡ PrPsP·Pë.

P†CḡPëPSPsC,PμPeP°PS PḡPjP°PeCḡP° CḡP»C-Pr PIPsPrPëC,Pë PīC-CḡP»Cḡ  
 P°PrPμPePIP°C,PSPsPiPs P·PSPëPePSPμPSPSCḡ CḡCḡC-C... PīPsP±C-C±PSPëC...  
 CḡPμP°PeC†C-PNë PrPs CḡC,CḡPīPμPSCḡ 0 P°P±Ps 1 P·P° CḡPeP°P»PsCḡ NCI-CTC  
 (P·P°PīP°P»CHPSC- PeCḡPëC,PμCḡC-C— PsC†C-PSPePë C,PsPeCḡPëC±PSPsCḡC,C-  
 PḡP°C†C-PsPSP°P»CHPSPsPiPs C-PSCḡC,PëC,CḡC,Cḡ CḡP°PeCḡ) C,P° PīC-CḡP»Cḡ  
 PīPsPIPSPsPiPs PīCḡPëPīPëPSPμPSPSCḡ PīPsPīBḡ™ CḡP·P°PSPsC— P· P»C-PeCḡPIP°PSPSCḡPj  
 PrC-P°CḡPμC—

PḡP° PīPsC±P°C,PeCḡ PSP°CḡC,CḡPīPSPsPiPs PeCḡCḡCḡCḡ PIPIPμPrPμPSPSCḡ  
 CḡP»CḡC...PsPj C-PSC,,CḡP·C-C— PrPsP·Cḡ PīCḡPμPīP°CḡP°C,Cḡ  
 P†CḡPëPSPsC,PμPeP°PS PḡPjP°PeCḡP° C,P° 5-PḡPJ, CḡPeC%Ps  
 P·P°CḡC,PsCḡPsPICḡCḡC,CHCḡCḡ, CḡP»C-Pr P·PSPëPḡCḡPIP°C,Pë P·P°P»PμPḡPSPs PIC-Pr  
 PīCḡPsCḡPIC-PI PīPsP±C-C±PSPëC... CḡPμP°PeC†C-PNë PSP°PNëC,CḡPḡC±PsPiPs  
 CḡC,CḡPīPμPSCḡ, C%Ps CḡPīPsCḡC,PμCḡC-PiP°P»PëCḡCḡ PīC-Pr C±P°Cḡ  
 PīPsPīPμCḡPμPrPSCḡPsC— C-PSC,,CḡP·C-C—. PḡP»C-Pr PIC-PrPeP»P°CḡC,Pë PīPsC±P°C,PsPe  
 P»C-PeCḡPIP°PSPSCḡ PSP° 1Bḡ“2 C,PëPḡPSC- PrP»Cḡ P·PSPëPePSPμPSPSCḡ  
 PīPsPīBḡ™ CḡP·P°PSPëC... P· P»C-PeCḡPIP°PSPSCḡPj PīPsP±C-C±PSPëC... CḡPμP°PeC†C-PNë.

PμCḡPë CḡPsP·PIPëC,PeCḡ PSPëPḡC±PμP·P°P·PSP°C±PμPSPëC... PīPsP±C-C±PSPëC...  
 CḡPμP°PeC†C-PNë PrPsP·Cḡ PīCḡPμPīP°CḡP°C,Cḡ P†CḡPëPSPsC,PμPeP°PS PḡPjP°PeCḡP°  
 C,P°/P°P±Ps 5-PḡPJ, CḡPeC%Ps P·P°CḡC,PsCḡPsPICḡCḡC,CHCḡCḡ, CḡP»C-Pr P·PSPëP·PëC,Pë  
 PSP° 15Bḡ“20 %:

- PīPμPjP°C,PsC,PsPeCḡPëC±PSC-CḡC,CH (PSPμPNëC,CḡPsPīPμPSC-Cḡ IV  
 CḡC,CḡPīPμPSCḡ, C,,PμP±CḡPëP»CHPSP° PSPμPNëC,CḡPsPīPμPSC-Cḡ  
 (PSPμPNëC,CḡPsPīPμPSC-Cḡ IIIBḡ“IV CḡC,CḡPīPμPSCḡ, C%Ps  
 CḡCḡPīCḡPsPIPPrPḡCḡCḡC,CHCḡCḡ PīP°CḡCḡC±PePsCḡ IIBḡ“IV CḡC,CḡPīPμPSCḡ),  
 C,CḡPsPjP±PsC†PëC,PsPīPμPSC-Cḡ C,P° P»PμPNëPePsPīPμPSC-Cḡ (IV CḡC,CḡPīPμPSCḡ));

- PSPμPīPμPjP°C,PsP»PsPiC-C±PSP° C,PsPeCḡPëC±PSC-CḡC,CH (IIIBḡ“IV  
 CḡC,CḡPīPμPSCḡ).

РҮР»С-Рr PrPsC,СҲРөРјСrPIP°С,РөСГГЦ ЦҲРµРёРsРјРµPSPrP°С†С-РN₂ Р·  
РјРsРrРөС,,С-РёР°С†С-С— РrPsР·Рө С†РµС,СrРёСГРөРјР°Р±Сr РiСҲРө РN₂РsРiРs  
Р·Р°СГГС,РsСГГСrPIP°PSPSC- РI РёРsРјР±С-РSP°С†С-С— Р· С-СҲРөРPSPsC,РµРёР°Р°РsРј  
Р·РiС-РrPSPs Р· С-РSC,,РsСҲРјР°С†С-С"СҲ, РSP°PIРµРrРµPSPsСҲ РI РёРsСҲРsC,РёС-РN₂  
С...Р°СҲР°РёС,РµСҲРөСГГС,РөС†С- С†РµС,СrРёСГРөРјР°Р±Сr.

Р†РSC,,РsСҲРјР°С†С-СҲ РiСҲРs РјРsРrРөС,,С-РёР°С†С-СҲ РrPsР·Рө Р±РµРµР°Р°С†РөР·СrРјР°Р±Сr  
РiСҲРө РёРsРјР±С-РSPsPIP°PSPsРјСr Р»С-РёСГРPIP°PSPSC- Р±РµРµР°Р°С†РөР·СrРјР°Р±Сr Р·  
С-СҲРөРPSPsC,РµРёР°Р°РsРј/5-Р±Рј/Р±Рµ РјРsРµPSP° Р·РSP°РN₂С,Рө РI РёРsСҲРsC,РёС-РN₂  
С...Р°СҲР°РёС,РµСҲРөСГГС,РөС†С- Р±РµРµР°Р°С†РөР·СrРјР°Р±Сr.

РµР°С†С-С"РSC,Р°Рј РIС-РёРsРј РIС-Рr 65 СҲРsРёС-РI РiСҲРө Р·Р°СГГС,РsСГГСrPIP°PSPSC-  
С-СҲРөРPSPsC,РµРёР°Р°РsРсr С,Р° РёР°РiРµС†РөС,Р°Р±С-РSCr СҲРµРёРsРјРµPSPrСrС"С,СҲСГГЦ  
Р·РSPөРµСrPIP°С,Рө РrPsР·Сr РёР°РiРµС†РөС,Р°Р±С-РSCr РrPs 800 РјРi/Рј² РiРsPIРµСҲС...РSC-  
С,С-Р»Р° 2 СҲР°Р·Рө РSP° РrPsР±Сr. Р"Р»Ц С-РSC,,РsСҲРјР°С†С-С— РiСҲРs  
РёРsСҲРөРiСrPIP°PSPSCЦ РrPsР·Рө Сr СҲР°Р·С- РёРsРјР±С-РSPsPIP°PSPsC— С,РµСҲР°РiС-С—  
Р·PIРµСҲРSC-С,СҲСГГЦ РrPs РёРsСҲРsC,РёРsC— С...Р°СҲР°РёС,РµСҲРөСГГС,РөРёРө  
РёР°РiРµС†РөС,Р°Р±С-РSCr.

РҮСҲРөРPIP°Р»С-СГГС,СҲ Р»С-РёСГРPIP°PSPSCЦ.

Р»С-РёСГРPIP°PSPSCЦ РiСҲРµРiР°СҲР°С,РsРј Р†СҲРөРPSPsC,РµРёР°Р°Рs РҲРјР°РёСГР° СГР»С-Рr  
РiСҲРsРrPsPIРµСrPIP°С,Рө РrPs РsР±СҲ™ С"РёС,РөPIРSPsРiРs РiСҲРsРiСҲРµСГГСrPIP°PSPSCЦ  
Р·Р°С...PIРsСҲСҲPIP°PSPSCЦ Р°Р±С РrPs СҲРsР·PIРөС,РёС РsР·РSP°Рё  
РSPµРiСҲРөРiСrСГГС,РөРјРsC— С,РsРёСГРөС±РSPsСГГС,С-.

*РµР°С†С-С"РSC,Рө Р· РiРsСҲСзСёРµРµPSPSCЦРјРө С,,СзРSPёС†С-С— РiРµС±С-РSPёРө.*

РҲРsPSPsC,РµСҲР°РiС-СЦ.

- РµР°С†С-С"РSC,Р°Рј Р· С-РSPrРµСГРsРј Р·Р°РiР°Р»СҲРSPsРiРs СГГС,Р°РSCr ≤ 2 Р·Р°  
СёРёР» Р»РsСҲ Р'РҲРҲР— РiРsС±Р°С,РёРsРIСr РrPsР·Сr Р»С-РёР°СҲСГГСРёРsРiРs  
Р·Р°СГРsР±Сr Р†СҲРөРPSPsC,РµРёР°Р°Рs РҲРјР°РёСГР° РSPµРsР±С...С-РrPSPs  
PIРөР·РSP°С±Р°С,Рө Р·Р° СҲС-PIРSPµРј Р±С-Р»С-СҲСrР±С-РSCr РI РёСҲРsРIС- (РiСҲРө  
Р·Р±С-Р»СҲСёРµРµPSPSC- СҲС-PIРSCЦ Р±С-Р»С-СҲСrР±С-РSCr PIРөС%Рµ  
PIРµСҲС...РSCHРsC— РјРµРµС- РSPsСҲРјРө РSPµ Р±С-Р»СҲСёРµ РSC-Рµ Сr 3 СҲР°Р·Рө). Рј  
С,Р°РёРөС... РiР°С†С-С"РSC,С-РI Р· РiС-РiРµСҲР±С-Р»С-СҲСrР±С-РSPµРјС-С"СҲ С,Р°  
РiСҲРsC,СҲРsРјР±С-РSPsPIРөРј С±Р°СГРsРј, Р±С-Р»СҲСёРөРј РSP° 50 %,  
РёР»С-СҲРµPSCГ С-СҲРөРPSPsC,РµРёР°Р°РsРсr Р·РSPөРµСrС"С,СҲСГГЦ (РrРөРi.  
СҲРsР·РrС-Р» Р«Р±Р°Р°СҲРјР°РёРsРёС-РSPµС,РөРёР°Р»»), PIРSP°СГР»С-РrPsРё С±РsРiРs  
Р·СҲРsСГГС,Р°С" СҲРөР·РөРё СҲРsР·PIРөС,РёС РiРµРјРјР°С,РsC,РsРёСГРөС±РSPsСГГС,С-.  
РҮРsРјСr С,Р°РёС-РN₂ РёР°С,РµРiРsСҲС-С— РiР°С†С-С"РSC,С-РI СГР»С-Рr  
С%РsC,РөРµPSCЦ РёРsPSC,СҲРsР»СҲPIP°С,Рө РiРsРёР°Р°Р·РSPөРёРө  
РёР»С-РSC-С±РSPsРiРs Р°РSP°Р»С-Р· РёСҲРsРIС-.

- РµР°С†С-С"РSC,Р°Рј С-Р· СҲС-PIРSPµРј Р±С-Р»С-СҲСrР±С-РSCr PIРөС%Рµ  
PIРµСҲС...РSCHРsC— РјРµРµС- РSPsСҲРјРө РSPµ Р±С-Р»СҲСёР РSC-Рµ Сr 1,5 СҲР°Р·РөРө  
СҲРµРёРsРјРµPSPrPsPIP°PSP° РrPsР·Р° РiСҲРµРiР°СҲР°С,Сr СГГС,Р°РSPsPIРөС,СҲ 350 РјРi/Рј²  
РiРsPIРµСҲС...РSC- С,С-Р»Р°.

- P<sub>μ</sub>P°C†C-C''PSC,P°Pj C-P· C<sub>7</sub>C-PIPS<sub>μ</sub>Pj P±C-P»C-C<sub>7</sub>C†P±C-PSC† PIPëC%P<sub>μ</sub>  
PIP<sub>μ</sub>C<sub>7</sub>C...PSC<sub>H</sub>PsC— PjP<sub>μ</sub>P¶C- PSp<sub>s</sub>C<sub>7</sub>PjPë C† 1,5B<sub>7</sub>“3 C<sub>7</sub>P°P·Pë C<sub>7</sub>P<sub>μ</sub>PePsPjP<sub>μ</sub>PSPrPsPIP°PSP°  
PrPsP·P° C†C,P°PSPsPIPëC,CH 200 PjPi/Pj<sup>2</sup> PīPsPIP<sub>μ</sub>C<sub>7</sub>C...PSC- C,C-P»P°.

- P<sub>μ</sub>P°C†C-C''PSC,P°Pj C-P· C<sub>7</sub>C-PIPS<sub>μ</sub>Pj P±C-P»C-C<sub>7</sub>C†P±C-PSC† PIPëC%P<sub>μ</sub>  
PIP<sub>μ</sub>C<sub>7</sub>C...PSC<sub>H</sub>PsC— PjP<sub>μ</sub>P¶C- PSp<sub>s</sub>C<sub>7</sub>PjPë P±C-P»CHC€ PSC-P¶ C† 3 C<sub>7</sub>P°P·Pë PSp<sub>μ</sub>  
C†P»C-Pr P·P°C†C,PsC†PsPIC†PIP°C,Pë C-C<sub>7</sub>PëPSPsC,P<sub>μ</sub>PeP°PS (PrPëPI. C<sub>7</sub>PsP·PrC-P»Pë  
B«P<sub>μ</sub>C<sub>7</sub>PsC,PëPīPsPeP°P·P°PSPSC¶B» C,P° B«PhC†PsP±P»PëIPsC†C,C-  
P·P°C†C,PsC†C†PIP°PSPSC¶B»).

P†PSC,,PsC<sub>7</sub>PjP°C†C-C¶ C%PsPrPs P·P°C†C,PsC†C†PIP°PSPSC¶  
C-C<sub>7</sub>PëPSPsC,P<sub>μ</sub>PeP°PSC† C† PePsPjP±C-PSP°C†C-C— P· C-PSC€PëPjPë  
PīC<sub>7</sub>P<sub>μ</sub>PīP°C<sub>7</sub>P°C,P°PjPë PīP°C†C-C''PSC,P°Pj P· C†C<sub>7</sub>P°P¶P<sub>μ</sub>PSPSC¶PjPë  
PīP<sub>μ</sub>C†C-PSPePë PIC-PrC†C†C,PSC¶.

*P<sub>μ</sub>P°C†C-C''PSC,Pë P· PīPsC<sub>7</sub>C¿C€P<sub>μ</sub>PSPSC¶PjPë C,,C¿PSPeC†C-C— PSPëC<sub>7</sub>PsPe.*

P—P°C†C,PsC†PsPIC†PIP°C,Pë P†C<sub>7</sub>PëPSPsC,P<sub>μ</sub>PeP°PS P<sub>H</sub>PjP°PeC†P° PīP°C†C-C''PSC,P°Pj  
C-P· PīPsC<sub>7</sub>C†C€P<sub>μ</sub>PSPSC¶PjPë C,,C†PSPeC†C-C— PSPëC<sub>7</sub>PsPe PSp<sub>μ</sub>  
C<sub>7</sub>P<sub>μ</sub>PePsPjP<sub>μ</sub>PSPrC†C''C,CHC†C¶, PsC†PeC-P»CHPePë PrPsC†P»C-PrP¶P<sub>μ</sub>PSPSC¶ C%PsPrPs  
P·P°C†C,PsC†C†PIP°PSPSC¶ PīC<sub>7</sub>P<sub>μ</sub>PīP°C<sub>7</sub>P°C,C† C,P°PeC-PN<sub>0</sub> PeP°C,P<sub>μ</sub>PiPsC<sub>7</sub>C-C—  
PīP°C†C-C''PSC,C-PI PSp<sub>μ</sub> PīC<sub>7</sub>PsPIPsPrPëP»PsC†C¶ (PrPëPI. C<sub>7</sub>PsP·PrC-P»Pë  
B«P<sub>μ</sub>P°C<sub>7</sub>PjP°PePsPeC-PSP<sub>μ</sub>C,PëPeP°B» C,P° B«PhC†PsP±P»PëIPsC†C,C-  
P·P°C†C,PsC†C†PIP°PSPSC¶B»).

*P<sub>μ</sub>P°C†C-C''PSC,Pë P»C-C,PSC<sub>H</sub>PsPiPs PIC-PeC¿.*

PŸPīP<sub>μ</sub>C†C-P°P»CH<sub>H</sub>PSPëC... C,,P°C<sub>7</sub>PjP°PePsPeC-PSP<sub>μ</sub>C,PëC†PSPëC...  
PrPsC†P»C-PrP¶P<sub>μ</sub>PSC<sub>H</sub> P·P° C†C†P°C†C,C<sub>H</sub> PīP°C†C-C''PSC,C-PI P»C-C,PSC<sub>H</sub>PsPiPs  
PIC-PeC† PSp<sub>μ</sub> PīC<sub>7</sub>PsPIPsPrPëP»Pë. P'PsPrPSPsC†P°C†, PīP°C†C-C''PSC,P°Pj C†C-C''C—  
PīC<sub>7</sub>C†PīPë C†P»C-Pr C<sub>7</sub>P<sub>μ</sub>C,P<sub>μ</sub>P»CH<sub>H</sub>PSPs PīC-PrP±PëC<sub>7</sub>P°C,Pë PrPsP·C†,  
PsC†PeC-P»CHPePë C† PSPëC... PSP°P±P°PīP°C,Ps C†P°C†C,C-C€P<sub>μ</sub>  
PIPëC¶IPIP»C¶C''C,CHC†C¶ P·PSPëP¶P<sub>μ</sub>PSPSC¶ P±C-PsP»PsPiC-C†PSPëC...  
C,,C†PSPeC†C-PN<sub>0</sub>. P<sub>μ</sub>P°C†C-C''PSC,Pë C†C-C''C— PīC<sub>7</sub>C†PīPë PīPsC,C<sub>7</sub>P<sub>μ</sub>P±C†C<sub>H</sub>C,CH  
P±C-P»CHC€ C-PSC,P<sub>μ</sub>PSC†PëPIPSPsPiPs C†PīPsC†C,P<sub>μ</sub>C<sub>7</sub>P<sub>μ</sub>P¶P<sub>μ</sub>PSPSC¶ (PrPëPI.  
C<sub>7</sub>PsP·PrC-P» B«PhC†PsP±P»PëIPsC†C,C- P·P°C†C,PsC†C†PIP°PSPSC¶B»).

P<sub>μ</sub>PsPrC-P±PSPs PrPs C-PSC€PëC... PīC<sub>7</sub>PsC,PëPīC†C...P»PëPSPSPëC...  
PīC<sub>7</sub>P<sub>μ</sub>PīP°C<sub>7</sub>P°C,C-PI, P†C<sub>7</sub>PëPSPsC,P<sub>μ</sub>PeP°PS P<sub>H</sub>PjP°PeC†P° C†P»C-Pr  
PīPsC,C†PIP°C,Pë PrPs P·P°C†C,PsC†C†PIP°PSPSC¶ C,P° PIPiPsPrPëC,Pë P·  
PsP±P<sub>μ</sub>C<sub>7</sub>P<sub>μ</sub>P¶PSC-C†C,C<sub>H</sub>. P'PëPePsC<sub>7</sub>PëC†C,P°PSPSC¶ P·P°C...PëC†PSPëC...  
PsPeC†P»C¶C<sub>7</sub>C-PI, PjP°C†PePë C,P° C<sub>7</sub>C†PeP°PIPëC†PsPe C''  
PsP±PsPiB<sub>7</sub><sup>TM</sup> C¶P·PePsPIPëPj.

Pj C<sub>7</sub>P°P·C- PīPsC,C<sub>7</sub>P°PīP»C¶PSPSC¶ PePsPSC†P<sub>μ</sub>PSC,C<sub>7</sub>P°C,C† P°P±Ps  
C<sub>7</sub>PsP·C†PëPSC† PrP»C¶ C-PSC,,C†P·C-C— PSP° C€PeC-C<sub>7</sub>C† C†P»C-Pr  
PSP<sub>μ</sub>PiP°PN<sub>0</sub>PSPs P·PjPëC,Pë C<sub>7</sub>PsP·C†PëPS C,P° C<sub>7</sub>P<sub>μ</sub>C,P<sub>μ</sub>P»CH<sub>H</sub>PSPs PIPëPjPëC,Pë  
PjC-C†C†P<sub>μ</sub> PePsPSC,P°PeC,C† PIPsPrPsC<sub>H</sub> P· PjPëP»PsPj, P° C† C<sub>7</sub>P°P·C-  
PīPsC,C<sub>7</sub>P°PīP»C¶PSPSC¶ PSP° C†P»PëP·PsPIC- PsP±PsP»PsPSPePë B<sub>7</sub>“ C†P»C-Pr  
PSP<sub>μ</sub>PiP°PN<sub>0</sub>PSPs P·PjPëC,Pë PIPsPrPsC<sub>H</sub>.

*PJC,PëP»C-P·P°C†C-CI.*

PJC†C- PjP°C,PμC†C-P°P»Pë, C%Ps P·P°C†C,Psc†PspIC†C†C,CHC†C†C P†P»C†C  
C†Psp·C†PëPSPμPSPSC†C C,P° PIPμP†PμPSPSC†C P†C†PμP†P°C†P°C,C†,  
P†C-P†P»C†P†P°C†C,CH C†C,PëP»C-P·P°C†C-C— PIC-P†P†PspIC-P†PSPs P†Ps  
C†C,P°PSP†P°C†C,PSPëC... P†C†PspC†PμP†C†C PjPμP†PëC†PSPsPiPs P·P°PëP»P°P†C†,  
C%Ps P·P°C†C,Psc†PspIC†C†C,CHC†C†C P†Ps C†PëC,Psc,PspëC†PëC†PSPëC...  
P†C†PμP†P°C†P°C,C-PI.

*P''C-C,Pë.*

PμC†PμP†P°C†P°C, P†C†PëP·PSP°C†PμPSPëPN P†P»C†C P·P°C†C,Psc†C†PIP°PSPSC†C  
C,C-P»CHPëPë P†Psc†PspC†P»PëPjPë.

***PμPμC†PμP†PsP·C¿PIP°PSPSC†C.***

P†C†P»Pë Psc,C†PëPjP°PSC- P†PspIC-P†PspjP»PμPSPSC†C P†C†Psp P†PμC†PμP†Psp·C†PIP°PSPSC†C,  
C%Ps PjPsp†Pμ PjP°C,Pë P»PμC,P°P»CHPSPëPN PSP°C†P»C-P†PspPë, P†C†Pë  
P·P°C†C,Psc†C†PIP°PSPSC- P†Psp· P†C†PμP†P°C†P°C,C†, C%Ps P†C†PëP±P»PëP·PSPs  
PIP†PIC-C†C- P†PμC†PμPIPëC%C†PIP°P»Pë C†PμPëPspjPμPSP†PspIP°PSC†  
C,PμC†P°P†PμPIC,PëC†PSC† P†Psp·C†. P†P°PN±C-P»CHC€ P·PSP°C†C†C%PëPjPë  
P†Psp±C-C†PSPëPjPë C†PμP°PëC†C-C†PjPë P±C†P»Pë PSPμPN,C†PspP†PμPSC-C†  
C,C†P†PëPspPiPs C†C,C†P†PμPSC†C C,P° P†C-P°C†PμC†C C,C†P†PëPspPiPs C†C,C†P†PμPSC†C.  
P†C-P†PspjPspPiPs P°PSC,PëP†Psc,C† P†Ps C-C†PëPSPsC,PμPëP°PSC† PSPμ C-C†PSC†C".  
P†P»C-P† P†C†PspIPsP†PëC,Pë PjP°PëC†PëPjP°P»CHPSPs C-PSC,PμPSC†PëPIPSPμ  
P†C-P†C,C†PëPjC†C†Pμ P»C-PëC†PIP°PSPSC†C, C%PsP± P·P°P†Psp±C-P†C,Pë  
P·PSPμIPsP†PSPμPSPSC† PIPSP°C†P»C-P†PspPë P†C-P°C†PμC— C,P° PIPëP»C-PëC†PIP°C,Pë  
PjPsp†P»PëPIC- C-PSC,,PμPëC†C-PN±PSC- C†C†PëP»P°P†PSPμPSPSC†C.

***PμPsp±C-C†PSC- C†PμP°PëC†C-C—.***

*PμP»C-PSC-C†PSC- P†Psc†P»C-P†P†PμPSPSC†C.*

P''P°PSC- C%PsP†Ps P†Psp±C-C†PSPëC... C†PμP°PëC†C-PN± P±C†P»Pë C†PμC,PμP»CHPSPs  
P·C-P±C†P°PSC- C† P†C†PspC†PμC†C- P†Psc†P»C-P†P†PμPSC†C PjPμC,P°C†C,P°C,PëC†PSPsPiPs  
PëPsp»Psc†PμPëC,P°P»CHPSPsPiPs C†P°PëC†, C†P°C†C,Psc,P° C—C... P†Psc†PIPë  
PSP°PIPμP†PμPSP° PSPëP†C†Pμ. PμC†Pë P·P°C†C,Psc†C†PIP°PSPSC- P†C†PμP†P°C†P°C,C†  
P†P»C†C C-PSC€PëC... P†PspPëP·P°PSC†, PspëC†C-Pj PëPsp»Psc†PμPëC,P°P»CHPSPsPiPs  
C†P°PëC†, Psc†C-PëC†C" C,CHC†C†C PIPëPSPëPëPSPμPSPSC†C C†C...Psp†PëC...  
P†Psp±C-C†PSPëC... C†PμP°PëC†C-PN±.

P†P°PN±P†Psc€PëC†PμPSC-C€PëPjPë (≥1/10) P†Psp·Psp»C-PjC-C,C†C†C†PëPjPë  
P†Psp±C-C†PSPëPjPë C†PμP°PëC†C-C†PjPë C-C†PëPSPsC,PμPëP°PSC†C"

PIC-PrCfC,ChPsC+PμPSP° PrC-P°ChPμCΠ (PIPëPSPëPeP°C" P±C-P»CHC€Pμ PSC-P¶ C+PμChPμP· 24 PiPsPrPëPSPë PiC-CfP»CΠ PIPμPrPμPSPSCΠ PiChPμPiP°ChP°C,Cr) C,P° ChPsP·P»P°PrPë P· P±PsPeCr PeChPsPIC-, PIPeP»ChC+P°ChC+Pë PSPμPNëC,ChPsPiPμPSC-Ch, P°PSPμPjC-Ch C- C,ChPsPjP±PsC+PëC,PsPiPμPSC-Ch.

PkPμPNëC,ChPsPiPμPSC-CΠ C" PrPsP·PsP»C-PjC-C,CrChC+PëPj C,PsPeCfPëC+PSPëPj PμC,,PμPeC,PsPj. PkPμPNëC,ChPsPiPμPSC-CΠ PjP°P»P° PsP±PsChPsC,PSPëPNë C...P°ChP°PeC,PμCh C- PSPμ P±CrP»P° PeCrPjCrP»CΠC,PëPIPSPsCh; PiC-Pr C+P°Cf PjPsPSPsC,PμChP°PiC-C— P°P±Ps PePsPjP±C-PSPsPIP°PSPsC— C,PμChP°PiC-C— CfPμChPμPrPSC-PNë C+P°Cf PrPs PrPsCfCΠPiPSPμPSPSCΠ PjC-PSC-PjP°P»CHPSPsPiPs ChC-PIPSCΠ PSPμPNëC,ChPsC,,C-P»C-PI CfC,P°PSPsPIPëPI 8 PrPSC-PI.

P"CrP¶Pμ C+P°CfC,Ps CfPiPsCfC,PμChC-PiP°PICfCΠ C,ChP°PSP·PëC,PsChPSPëPNë PiPsCfC,ChPëPNë C...PsP»C-PSPμChPiC-C+PSPëPNë CfPëPSPrChPsPj C,CΠP¶PePsPiPs CfC,CrPiPμPSCΠ.

PhCfPSPsPIPSPëPjPë PNëPsPiPs CfPëPjPiC,PsPjP°PjPë P±CrP»Pë ChP°PSPSCΠ PrC-P°ChPμCΠ C,P° ChC-P·PSC- C-PSC€C- CfPëPjPiC,PsPjPë, C,P°PeC- CΠPe P±C-P»CH Cr P¶PëPIPsC,C-, PiC-PrPIPëC%PμPSP° PiC-C,P»PëPIC-CfC,Ch, PjC-PsP· C- PiC-PrPIPëC%PμPSPμ CfP»PëPSPsPIPëPrC-P»PμPSPSCΠ, C%Ps PIPëPSPëPeP°P»Pë PiChPsC,CΠPiPsPj C-PSC,,CrP·C-C— C-ChPëPSPsC,PμPeP°PSCr P°P±Ps PIPiChPsPrPsPIP¶ PiPμChC€PëC... 24 PiPsPrPëPS PiC-CfP»CΠ C-PSC,,CrP·C-C—. PjC- CfPëPjPiC,PsPjPë P·PSPëPeP°P»Pë PiC-CfP»CΠ P·P°CfC,PsCfCrPIP°PSPSCΠ P°C,ChPsPiC-PSCr (PrPëPI. ChPsP·PrC-P» B«PhCfPsP±P»PëPIPsCfC,C- P·P°CfC,PsCfCrPIP°PSPSCΠB»).

#### PμPsPSPsC,PμChP°PiC-CΠ

PμChPs PiPμChPμP»C-C+PμPSC- PSPëP¶C+Pμ PiPsP±C-C+PSC- ChPμP°PeC+C-C—, ChPsP·C+C-PSPμPSC- CΠPe PjPsP¶P»PëPIPs P°P±Ps PNëPjPsPIC-ChPSPs PiPsPIB¶™ CΠP·P°PSC- C-P· P·P°CfC,PsCfCrPIP°PSPSCΠPj PiChPμPiP°ChP°C,Cr P+ChPëPSPsC,PμPeP°PS PhPjP°PeCfP°, PiPsPIC-PrPsPjP»CΠP»PsCfCΠ PrP»CΠ 765 PiP°C+C-C" PSC,C-PI, CΠPeC- PsC,ChPëPjCrPIP°P»Pë ChPμPePsPjPμPSPrPsPIP°PSCr PrPsP·Cr 350 PjPi/Pj² Cr PIPëPiP»CΠPrC- PjPsPSPsC,PμChP°PiC-C—. Pj PjPμP¶P°C... PePsP¶PSPsC— C+P°CfC,PsC,PSPsC— PiChCrPiPë PiPsP±C-C+PSC- ChPμP°PeC+C-C— PSP°PIPμPrPμPSC- Cr PiPsChCΠPrPeCr P·PjPμPSC€PμPSPSCΠ CfC,CrPiPμPSCΠ C,CΠP¶PePsCfC,C-. P§P°CfC,PsC,P° PiPsP±C-C+PSPëC... ChPμP°PeC+C-PNë PeP»P°CfPëC,,C-PeCrC"C,ChCfCΠ C,P°PePëPj C+PëPSPsPj: PrCrP¶Pμ C+P°CfC,Ps (≥1/10); C+P°CfC,Ps (PIC-Pr ≥1/100 PrPs <1/10); PSPμC+P°CfC,Ps (PIC-Pr ≥1/1000 PrPs <1/100); ChC-PrPePs (PIC-Pr ≥1/10000 PrPs <1/1000); PrCrP¶Pμ ChC-PrPePs (<1/10000); C+P°CfC,PsC,P° PSPμPIC-PrPsPjP° (PSPμ PjPsP¶Pμ P±CrC,Pë PsC+C-PSPμPSP° P· PSP°CΠIPSPëC... PrP°PSPëC...).

|                                                                                                                                                                                              |                |                               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|-------------------------------|
| PμPsP±C-C+PSC- ChPμP°PeC+C-C—, PiChPs CΠPeC- PiPsPIC-PrPsPjP»CΠP»Pë PiC-Pr C+P°Cf PjPsPSPsC,PμChP°PiC-C— C-ChPëPSPsC,PμPeP°PSPsPj (P·P° CfC...PμPjPsCh 350 PjPi/Pj² PePsP¶PSC- 3 C,PëP¶PSC-) |                |                               |
| PμP»P°Cf CfPëCfC,PμPjPë PsChPiP°PSC-PI MedDRA                                                                                                                                                | P§P°CfC,PsC,P° | PμPsP±C-C+PSP° ChPμP°PeC+C-CΠ |
| P+PSC,,PμPeC+C-C— C,P° C-PSPIP°P·C-C—                                                                                                                                                        | P§P°CfC,Ps     | P+PSC,,PμPeC+C-C—             |

|                                                                                                                |                        |                                                                                                                                                                                                                                                                                                              |
|----------------------------------------------------------------------------------------------------------------|------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| P— P±PsPeCf CÍPëCfC,PµPjPë<br>PeCĤPsPIC- C,P°<br>P»C-PjC,,P°C,PëC±PSPsC—<br>CÍPëCfC,PµPjPë                     | P"CrP¶Pµ<br>C±P°CfC,Ps | PkPµPNëC,CĤPsPiPµPSC-CĬ,<br>P°PSPµPjC-CĬ                                                                                                                                                                                                                                                                     |
|                                                                                                                | P§P°CfC,Ps             | PŸCĤPsPjP±PsC†PëC,PsPiPµPSC-CĬ,<br>C,,PµP±CĤPëP»CHßPSP°<br>PSPµPNëC,CĤPsPiPµPSC-CĬ                                                                                                                                                                                                                           |
| P— P±PsPeCf C,CĤP°PIP»PµPSPSCĬ<br>C,P° PjPµC,P°P±PsP»C-P·PjCf                                                  | P"CrP¶Pµ<br>C±P°CfC,Ps | P—PSPëP¶PµPSPSCĬ P°PiPµC,PëC,Cf                                                                                                                                                                                                                                                                              |
| P— P±PsPeCf PSPµCĤPIPsPIPsC—<br>CÍPëCfC,PµPjPë                                                                 | P"CrP¶Pµ<br>C±P°CfC,Ps | PfPsP»C-PSPµCĤPiC-C±PSPëPNë<br>CÍPëPSPrCĤPsPj                                                                                                                                                                                                                                                                |
| P— P±PsPeCf CëP»CrPSPePsPIPs-<br>PePëCëPePsPIPsPiPs C,CĤP°PeC,Cf                                               | P"CrP¶Pµ<br>C±P°CfC,Ps | P"C-P°CĤPµCĬ, P±P»CĤPIP°PSPSCĬ,<br>PSCfPrPsC,P°, P±C-P»CHß Cf<br>P¶PëPIPsC,C-                                                                                                                                                                                                                                |
|                                                                                                                | P§P°CfC,Ps             | P—P°PiPsCĤ                                                                                                                                                                                                                                                                                                   |
| P— P±PsPeCf CëPeC-CĤPë C,P°<br>PiC-PrCëPeC-CĤPSPsC—<br>C,PeP°PSPëPSPë                                          | P"CrP¶Pµ<br>C±P°CfC,Ps | PĥP»PsPiPµC†C-CĬ (PsP±PsCĤPsC,PSP°)                                                                                                                                                                                                                                                                          |
| P—P°PiP°P»CHßPSC- CĤPsP·P»P°PrPë<br>C,P° CĤPµP°PeC†C-C— Cf PjC-CfC†C-<br>PIPIPµPrPµPSPSCĬ<br>C-PSBĤ™C"PeC†C-C— | P"CrP¶Pµ<br>C±P°CfC,Ps | P—P°PiP°P»PµPSPSCĬ<br>CÍP»PëP·PsPIPëC... PsP±PsP»PsPSPsPe,<br>PiP°CĤCĬC±PeP°, P°CfC,PµPSC-CĬ                                                                                                                                                                                                                 |
| P·P°P±PsCĤP°C,PsCĤPSC-<br>PrPsCfP»C-PrP¶PµPSPSCĬ                                                               | P§P°CfC,Ps             | PµC-PrPIPëC%PµPSPSCĬ CĤC-PIPSCĬ<br>PeCĤPµP°C,PëPSC-PSCf PI PeCĤPsPIC-,<br>PiC-PrPIPëC%PµPSPSCĬ CĤC-PIPSCĬ<br>C,CĤP°PSCfP°PjC-PSP°P· (PĥP·PŸ C-<br>PĥPŸPŸ), PiC-PrPIPëC%PµPSPSCĬ<br>CĤC-PIPSCĬ P±C-P»C-CĤCfP±C-PSCf,<br>PiC-PrPIPëC%PµPSPSCĬ CĤC-PIPSCĬ<br>P»CfP¶PSPsC— C,,PsCfC,,P°C,P°P·Pë PI<br>PeCĤPsPIC- |

PĥPiPëCf PsPeCĤPµPjPëC... PiPsP±C-C±PSPëC... CĤPµP°PeC†C-PNë (PiCĤPë  
PjPsPSPsC,PµCĤP°PiC-C—).

PŸCĬP¶PeP° PrC-P°CĤPµCĬ CÍPiPsCfC,PµCĤC-PiP°P»P°CfCĬ Cf 20 % PiP°C†C-C"PSC,C-PI,  
CĬPeC- PrPsC,CĤPëPjCfPIP°P»PëCfCĬ CĤPµPePsPjPµPSPrP°C†C-PNë P· PePsPSC,CĤPsP»CĤ  
PrC-P°CĤPµC—. PJ C†PëPeP»P°C... C,PµCĤP°PiC-C—, C%Ps PiC-PrP»CĬPiP°P»Pë  
PsC†C-PSCĤPIP°PSPSCĤ, C,CĬP¶PeP° PrC-P°CĤPµCĬ CÍPiPsCfC,PµCĤC-PiP°P»P°CfCĬ Cf  
14 %. PŸPµCĤPµPrPSC-PNë C±P°Cf PrPs PiPsCĬPIPë CĤC-PrPePëC... PIPëPiPsCĤPsP¶PSPµPSCĤ  
PiC-CÍP»CĬ C-PSC,,CfP·C-C— C-CĤPëPSPsC,PµPeP°PSCf CÍC,P°PSPsPIPëPI 5 PrPSC-PI.

PkCzPrPsC,P° C- P±P»CĤPIP°PSPSCĬ PjP°P»Pë C,CĬP¶PePëPNë PiPµCĤPµP±C-Pi Cf  
PiCĤPëP±P»PëP·PSPs 10 % PiP°C†C-C"PSC,C-PI, CĬPeC- PsC,CĤPëPjCfPIP°P»Pë  
PiCĤPsC,PëP±P»CĤPIP°P»CHßPSC- PiCĤPµPiP°CĤP°C,Pë.

P—P°PiPsCĤ CÍPiPsCfC,PµCĤC-PiP°PICfCĬ Cf PjPµPSCë PSC-P¶ 10 % PiP°C†C-C"PSC,C-PI.

PkPµPNëC,CĤPsPiPµPSC-CĬ CÍPiPsCfC,PµCĤC-PiP°P»P°CfCĬ Cf 78,7 % PiP°C†C-C"PSC,C-PI,  
CÍPµCĤPµPr CĬPePëC... C,CĬP¶PePëPNë CÍC,CfPiC-PSCH PiPµCĤPµP±C-PiCf  
(PeC-P»CHßPeC-CfC,CHß PSPµPNëC,CĤPsC,,C-P»C-PI <500 PeP»C-C,PëPS/PjPj³)  
CÍPiPsCfC,PµCĤC-PiP°PICfCĬ Cf 22,6 % PiP°C†C-C"PSC,C-PI. PJ C†PëPeP»P°C...  
C,PµCĤP°PiC-C—, C%Ps PiC-PrP»CĬPiP°P»Pë PsC†C-PSCHPIP°PSPSCĤ, Cf 18 %  
PeC-P»CHßPeC-CfC,CHß PSPµPNëC,CĤPsC,,C-P»C-PI P±CfP»P° PjPµPSCëPµ

1000 PeP»C-C,PëPS/PjPj<sup>3</sup>, PIPeP»CĤC†P°CĤC†Pë 7,6 % P· PeC-P»CHĤPeC-CĤC,CĤ  
PSPµPNëC,CĤPsC,,C-P»C-PI <500 PeP»C-C,PëPS/PjPj<sup>3</sup>. PµPsPIPSPµ PIC-PrPSPsPIP»PµPSPSCĬ  
PĭPsPeP°P·PSPëPeC-PI P·P°P·PIPëC†P°PNë C,CĤPëPIP°P»Ps PrPs 22 PrPSC-PI.

P°P°CĤCĬC†PeP° P· PSPµPNëC,CĤPsPiPµPSC-C°CĤ C,CĬP¶PePsPiPs CĤC,CžPiPµPSCĬ  
CĤPiPsCĤC,PµCĤC-PiP°P»P°CĤCĬ Cr 6,2 % PiP°C†C-C°PSC,C-PI C,P° 1,7 % PICĤC-C...  
C†PëPeP»C-PI C,PµCĤP°PiC-C—.

P·PiC-P·PsPrPë C-PSC,,PµPeC†C-PNë C,CĤP°PiP»CĬP»PëCĤCĬ PiCĤPëP±P»PëP·PSPs Cr 10,3 %  
PiP°C†C-C°PSC,C-PI (2,5 % PICĤC-C... C†PëPeP»C-PI C,PµCĤP°PiC-C—) C,P° P±CrP»Pë  
PiPsPiBĤ™ CĬP·P°PSC- P· C,CĬP¶PePsCĤ PSPµPNëC,CĤPsPiPµPSC-C°CĤ PiCĤPëP±P»PëP·PSPs Cr  
5,3 % PiP°C†C-C°PSC,C-PI (1,1 % PICĤC-C... C†PëPeP»C-PI C,PµCĤP°PiC-C—); Cr  
PrPIPsC... PIPëPiP°PrPeP°C... C†Pµ CrCĤPeP»P°PrPSPµPSPSCĬ PiCĤPëP·PIPµP»Ps PrPs  
P»PµC,P°P»CHĤPSPsPiPs PSP°CĤP»C-PrPeCĤ.

PµCĤPs P°PSPµPjC-CĤ PiPsPIC-PrPsPjP»CĬP»Pë PiCĤPëP±P»PëP·PSPs Cr 58,7 %  
PiP°C†C-C°PSC,C-PI (8 % C-P· CĤC-PIPSµPj PiPµPjPsPiP»PsP±C-PSCr <8 Pi/PrP» C,P° 0,9 %  
C-P· CĤC-PIPSµPj PiPµPjPsPiP»PsP±C-PSCr <6,5 Pi/PrP»).

PŷCĤPsPjP±PsC†PëC,PsiPiPµPSC-CĬ (<100000 PeP»C-C,PëPS/PjPj<sup>3</sup>)  
CĤPiPsCĤC,PµCĤC-PiP°P»P°CĤCĬ Cr 7,4 % PiP°C†C-C°PSC,C-PI (1,8 % PICĤC-C...  
C†PëPeP»C-PI C,PµCĤP°PiC-C—), CĤPµCĤPµPr CĬPePëC... Cr 0,9 % PiP°C†C-C°PSC,C-PI  
(0,2 % C†PëPeP»C-PI C,PµCĤP°PiC-C—) PeC-P»CHĤPeC-CĤC,CĤ  
C,CĤPsPjP±PsC†PëC,C-PI P±CrP»P° PSP° CĤC-PIPS- £50000 PeP»C-C,PëPS/PjPj<sup>3</sup>. Pj  
PjP°PNëP¶Pµ PICĤC-C... PiP°C†C-C°PSC,C-PI PIC-PrPSPsPIP»PµPSPSCĬ  
PĭPsPeP°P·PSPëPeC-PI C,CĤPëPIP°P»Ps PrPs 22 PrPSC-PI.

P°P°CĤC,CĤPëPNë C...PsP»C-PSPµCĤPiC-C†PSPëPNë CĤPëPSPrCĤPsPj.

PŷCĤP°PSP·PëC,PsiCĤPSPëPNë PiPsCĤC,CĤPëPNë C...PsP»C-PSPµCĤPiC-C†PSPëPNë  
CĤPëPSPrCĤPsPj C,CĬP¶PePsPiPs CĤC,CĤPiPµPSCĬ CĤPiPsCĤC,PµCĤC-PiP°PICĤCĬ Cr 9 %  
PiP°C†C-C°PSC,C-PI, CĬPeC- PsC,CĤPëPjCrPIP°P»Pë PjPsPSPsC,PµCĤP°PiC-CĤ.

PĤCĤC,PµPSC-CĬ PjP°P»P° C,CĬP¶PePëPNë PiPµCĤPµP±C-Pi Cr PjPµPSC€Pµ 10 %  
PiP°C†C-C°PSC,C-PI, CĬPeC- PsC,CĤPëPjCrPIP°P»Pë PjPsPSPsC,PµCĤP°PiC-CĤ.  
PµCĤPëC†PëPSPSPs-PSP°CĤP»C-PrPePsPIPëPNë P·PiBĤ™ CĬP·PsPe PjC-P¶ C†PëPj CĬPIPëC%PµPj  
C,P° P·P°CĤC,PsiCĤC†PIP°PSPSCĬPj C-CĤPëPSPsC,PµPeP°PSCr PSPµ P±CrPI C†C-C,PePs  
PICĤC,P°PSPsPIP»PµPSPëPNë. P°P°CĤCĬC†PeP° Cr CĤP°P·C- PIC-PrCĤCĤC,PSPsCĤC,C-  
C-PSC,,PµPeC†C-C— P°P±Ps CĤC†PiCĤC,PSCĤPsC— C,CĬP¶PePsC— PSPµPNëC,CĤPsPiPµPSC-C—  
C,CĤP°PiP»CĬP»P°CĤCĬ Cr 12 % PiP°C†C-C°PSC,C-PI, CĬPeC- PsC,CĤPëPjCrPIP°P»Pë  
PjPsPSPsC,PµCĤP°PiC-CĤ.

P>P°P±PsCĤP°C,PsiCĤPSC- PiPsPeP°P·PSPëPePë

PĤPµPIPµP»PëPePµ P°P±Ps PiPsPjC-CĤPSPµ C,CĤP°PSP·PëC,PsiCĤPSPµ PiC-PrPIPëC%PµPSPSCĬ  
CĤPëCĤPsPIP°C,PePsPIPëC... CĤC-PIPS-PI C,CĤP°PSCĤP°PjC-PSP°P·, P»CrP¶PSPsC—  
C,,PsiCĤC,,P°C,P°P·Pë C†Pë P±C-P»C-CĤC†P±C-PSCr CĤPiPsCĤC,PµCĤC-PiP°P»PsCĤCĬ Cr 9,2 %,  
8,1 % C,P° 1,8 % PiP°C†C-C°PSC,C-PI PIC-PrPiPsPIC-PrPSPs Cr CĤP°P·C-  
PIC-PrCĤCĤC,PSPsCĤC,C- PiCĤPsPiCĤPµCĤC†PëC... PjPµC,P°CĤC,P°P·C-PI Cr  
PiPµC†C-PSC†C-. PĤPµPIPµP»PëPePµ P°P±Ps PiPsPjC-CĤPSPµ C,CĤP°PSP·PëC,PsiCĤPSPµ  
PiC-PrPIPëC%PµPSPSCĬ CĤC-PIPSĬ CĤPëCĤPsPIP°C,PePsPIPsiPs PeCĤPµP°C,PëPSC-PSCr  
CĤPiPsCĤC,PµCĤC-PiP°P»PsCĤCĬ Cr 7,3 % PiP°C†C-C°PSC,C-PI.

$P^{\circ}P \gg C - PSP^{\circ}PIP_{\mu}PrP_{\mu}PSC - \bar{P}iPsP \pm C - C \ddagger PSC - C\bar{H}P_{\mu}P^{\circ}PeC \ddagger C - C - III$  C-  
 IV  $C\bar{I}C, C\bar{r}\bar{P}iP_{\mu}PSC - PI$  C,  $C\bar{I}P\bar{I}PePsC\bar{I}C, C-, \bar{P}iC\bar{H}Ps$   $C\bar{I}PeC - \bar{P}iPsPIC - PrPsPjP \gg C\bar{I}P \gg P\bar{e}$   $C\bar{r}$   
 $\bar{P}iP^{\circ}C \ddagger C - C''PSC, C - PI, C\bar{I}PeC - PsC, C\bar{H}P\bar{e}PjC\bar{r}PIP^{\circ}P \gg P\bar{e}$   $PeP^{\circ}\bar{P}iP_{\mu}C \ddagger P\bar{e}C, P^{\circ}P \pm C - PS$   $C\bar{r}$   
 $PePsPjP \pm C - PSP^{\circ}C \ddagger C - C - P \cdot C - C\bar{H}P\bar{e}PSPsC, P_{\mu}PeP^{\circ}PSPsPj$  C,  $P^{\circ}$   
 $P \pm P_{\mu}PIP^{\circ}C \ddagger P\bar{e}P \cdot C\bar{r}PjP^{\circ}P \pm PsPj, PrPsPrP^{\circ}C, PePsPIP_s PrPs$  C,  $P\bar{e}C \dots C\bar{H}P_{\mu}P^{\circ}PeC \ddagger C - PN_2,$   
 $C\%Ps$   $C\bar{I}\bar{P}iPsC\bar{I}C, P_{\mu}C\bar{H}C - PiP^{\circ}P \gg P\bar{e}C\bar{I}C\bar{I} \bar{P}iC\bar{H}P\bar{e}$   $PjPsPSPsC, P_{\mu}C\bar{H}P^{\circ}\bar{P}iC - C -$   
 $PeP^{\circ}\bar{P}iP_{\mu}C \ddagger P\bar{e}C, P^{\circ}P \pm C - PSPsPj$   $P^{\circ}P \pm Ps$  C,  $C\bar{H}P^{\circ}\bar{P}iP \gg C\bar{I}P \gg P\bar{e}C\bar{I}C\bar{I} P \cdot PIP\bar{e}C\%PsC\bar{H}$   
 $C \ddagger P^{\circ}C\bar{I}C, PsC, PsC\bar{H}$   $\bar{P}iPsC\bar{H}C - PIPSC\bar{I}PSPs$   $P \cdot PjPsPSPsC, P_{\mu}C\bar{H}P^{\circ}\bar{P}iC - C''C\bar{H}$

PeP°PiPμC†PëC,P°P±C-PSPsPj.

PšP°CÍC,Ps, PiPsP±C-C†PSC- CĤPμP°PeC†C-C— III C,P° IV CÍC,CžPiPμPSC-PI:  
PSPμPNëC,CĤPsPiPμPSC-CĬ, C,CĤPsPjP±PsP/PμPjP±PsP»C-CĬ, P°CĤC,PμCĤC-P°P»CHbPSP°  
PiC-PiPμCĤC,PμPSP·C-CĬ, C-CëPμPjC-CĬ/C-PSC,,P°CĤPeC, PjC-PsPeP°CĤPrP°.

PμPsPIPSP° C-PSC,,PsCĤPjP°C†C-CĬ PiCĤPs PiPsP±C-C†PSC- CĤPμP°PeC†C-C—  
PeP°PiPμC†PëC,P°P±C-PSCr C,P° P±PμPIP°C†PëP·C†PjP°P±C† PSP°PIPμPrPμPSP° PI  
C-PSCÍC,CĤC†PeC†C-C— PrP»CĬ PjPμPrPëC†PSPsPiPs P·P°CÍC,PsCÍC†PIP°PSPSCĬ  
C†PëC... P»C-PeP°CĤCÍCHbPePëC... P·P°CÍPsP±C-PI.

P PsP·PIPëC,PsPe P°CĤC,PμCĤC-P°P»CHbPSPsC— PiC-PiPμCĤC,PμPSP·C-C— III CÍC,C†PiPμPSCĬ  
P±C†PI PsCÍPSPsPIPSPëPj CÍC†C,C,C”PIPëPj CĤPëP·PëPePsPj, PiPsPIbĤ™ CĬP·P°PSPëPj C-P·  
PrPsPrP°PIP°PSPSCĬPj P±PμPIP°C†PëP·C†PjP°P±C† PrPs P±PsP»CHCÍPSPsC— PrPsP·Pë  
PiCĤPμPiP°CĤP°C,C-PI C-CĤPëPSPsC,PμPeP°PS/5-PαPJ/PαPĤ. PĤCĤC-Pj C,PsPiPs, PiCĤPë  
P·P°CÍC,PsCÍC†PIP°PSPSC- C†C-C”C— CÍC...PμPjPë P»C-PeC†PIP°PSPSCĬ  
CÍPiPsCÍC,PμCĤC-PiP°P»PsCÍCĬ PSPμPIPμP»PëPePμ P·CĤPsCÍC,P°PSPSCĬ C†P°CÍC,PsC,Pë  
PiPsP±C-C†PSPëC... CĤPμP°PeC†C-PNë C...C-PjC-PsC,PμCĤP°PiC-C— III/IV CÍC,C†PiPμPSCĬ bĤ“  
PrC-P°CĤPμC— C,P° P»PμPNëPePsPiPμPSC-C—, PiPsCĤC-PIPSCĬPSPs P· PiP°C†C-C”PSC,P°PjPë,  
CĬPeC- PsC,CĤPëPjC†PIP°P»Pë C,C-P»CHbPePë P±PsP»CHCÍPSCr PrPsP·C†  
C-CĤPëPSPsC,PμPeP°PS/5-PαPJ/PαPĤ. P†PSCëP° C-PSC,,PsCĤPjP°C†C-CĬ PiCĤPs  
PiPsP±C-C†PSC- CĤPμP°PeC†C-C— PePsPjP±C-PSPsPIP°PSPsC— C,PμCĤP°PiC-C— P·  
P±PμPIP°C†PëP·C†PjP°P±PsPj PSP°PIPμPrPμPSP° PI C-PSCÍC,CĤC†PeC†C-C— PrP»CĬ  
PjPμPrPëC†PSPsPiPs P·P°CÍC,PsCÍC†PIP°PSPSCĬ C†CHbPsPiPs P»C-PeP°CĤCÍCHbPePsPiPs  
P·P°CÍPsP±C†.

P·C†P»Pë PiCĤPsPIPμPrPμPSC- PrPsCÍP»C-PrP¶PμPSPSCĬ P·P°CÍC,PsCÍC†PIP°PSPSCĬ  
C-CĤPëPSPsC,PμPeP°PSCr C† PePsPjP±C-PSP°C†C-C— P· 5-PαPJ C,P° PαPĤ PrP»CĬ  
P»C-PeC†PIP°PSPSCĬ PjPμC,P°CÍC,P°C,PëC†PSPsPiPs PePsP»PsCĤPμPeC,P°P»CHbPSPsPiPs  
CĤP°PeC†.

P”P°PSC- P±PμP·PiPμPePë C%PsPrPs PiPsP±C-C†PSPëC... CĤPμP°PeC†C-PNë,  
PsC,CĤPëPjP°PSC- C† PiCĤPsC†PμCÍC- PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PμPSCĤb,  
PiPsPeP°P·C†CHC,CHb, C%Ps PrC†P¶Pμ C†P°CÍC,Ps  
CÍPiPsCÍC,PμCĤC-PiP°CHC,CHbCÍCĬ PiPsP±C-C†PSC- CĤPμP°PeC†C-C— III P°P±Ps  
IV CÍC,C†PiPμPSCĬ P·P° CëPeP°P»PsCĤ PkP°C†C-PsPSP°P»CHbPSPsPiPs  
C-PSCÍC,PëC,C†C,C† CĤP°PeC†, CĬPeC-, PjPsP¶P»PëPIPs P°P±Ps PNëPjPsPIC-CĤPSPs,  
PiPsPIbĤ™ CĬP·P°PSC- C-P· P·P°CÍC,PsCÍC†PIP°PSPSCĬPj C,PμCĤP°PiC-C—, P·  
P±PsPeC† C,P°PePëC... PeP»P°CÍC-PI CÍPëCÍC,PμPj PsCĤPiP°PSC-PI: PeCĤPsPI C,P°  
P»C-PjC,,P°C,PëC†PSP° CÍPëCÍC,PμPjP°, CëP»C†PSPePsPIPs-PePëCëPePsPIPëPNë  
C,CĤP°PeC,, CëPeC-CĤP° C,P° PiC-PrCëPeC-CĤPSP° C,PeP°PSPëPSP°.

P”P°P»C- PSP°PIPμPrPμPSC- PiPsP±C-C†PSC- CĤPμP°PeC†C-C—, C%Ps, PjPsP¶P»PëPIPs P°P±Ps  
B PNëPjPsPIC-CĤPSPs, P±C†P»Pë PiPsPIbĤ™ CĬP·P°PSC- C-P· P·P°CÍC,PsCÍC†PIP°PSPSCĬPj  
C-CĤPëPSPsC,PμPeP°PSCr C- PiCĤPs CĬPeC- PiPsPIC-PrPsPjP»CĬP»Pë C†  
145 PiP°C†C-C”PSC,C-PI, CĬPeC- PsC,CĤPëPjC†PIP°P»Pë C-CĤPëPSPsC,PμPeP°PS C†  
CĤPμPePsPjPμPSPPrPsPIP°PSC-PNë PrPsP·C- 180 PjPi/Pj² C† PePsPjP±C-PSPsPIP°PSC-PNë  
C,PμCĤP°PiC-C— P· 5-PαPJ/PαPĤ PePsP¶PSC- 2 C,PëP¶PSC-.

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| P <sub>μ</sub> PsP±C-C±PSC- C <sub>7</sub> P <sub>μ</sub> P°PeC†C-C—, P <sub>i</sub> C <sub>7</sub> Ps C <sub>1</sub> PeC- P <sub>i</sub> PsPIC-PrPsPjP»C <sub>1</sub> P»Pë P <sub>i</sub> C-Pr C±P°C <sub>1</sub> PePsPjP±C-PSPsPIP°PSPsC— C,P <sub>μ</sub> C <sub>7</sub> P°P <sub>i</sub> C-C— P· C-C <sub>7</sub> PëPSPsC,P <sub>μ</sub> PeP°PSPsPj (P·P°C <sub>1</sub> C...P <sub>μ</sub> PjPsC <sub>7</sub> 180 PjPi/Pj <sup>2</sup> PePsP <sub>1</sub> PSC- 2 C,PëP <sub>1</sub> PSC-) |                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| P <sub>7</sub> P»P°C <sub>1</sub> C <sub>1</sub> PëC <sub>1</sub> C,P <sub>μ</sub> PjPë PsC <sub>7</sub> PiP°PSC-PI MedDRA                                                                                                                                                                                                                                                                                                                                                                    | P <sub>7</sub> P°C <sub>1</sub> C,P <sub>μ</sub> C,P°                              | P <sub>μ</sub> PsP±C-C±PSP° C <sub>7</sub> P <sub>μ</sub> P°PeC†C-C <sub>1</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| P†PSC,,P <sub>μ</sub> PeC†C-C— C,P° C-PSIPiP°P·C-C—                                                                                                                                                                                                                                                                                                                                                                                                                                           | P <sub>7</sub> P°C <sub>1</sub> C,P <sub>μ</sub>                                   | P†PSC,,P <sub>μ</sub> PeC†C-C—                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| P— P±PsPeC <sub>1</sub> C <sub>1</sub> PëC <sub>1</sub> C,P <sub>μ</sub> PjPë PeC <sub>7</sub> PsPIC- C,P° P»C-PjC,,P°C,PëC±PSPsC— C <sub>1</sub> PëC <sub>1</sub> C,P <sub>μ</sub> PjPë                                                                                                                                                                                                                                                                                                      | P°C <sub>1</sub> P <sub>1</sub> P <sub>μ</sub> C±P°C <sub>1</sub> C,P <sub>μ</sub> | P <sub>7</sub> C <sub>7</sub> PsPjP±PsC†PëC,P <sub>μ</sub> PiP <sub>μ</sub> PSC-C <sub>1</sub> , PSP <sub>μ</sub> PNëC,C <sub>7</sub> PsPiP <sub>μ</sub> PSC-C <sub>1</sub> , P°PSP <sub>μ</sub> PjC-C <sub>1</sub>                                                                                                                                                                                                                                                                                                                                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | P <sub>7</sub> P°C <sub>1</sub> C,P <sub>μ</sub>                                   | P <sub>μ</sub> P±C <sub>7</sub> PëP»C <sub>7</sub> PSP° PSP <sub>μ</sub> PNëC,C <sub>7</sub> PsPiP <sub>μ</sub> PSC-C <sub>1</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| P— P±PsPeC <sub>1</sub> C,C <sub>7</sub> P°PIP»P <sub>μ</sub> PSPSC <sub>1</sub> C,P° PjP <sub>μ</sub> C,P°P±PsP»C-P·PjC <sub>1</sub>                                                                                                                                                                                                                                                                                                                                                         | P°C <sub>1</sub> P <sub>1</sub> P <sub>μ</sub> C±P°C <sub>1</sub> C,P <sub>μ</sub> | P—PSPëP <sub>1</sub> P <sub>μ</sub> PSPSC <sub>1</sub> P°PiP <sub>μ</sub> C,PëC,C <sub>1</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| P— P±PsPeC <sub>1</sub> PSP <sub>μ</sub> C <sub>7</sub> PIPsPIPsC— C <sub>1</sub> PëC <sub>1</sub> C,P <sub>μ</sub> PjPë                                                                                                                                                                                                                                                                                                                                                                      | P°C <sub>1</sub> P <sub>1</sub> P <sub>μ</sub> C±P°C <sub>1</sub> C,P <sub>μ</sub> | P <sub>1</sub> PsP»C-PSP <sub>μ</sub> C <sub>7</sub> PiC-C±PSPëPNë C <sub>1</sub> PëPSP <sub>1</sub> C <sub>7</sub> PsPj                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| P— P±PsPeC <sub>1</sub> CëP»C <sub>1</sub> PSPePsPIPs-PePëCëPePsPIPsPiPs C,C <sub>7</sub> P°PeC,C <sub>1</sub>                                                                                                                                                                                                                                                                                                                                                                                | P°C <sub>1</sub> P <sub>1</sub> P <sub>μ</sub> C±P°C <sub>1</sub> C,P <sub>μ</sub> | P°C-P°C <sub>7</sub> P <sub>μ</sub> C <sub>1</sub> , P±P»C <sub>7</sub> PIP°PSPSC <sub>1</sub> , PSC <sub>1</sub> PrPsC,P°                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | P <sub>7</sub> P°C <sub>1</sub> C,P <sub>μ</sub>                                   | P°C-P»C <sub>7</sub> C <sub>1</sub> P <sub>1</sub> PëPIPsC,C-, P·P°PiPsC <sub>7</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| P— P±PsPeC <sub>1</sub> CëPeC-C <sub>7</sub> Pë C,P° P <sub>i</sub> C-PrCëPeC-C <sub>7</sub> PSPsC— C,PeP°PSPëPSPë                                                                                                                                                                                                                                                                                                                                                                            | P°C <sub>1</sub> P <sub>1</sub> P <sub>μ</sub> C±P°C <sub>1</sub> C,P <sub>μ</sub> | P <sub>7</sub> P»PsPiP <sub>μ</sub> C†C-C <sub>1</sub> (PsP±PsC <sub>7</sub> PsC,PSP°)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| P—P°PiP°P»C <sub>7</sub> PSC- C <sub>7</sub> PsP·P»P°PrPë C,P° C <sub>7</sub> P <sub>μ</sub> P°PeC†C-C— C <sub>1</sub> PjC-C <sub>1</sub> C†C-PIPIP <sub>μ</sub> PrP <sub>μ</sub> PSPSC <sub>1</sub> C-PSB <sub>7</sub> ™C°PeC†C-C—                                                                                                                                                                                                                                                           | P°C <sub>1</sub> P <sub>1</sub> P <sub>μ</sub> C±P°C <sub>1</sub> C,P <sub>μ</sub> | P—P°PiP°P»P <sub>μ</sub> PSPSC <sub>1</sub> C <sub>1</sub> P»PëP·PsPIPëC... PsP±PsP»PsPSPsPe, P°C <sub>1</sub> C,P <sub>μ</sub> PSC-C <sub>1</sub>                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | P <sub>7</sub> P°C <sub>1</sub> C,P <sub>μ</sub>                                   | P°C <sub>7</sub> C <sub>1</sub> C±PeP°                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| P·P°P±PsC <sub>7</sub> P°C,P <sub>μ</sub> C <sub>7</sub> PSC-PrPsC <sub>1</sub> P»C-PrP <sub>1</sub> P <sub>μ</sub> PSPSC <sub>1</sub>                                                                                                                                                                                                                                                                                                                                                        | P°C <sub>1</sub> P <sub>1</sub> P <sub>μ</sub> C±P°C <sub>1</sub> C,P <sub>μ</sub> | P <sub>μ</sub> C-PrPIPëC%P <sub>μ</sub> PSPSC <sub>1</sub> C <sub>7</sub> C-PIPS <sub>1</sub> C,C <sub>7</sub> P°PSC <sub>1</sub> P°PjC-PSP°P· (P <sub>7</sub> P·P <sub>7</sub> C-P <sub>7</sub> P <sub>7</sub> P <sub>7</sub> ), P <sub>i</sub> C-PrPIPëC%P <sub>μ</sub> PSPSC <sub>1</sub> C <sub>7</sub> C-PIPS <sub>1</sub> P±C-P»C-C <sub>7</sub> C <sub>1</sub> P±C-PSC <sub>1</sub> , P <sub>i</sub> C-PrPIPëC%P <sub>μ</sub> PSPSC <sub>1</sub> C <sub>7</sub> C-PIPS <sub>1</sub> P»C <sub>1</sub> P <sub>1</sub> PSPsC— C,,PsC <sub>1</sub> C,,P°C,P°P·Pë PI PeC <sub>7</sub> PsPIC- |

P<sub>7</sub>PiPëC<sub>1</sub> PsPeC<sub>7</sub>P<sub>μ</sub>PjPëC... P<sub>i</sub>PsP±C-C±PSPëC... C<sub>7</sub>P<sub>μ</sub>P°PeC†C-PNë (P<sub>i</sub>C<sub>7</sub>Pë PePsPjP±C-PSPsPIP°PSC-PNë C,P<sub>μ</sub>C<sub>7</sub>P°P<sub>i</sub>C-C—).

P<sub>7</sub>C<sub>1</sub>P<sub>1</sub>P<sub>μ</sub>PeP° PrC-P°C<sub>7</sub>P<sub>μ</sub>C<sub>1</sub> C<sub>1</sub>PiPsC<sub>1</sub>C,P<sub>μ</sub>C<sub>7</sub>C-PiP°P»P°C<sub>1</sub>C<sub>1</sub> C<sub>1</sub> 13,1 % P<sub>i</sub>P°C†C-C°PSC,C-PI, C<sub>1</sub>PeC- PrPsC,C<sub>7</sub>PëPjC<sub>1</sub>PIP°P»PëC<sub>1</sub>C<sub>1</sub> C<sub>7</sub>P<sub>μ</sub>PePsPjP<sub>μ</sub>PSP<sub>1</sub>P°C†C-PNë P· PePsPSC,C<sub>7</sub>PsP»C<sub>7</sub>PrC-P°C<sub>7</sub>P<sub>μ</sub>C—. Pj C†PëPeP»P°C... C,P<sub>μ</sub>C<sub>7</sub>P°P<sub>i</sub>C-C—, C%Ps P<sub>i</sub>C-PrP»C<sub>1</sub>PiP°P»Pë PsC†C-PSC<sub>1</sub>PIP°PSPSC<sub>7</sub>, C,C<sub>1</sub>P<sub>1</sub>PeP° PrC-P°C<sub>7</sub>P<sub>μ</sub>C<sub>1</sub> C<sub>1</sub>PiPsC<sub>1</sub>C,P<sub>μ</sub>C<sub>7</sub>C-PiP°P»P°C<sub>1</sub>C<sub>1</sub> C<sub>1</sub> 3,9 %.

P<sub>7</sub>C<sub>1</sub>PrPsC,P° C- P±P»C<sub>7</sub>PIP°PSPSC<sub>1</sub> C,C<sub>1</sub>P<sub>1</sub>PePsPiPs C<sub>1</sub>C,C<sub>1</sub>PiP<sub>μ</sub>PSC<sub>1</sub> C<sub>1</sub>PiPsC<sub>1</sub>C,P<sub>μ</sub>C<sub>7</sub>C-PiP°P»PëC<sub>1</sub>C<sub>1</sub> P· PSPëP<sub>1</sub>C±PsC<sub>7</sub> C±P°C<sub>1</sub>C,P<sub>μ</sub>C,P<sub>μ</sub>C<sub>7</sub> (C<sub>1</sub> 2,1 % C,P° 2,8 % P<sub>i</sub>P°C†C-C°PSC,C-PI PIC-PrPiPsPIC-PrPSPs).

P—P°PiPsC<sub>7</sub> PIPSP°C<sub>1</sub>P»C-PrPsPe P·P°C<sub>1</sub>C,P<sub>μ</sub>C<sub>1</sub>C<sub>1</sub>PIP°PSPSC<sub>1</sub> C-C<sub>7</sub>PëPSPsC,P<sub>μ</sub>PeP°PSC<sub>1</sub> C,P°/P°P±Ps P»PsPiP<sub>μ</sub>C<sub>7</sub>P°PjC-PrC<sub>1</sub> C<sub>1</sub>PiPsC<sub>1</sub>C,P<sub>μ</sub>C<sub>7</sub>C-PiP°PIC<sub>1</sub>C<sub>1</sub> C<sub>1</sub> 3,4 % P<sub>i</sub>P°C†C-C°PSC,C-PI.

P<sub>7</sub>P<sub>μ</sub>PNëC,C<sub>7</sub>PsPiP<sub>μ</sub>PSC-C<sub>1</sub> C<sub>1</sub>PiPsC<sub>1</sub>C,P<sub>μ</sub>C<sub>7</sub>C-PiP°P»P°C<sub>1</sub>C<sub>1</sub> C<sub>1</sub> 82,5 % P<sub>i</sub>P°C†C-C°PSC,C-PI,

$\text{Cl}^+\text{P}\mu\text{C}\text{H}_3\text{P}\mu\text{Pr} \text{ ClP}\text{eP}\text{eC}\dots \text{C}, \text{ClP}\mu\text{P}\text{eP}\text{eP}\text{N}\text{e} \text{ Cl}^+\text{C}, \text{Cr}^+\text{P}\text{ic}-\text{PSC}\text{H} \text{ P}\text{ip}\mu\text{C}\text{H}_3\text{P}\mu\text{P}\pm\text{C}-\text{PiCr}$   
 $(\text{PeC}-\text{P}\gg\text{CH}\text{PeC}-\text{Cl}^+\text{C}, \text{CH} \text{ PSP}\mu\text{PN}\text{eC}, \text{C}\text{H}_3\text{PsC}, \text{C}-\text{P}\gg\text{C}-\text{PI} <500 \text{ PeP}\gg\text{C}-\text{C}, \text{P}\text{ePS}/\text{PjPj}^3) \text{ P}\pm\text{CrPI} \text{ Cr}^+ 9,8 \%$   
 $\text{P}\text{ip}^+\text{C}^+\text{C}-\text{C}^-\text{PSC}, \text{C}-\text{PI}. \text{PJ} \text{ C}^+\text{P}\text{eP}\text{eP}\gg\text{P}^+\text{C}\dots \text{C}, \text{P}\mu\text{C}\text{H}_3\text{P}^+\text{P}\text{ic}-\text{C}-, \text{C}\%_{\text{oo}}\text{Ps} \text{ P}\text{ic}-\text{PrP}\gg\text{ClP}\text{ip}\text{P}^+\text{P}\gg\text{P}\text{e}$   
 $\text{PsC}^+\text{C}-\text{PSC}\text{HPIP}^+\text{PSPSC}\text{H}, \text{Cr}^+ 67,3 \%$ 
 $\text{P}\text{ip}^+\text{C}^+\text{C}-\text{C}^-\text{PSC}, \text{C}-\text{PI} \text{ PeC}-\text{P}\gg\text{CH}\text{PeC}-\text{Cl}^+\text{C}, \text{CH}$   
 $\text{PSP}\mu\text{PN}\text{eC}, \text{C}\text{H}_3\text{PsC}, \text{C}-\text{P}\gg\text{C}-\text{PI} \text{ P}\pm\text{CrP}\gg\text{P}^+ \text{ PjP}\mu\text{PSC}\text{eP}\mu 1000 \text{ PeP}\gg\text{C}-\text{C}, \text{P}\text{ePS}/\text{PjPj}^3,$   
 $\text{PIPeP}\gg\text{C}\text{H}\text{C}\ddagger\text{P}^+\text{C}\text{H}\text{C}\ddagger\text{P}\text{e} 2,7 \%$ 
 $\text{P}\cdot \text{PeC}-\text{P}\gg\text{CH}\text{PeC}-\text{Cl}^+\text{C}, \text{C}\text{H} \text{ PSP}\mu\text{PN}\text{eC}, \text{C}\text{H}_3\text{PsC}, \text{C}-\text{P}\gg\text{C}-\text{PI} <500$   
 $\text{PeP}\gg\text{C}-\text{C}, \text{P}\text{ePS}/\text{PjPj}^3. \text{P}\mu\text{PsPIPSP}\mu \text{ PIC}-\text{PrPSPsPIP}\gg\text{P}\mu\text{PSPSC}\text{Cl} \text{ P}\text{ipPsPeP}^+\text{P}\cdot\text{PSP}\text{ePeC}-\text{PI}$   
 $\text{P}\cdot\text{P}^+\text{P}\cdot\text{PIP}\text{eC}\ddagger\text{P}^+\text{PN}\text{e} \text{ C}, \text{C}\text{H}_3\text{P}\text{ePIP}^+\text{P}\gg\text{Ps} \text{ PrPs} 7\text{b}\text{H}^+ 8 \text{ PrPSC}-\text{PI}.$

[illegible]

$P\check{y}C\check{H}PsPjP\pm PsC\check{t}P\check{e}C,PsPiP\mu PSC-Cl$  ( $<100000$   $PeP\gg C-C, P\check{e}PS/PjPj^3$ )  
 $C\acute{r}PiPsC\acute{r}C, P\mu C\check{H}C-PiP^\circ P\gg P^\circ C\acute{r}C\check{Cl}$   $Cr$  32,6 %  $PiP^\circ C\check{t}C-C''PSC, C-PI$   $C, P^\circ$  21,8 %  $PI C\acute{r}C-C...$   
 $C\check{t}P\check{e}PeP\gg C-PI$   $C, P\mu C\check{H}P^\circ PiC-C-$ .  $P'P\check{e}PiP^\circ PrPeC-PI$   $C, C\check{H}PsPjP\pm PsC\check{t}P\check{e}C, PsPiP\mu PSC-C-$   
 $C, ClP\check{r}PePsPiPs$   $C\acute{r}C, C\acute{r}PiP\mu PSC\check{Cl}$  ( $<50000$   $PeP\gg C-C, P\check{e}PS/PjPj^3$ )  $PSP\mu$   
 $C\acute{r}PiPsC\acute{r}C, P\mu C\check{H}C-PiP^\circ P\gg PsC\acute{r}C\check{Cl}$ .

$\text{P}\ddot{\text{Y}}\text{C}\ddot{\text{H}}\text{P}^{\circ}\text{PSP}\cdot\text{P}\ddot{\text{e}}\text{C}, \text{PsC}\ddot{\text{H}}\text{PSP}\ddot{\text{e}}\text{PN}_{\text{e}} \text{ PiPsC}\acute{\text{I}}\text{C}, \text{C}\ddot{\text{H}}\text{P}\ddot{\text{e}}\text{PN}_{\text{e}} \text{ C} \dots \text{PsP} \gg \text{C} - \text{PSP}_{\text{p}}\text{C}\ddot{\text{H}}\text{PiC} - \text{C}\ddagger\text{PSP}\ddot{\text{e}}\text{PN}_{\text{e}}$   
 $\text{C}\acute{\text{I}}\text{P}\ddot{\text{e}}\text{PSPrC}\ddot{\text{H}}\text{PsPj} \text{ C}, \text{C}\ddot{\text{I}}\text{P}\text{¶PePsPiPs} \text{ C}\acute{\text{I}}\text{C}, \text{C}\acute{\text{r}}\text{P}\ddot{\text{i}}\text{P}_{\text{p}}\text{PSC}\ddot{\text{I}} \text{ C}\acute{\text{I}}\text{P}\ddot{\text{i}}\text{PsC}\acute{\text{I}}\text{C}, \text{P}_{\text{p}}\text{C}\ddot{\text{H}}\text{C} - \text{PiP}^{\circ}\text{PiC}\acute{\text{I}}\text{C}\ddot{\text{I}} \text{ C}\acute{\text{r}} \text{ 1,4 \%}$   
 $\text{P}\ddot{\text{i}}\text{P}^{\circ}\text{C}\ddagger\text{C} - \text{C}^{\circ}\text{PSC}, \text{C} - \text{PI}, \text{C}\ddot{\text{I}}\text{PeC} - \text{PsC}, \text{C}\ddot{\text{H}}\text{P}\ddot{\text{e}}\text{PjC}\acute{\text{r}}\text{PiP}^{\circ}\text{P} \gg \text{P}\ddot{\text{e}} \text{ PePsPjP} \pm \text{C} - \text{PSPsPiP}^{\circ}\text{PSC}\acute{\text{r}}$   
 $\text{C}, \text{P}_{\text{p}}\text{C}\ddot{\text{H}}\text{P}^{\circ}\text{PiC} - \text{C}\ddot{\text{H}}.$

[illegible]

PyC<sub>7</sub>H<sub>5</sub>P<sup>o</sup>PSP·PëC,PsC<sub>7</sub>H<sub>5</sub>PSP<sub>μ</sub> PiC-PrPIPeC%<sub>0</sub>P<sub>μ</sub>PSPSC<sub>Π</sub> (I C,P<sup>o</sup> II C<sub>1</sub>C,C<sub>1</sub>PiP<sub>μ</sub>PSC-PI  
C,C<sub>Π</sub>P<sub>¶</sub>PePsC<sub>1</sub>C,C-) C<sub>1</sub>PëC<sub>7</sub>H<sub>5</sub>PsPIP<sup>o</sup>C,PePsPIPëC... C<sub>7</sub>H<sub>5</sub>-PIPSC-PI P<sub>h</sub>P<sub>¶</sub>P<sub>¶</sub>, P<sub>h</sub>P<sub>¶</sub>P<sub>¶</sub>, P<sub>¶</sub>C<sub>1</sub>P<sub>¶</sub>PSPsC-

C,,PsCfC,,P°C,P°P·Pë P°P±Ps P±C-P»C-CfCfP±C-PSCf CfPïPsCfC,PµCfC-PiP°P»PsCfCf Cf  
15 %, 11 %, 11 % C,P° 10 % PiP°C†C-C"PS C,C-PI PIC-PrPiPsPIC-PrPSPs Cf CfP°P·C-  
PIC-PrCfCfC,PSPsCfC,C- PiCfPsPiCfPµCfCfCfC±PëC... PjPµC,P°CfC,P°P·C-PI Cf  
PiPµC±C-PSC†C-. PÿCfP°PSP·PëC,PscfPSPµ PiC-PrPiPëC%PµPSPSCf CfC-PIPS C-PI C†PëC...  
PiPsPeP°P·PSPëPeC-PI III CfC,CfPiPµPSCf C,CfP¶PePsCfC,C- CfPiPsCfC,PµCfC-PiP°P»PsCfCf  
Cf 0 %, 0 %, 0 % C,P° 1 % PiP°C†C-C"PS C,C-PI PIC-PrPiPsPIC-PrPSPs. P'PëPiP°PrPeC-PI  
IV CfC,CfPiPµPSCf C,CfP¶PePsCfC,C- PrP°PSPsC— PiPsP±C-C±PSPsC— CfPµP°PeC†C-C—  
PSPµ CfPiPsCfC,PµCfC-PiP°P»PsCfCf.

P"CrP¶Pµ CfC-PrPePs PSP°PrC...PsPrPëP»Pë PiPsPIC-PrPsPjP»PµPSPSCf PiCfPs  
PiC-PrPiPëC%PµPSPSCf CfC-PIPS C-PI P°PjC-P»P°P·Pë C,P°/P°P±Ps P»C-PiP°P·Pë.

PµPsPIC-PrPsPjP»CfP»Pë PiCfPs CfC-PrPeC-CfPSC- PIPëPiP°PrPePë  
PiC-PiPsPeP°P»C-C"PjC-C— C,P° PiC-PiPsPSP°C,CfC-C"PjC-C—, PiPsCfPIP° CfPePëC...  
P±CfP»P° PiPµCfPµPiP°P¶PSPs PiPsPiBf™ CfP·P°PSP° P· PrC-P°CfPµC"CF C-  
P±P»CfPIP°PSPSCfPj.

P†PSC€C- PiPsP±C-C±PSC- CfPµP°PeC†C-C—, PiCfPs CfPeC- PiPsPIC-PrPsPjP»CfP»Pë Cf  
PeP»C-PSC-C±PSPëC... PrPsCfP»C-PrP¶PµPSPSCfC... P·P°CfC,PscfCfPIP°PSPSCf  
C-CfPëPSPsC,PµPeP°PSCf P·P° CfC...PµPjPsCf 1 CfP°P· PSP° C,PëP¶PrPµPSCf.

Pj PeP»C-PSC-C±PSPëC... PrPsCfP»C-PrP¶PµPSPSCfC... P·P°CfC,PscfCfPIP°PSPSCf  
C-CfPëPSPsC,PµPeP°PSCf PiPsPIC-PrPsPjP»CfP»Pë PiCfPs PSP°CfC,CfPiPSC- PiPsP±C-C±PSC-  
CfPµP°PeC†C-C—, PiPsPiBf™ CfP·P°PSC- C-P· P·P°CfC,PscfCfPIP°PSPSCfPj  
PiCfPµPiP°CfP°C,Cf: P±C-P»Cf, CfPµPiCfPëCf, CfPsP·P»P°PrPë P· P±PsPeCf PiCfCfPjPsC—  
PePëC€PePë, PeP°PSPPrPëPrPsPjC-PePsP· C€P»CfPSPePsIPs-PePëC€PePsPiPs C,CfP°PeC,Cf,  
PiC-PiPsPjP°PiPSC-C"PjC-Cf, PIPëCfPëPiP°PSPSCf, CfPëPjPiC,PsPjPë P· P±PsPeCf  
C€PeC-CfPë, PiPsCfCfC€PµPSPSCf C...PsPrPë, CfPiP»CfC,P°PSC-CfC,Cf  
CfPIC-PrPsPjPsCfC,C-, PiPsP»PsPIPSPëPN± P±C-P»Cf, PSPµPiCfPëC,PsPjPSC-CfC,Cf,  
PiCfPëPiP»PëPIPë, P±CfP°PrPëPeP°CfPrC-Cf, C-PSC,,PµPeC†C-C—  
CfPµC±PsPIPëPIC-PrPSPëC... C€P»CfC...C-PI, P±C-P»Cf Cf PiCfCfPrCfC...,  
PiC-PrPiPëC%PµPSPSCf PiP°PjPjP°PiP»CfC,P°PjC-P»C,CfP°PSCfC,,PµCfP°P·Pë,  
PeCfPsPIPsPIPëP»PëPIPë, CfPëPSPrCfPsPj P»C-P·PëCfCf PiCfC...P»PëPSPë, CfPµCfC†PµPIPs-  
CfCfPrPëPSPSC- P·P°C...PIPsCfCfPIP°PSPSCf (CfC,PµPSPsPeP°CfPrC-Cf, P·CfPiPëPSPeP°  
CfPµCfC†Cf, C-PSC,,P°CfPeC, PjC-PsPeP°CfPrP°, C-C€PµPjC-Cf PjC-PsPeP°CfPrP°,  
CfPsP·P»P°PrPë P· P±PsPeCf PiPµCfPëC,,PµCfPëC±PSPëC... CfCfPrPëPS, CfCfPrPëPSPSC-  
P·P°C...PIPsCfCfPIP°PSPSCf) C- C,CfPsPjP±PsPµPjP±PsP»C-C±PSC- CfPIPëC%P°  
(P°CfC,PµCfC-P°P»CfPSPëPN± C,CfPsPjP±PsP·, C-C€PµPjC-C±PSPëPN± C-PSCfCfP»CfC,,  
PiPsCfCfC€PµPSPSCf PjPsP·PePsPIPsPiPs PeCfPsPIPsPsP±C-PiCf, PiP»PëP±PsPePëPN±  
C,CfPsPjP±PsC,,P»PµP±C-C,, PµPjP±PsP»C-Cf CfCfPrPëPS PSPëP¶PSCfPsC—  
PeC-PSC†C-PIPePë, P»PµPiPµPSPµPIP° PµPjP±PsP»C-Cf, C,CfPsPjP±PsC,,P»PµP±C-C,,  
C,CfPsPjP±PsP· C- CfP°PiC,PsPIPëPN± P»PµC,P°P»CfPSPëPN± PSP°CfP»C-PrPsPe) (PrPëPI.  
CfPsP·PrC-P» B«PhCfPsP±P»PëPIPsCfC,C- P·P°CfC,PscfCfPIP°PSPSCfB»).

PµC-CfP»CfCfPµC"CfC,CfP°C†C-PN±PSPµ CfPiPsCfC,PµCfPµP¶PµPSPSCf.

PfP°CfC,Psc,P° PIPëPSPëPePSPµPSPSCf PiPsP±C-C±PSPëC... CfPµP°PeC†C-PN± Cf  
PiPµCfC-PsPrC- PiC-CfP»CfCfPµC"CfC,CfP°C†C-PN±PSPsPiPs  
CfPiPsCfC,PµCfPµP¶PµPSPSCf PSPµPIC-PrPsPjP° (PSPµPjPsP¶P»PëPIPs PICfC,P°PSPsPIPëC,Pë  
PSP° PsCfPSPsPIC- C-CfPSCfCfC±PëC... PrP°PSPëC...).

[illegible]

|                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|----------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| P— P±PsPeCf C€P»CfPSPePsPIPs-<br>PeP€C€PePsPIPsPiPs C,ChP°PeC,Cf                                               | PљP€C€PePsPIP° PSPµPiCћPsC...C-PrPSC-CfC,Ch;<br>C-P»PµCfCf: C,P°PePsP¶ PiPsPIC-PrPsPjP»C¶P»P€ PiCћPs<br>PIP€PiP°PrPeP€ C-P»PµCfCfCf P±PµP·<br>PiPsPiPµCћPµPrPSCћPsPiPs PIP€PSP€PePSPµPSPSC¶<br>PePsP»C-C,Cf; PjPµPiP°PePsP»PsPS; C€P»CfPSPePsPIPs-<br>PeP€C€PePsPIP€PNё PeCћPsPIPsPIP€P»P€PI; PePsP»C-C,, PI<br>PsPeCћPµPjP€C... PIP€PiP°PrPeP°C... PePsP»C-C, P±CfPI<br>CfCfPeP»P°PrPSPµPSP€PNё PIP€CћP°P·PeP°PjP€,<br>PeCћPsPIPsC,PµC†PµCћ, C-P»PµCfCfPsPj P°P±Ps<br>C-PSC,,PµPeC†C-C”Cћ; C,P€C,,P»C-C,;<br>C-C€PµPjC-C†PSP€PNё PePsP»C-C,; PIP€CћP°P·PePsPIP€PNё<br>PePsP»C-C,; C€P»CfPSPePsPIPs-PeP€C€PePsPIP°<br>PeCћPsPIPsC,PµC†P°; CfP€PjPiC,PsPjP°C,P€C†PSPµ P°P±Ps<br>P±PµP·CfP€PjPiC,PsPjPSPµ PiC-PrPIP€C%PµPSPSC¶<br>CћC-PIPS¶ C,,PµCћPjPµPSC,C-PI<br>PiC-PrC€P»CfPSPePsPIPsC— P·P°P»PsP·P€;<br>PiPµCћC,,PsCћP°C†C-C¶ PeP€C€PµC†PSP€PeCf |
| P— P±PsPeCf C€PeC-CћP€ C,P°<br>PiC-PrC€PeC-CћPSPsC—<br>C,PeP°PSP€PSP€                                          | P€PeC-CћPSC- CћPµP°PeC†C-C—                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| P—P°PiP°P»CHPSC- CћPsP·P»P°PrP€<br>C,P° CћPµP°PeC†C-C— Cf PjC-CfC†C-<br>PIPIPµPrPµPSPSC¶<br>C-PSбћ™C”PeC†C-C—  | P PµP°PeC†C-C— Cf PjC-CfC†C- C-PSC,,CfP·C-C—                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| P>P°P±PsCћP°C,PsCћPSC-<br>PrPsCfP»C-PrP¶PµPSPSC¶                                                               | PµC-PrPIP€C%PµPSPSC¶ CћC-PIPS¶ P°PjC-P»P°P·P€ PI<br>PeCћPsPIC-; PiC-PrPIP€C%PµPSPSC¶ CћC-PIPS¶<br>P»C-PiP°P·P€; PiC-PiPsPeP°P»C-C”PjC-C¶;<br>PiC-PiPsPSP°C,CћC-C”PjC-C¶, C%Ps PiPµCћPµPIP°P¶PSPs<br>PiPsPiбћ™C¶P·P°PSP° P· PrC-P°CћPµC”Cћ C,P°<br>P±P»CћPIP°PSPSC¶Pj; PrCfP¶Pµ CћC-PrPePs<br>PSP°PrC...PsPrP€P»P€ PiPsPIC-PrPsPjP»PµPSPSC¶ PiCћPs<br>PIP€PiP°PrPeP€ PiC-PrPIP€C%PµPSPSC¶<br>CfP€CћPsPIP°C,PePsPIP€C... CћC-PIPS-C-PI<br>C,CћP°PSCfP°PjC-PSP°P· (PћPŸPŸ C- PћP·PŸ) Cf CћP°P·C-<br>PIC-PrCfCfC,PSPsCfC,C- PiCћPsPiCћPµCfCfCћC†P€C...<br>PjPµC,P°CfC,P°P·C-PI PiPµC†C-PSPeP€                                                                                                                                                                                                                                                           |
| P— P±PsPeCf Pjбћ™C¶P·PsPIPs-<br>CfPePµP»PµC,PSPsC— CfP€CfC,PµPjP€<br>C,P° CfPiPsP»CfC†PSPsC—<br>C,PeP°PSP€PSP€ | PŸPePsCћPsC†PµPSPSC¶ Pjбћ™C¶P·C-PI P°P±Ps<br>CfCfPrPsPjP€                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| P— P±PsPeCf PSP€CћPsPe C,P°<br>CfPµC†PsPIP€PrC-P»CHPSPsC—<br>CfP€CfC,PµPjP€                                    | PµPsCћCfC€PµPSPSC¶ C,,CfPSPeC†C-C— PSP€CћPsPe C-<br>PiPsCfC,CћP° PSP€CћPePsPIP°<br>PSPµPrPsCfC,P°C,PSC-CfC,Ch P·P°P·PIP€C†P°PNё<br>CfPiPsCfC,PµCћC-PiP°P»P€CfC¶ Cf PiP°C†C-C”PSC,C-PI P·<br>C-PSC,,C-PeCfPIP°PSPSC¶Pj C,P°/P°P±Ps<br>PiC-PiPsPIPsP»PµPjC-C”Cћ, C%Ps<br>CћPsP·PIP€PSCfP»P°CfC¶ PIPSP°CfP»C-PrPsPe<br>C,C¶P¶PePsC— C€P»CfPSPePsPIPs-PeP€C€PePsPIPsC—<br>C,PsPeCfP€C†PSPsCfC,C-***; PSP€CћPePsPIP°<br>PSPµPrPsCfC,P°C,PSC-CfC,Ch***                                                                                                                                                                                                                                                                                                                                                                                                    |
| P— P±PsPeCf CfCfPrP€PS                                                                                         | P”C-PiPsC,PµPSP·C-C¶***                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| P— P±PsPeCf<br>PiPµPiP°C,PsP±C-P»C-P°CћPSPsC—<br>CfP€CfC,PµPjP€                                                | PŸC,PµP°C,PsPiPµPiP°C,P€C,; CfC,PµP°C,PsP·<br>PiPµC†C-PSPeP€                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |

\*PќP°PiCћP€PeP»P°Pr, PiPSPµPIPIPsC†P€CfC,PSP° PiPSPµPIPIPsPSC-C¶,  
P±CћPsPSC...PsP»PµPiPµPSPµPIP€PNё P°CfPiPµCћPiC-P»CHPsP·, CfP€CfC,PµPjPSP€PNё  
PeP°PSPrP€PrPsP·.

**\*\*P<sub>h</sub>PiP<sub>μ</sub>CH<sub>3</sub>C-P·C<sub>r</sub>PIP°P»CH<sub>3</sub>PSPëPN<sub>2</sub> PiP<sub>μ</sub>CH<sub>3</sub>PiP<sub>μ</sub>CT<sub>r</sub>, PiCH<sub>3</sub>PëPi<sub>r</sub>, CH<sub>3</sub>P<sub>μ</sub>P°PeC,PëPIP°CT<sub>r</sub>C-CT<sub>r</sub> PiP<sub>μ</sub>PiP°C,PëC,C<sub>r</sub> P', C<sub>t</sub>PëC,PsPjP<sub>μ</sub>PiP°P»PsPIC-CH<sub>3</sub>C<sub>r</sub>CT<sub>r</sub>PSPëPN<sub>2</sub> PePsP»C-C,,.**

**\*\*\*P C-PrPeC-CT<sub>r</sub>PSC- PIPëPiP°PrPePë PSPëCH<sub>3</sub>PePsPIPsC— PSP<sub>μ</sub>PrPsCT<sub>r</sub>C,P°C,PSPsCT<sub>r</sub>C,C-, PiC-PiPsC,P<sub>μ</sub>PSP·C-C— P°P±Ps CT<sub>r</sub>P<sub>μ</sub>CH<sub>3</sub>C<sub>t</sub>P<sub>μ</sub>PIPs-CT<sub>r</sub>C<sub>r</sub>PrPëPSPSPsC— PSP<sub>μ</sub>PrPsCT<sub>r</sub>C,P°C,PSPsCT<sub>r</sub>C,C- CT<sub>r</sub>PiPsCT<sub>r</sub>C,P<sub>μ</sub>CH<sub>3</sub>C-PiP°P»PëCT<sub>r</sub>CT<sub>r</sub> C<sub>r</sub> PiP°CT<sub>r</sub>C-C”PSC,C-PI, CT<sub>r</sub>PeC- PiP<sub>μ</sub>CH<sub>3</sub>P<sub>μ</sub>PSP<sub>μ</sub>CT<sub>r</sub>P»Pë P·PSP<sub>μ</sub>PIPsPrPSP<sub>μ</sub>PSPSCCT<sub>r</sub> PIPSP°CT<sub>r</sub>P»C-PrPsPe PrC-P°CH<sub>3</sub>P<sub>μ</sub>C— C,P°/P°P±Ps P±P»CH<sub>3</sub>PIP°PSPSCCT<sub>r</sub> C<sub>t</sub>Pë CT<sub>r</sub>P<sub>μ</sub>PiCT<sub>r</sub>PëCT<sub>r</sub>C<sub>r</sub>.**

**P<sub>μ</sub>PsPIC-PrPsPjP»P<sub>μ</sub>PSPSCCT<sub>r</sub> PiCH<sub>3</sub>Ps PiC-PrPsP·CH<sub>3</sub>CH<sub>3</sub>PIP°PSC- PiPsP±C-C<sub>t</sub>PSC- CH<sub>3</sub>P<sub>μ</sub>P°PeCT<sub>r</sub>C-C—**

**P—PIC-C,C<sub>r</sub>PIP°PSPSCCT<sub>r</sub> PiCH<sub>3</sub>Ps PiC-PrPsP·CH<sub>3</sub>CH<sub>3</sub>PIP°PSC- PiPsP±C-C<sub>t</sub>PSC- CH<sub>3</sub>P<sub>μ</sub>P°PeCT<sub>r</sub>C-C— PiC-CT<sub>r</sub>P»CT<sub>r</sub> CH<sub>3</sub>P<sub>μ</sub>C”CT<sub>r</sub>C,CH<sub>3</sub>P°CT<sub>r</sub>C-C— P»C-PeP°CH<sub>3</sub>CT<sub>r</sub>CH<sub>3</sub>PePsPiPs P·P°CT<sub>r</sub>PsP±C<sub>r</sub> C” PIP°P¶P»PëPIPëPj. P’PsPSPs PrP°C” P·PjPsPiC<sub>r</sub> PiCH<sub>3</sub>PsPrPsPIP¶C<sub>r</sub>PIP°C,Pë PjPsPSC-C,PsCH<sub>3</sub>PëPSPi CT<sub>r</sub>PiC-PIPIC-PrPSPsC€P<sub>μ</sub>PSPSCCT<sub>r</sub> PePsCH<sub>3</sub>PëCT<sub>r</sub>C,CH<sub>3</sub>/CH<sub>3</sub>PëP·PëPe P»C-PeP°CH<sub>3</sub>CT<sub>r</sub>CH<sub>3</sub>PePsPiPs P·P°CT<sub>r</sub>PsP±C<sub>r</sub>.**

**P<sub>3</sub>P<sub>μ</sub>CH<sub>3</sub>PjC-PS PiCH<sub>3</sub>PëPrP°C,PSPsCT<sub>r</sub>C,C-.**

**P—P°PiP<sub>μ</sub>C<sub>t</sub>P°C,P°PSPëPN<sub>2</sub> C,,P»P°PePsPS: 4 CH<sub>3</sub>PsPePë.**

**P<sub>μ</sub>C-CT<sub>r</sub>P»CT<sub>r</sub> CH<sub>3</sub>PsP·P±P°PIP»P<sub>μ</sub>PSPSCCT<sub>r</sub>: C...C-PjC-C<sub>t</sub>PSP° C- C,,C-P·PëC<sub>t</sub>PSP° CT<sub>r</sub>C,P°P±C-P»CH<sub>3</sub>PSC-CT<sub>r</sub>C,CH<sub>3</sub> PiCH<sub>3</sub>Pë P·P°CT<sub>r</sub>C,PsCT<sub>r</sub>C<sub>r</sub>PIP°PSPSC- P±C<sub>t</sub>P»P° PiCH<sub>3</sub>PsPrP<sub>μ</sub>PjPsPSCCT<sub>r</sub>,CH<sub>3</sub>PsPIP°PSP° C<sub>r</sub> CH<sub>3</sub>PsP·C<sub>t</sub>PëPSP°C... PrP»CT<sub>r</sub> C-PSC,,C<sub>r</sub>P·C-PN<sub>2</sub> (0,9 % CH<sub>3</sub>PsP·C<sub>t</sub>PëPS (PjP°CT<sub>r</sub>P°/PsP±B<sub>7</sub><sup>TM</sup> C”Pj) PSP°C,CH<sub>3</sub>C-CH C...P»PsCH<sub>3</sub>PëPrC<sub>r</sub> C,P° 5 % CH<sub>3</sub>PsP·C<sub>t</sub>PëPS (PjP°CT<sub>r</sub>P°/PsP±B<sub>7</sub><sup>TM</sup> C”Pj) PiP»CH<sub>3</sub>PePsP·Pë) PiCH<sub>3</sub>Pë C,P<sub>μ</sub>PjPiP<sub>μ</sub>CH<sub>3</sub>P°C,C<sub>r</sub>CH<sub>3</sub>C- 15B<sub>7</sub>”25 B°C PiCH<sub>3</sub>PsC,CT<sub>r</sub>PiPsPj 12 PiPsPrPëPS P°P±Ps PiCH<sub>3</sub>Pë C,P<sub>μ</sub>PjPiP<sub>μ</sub>CH<sub>3</sub>P°C,C<sub>r</sub>CH<sub>3</sub>C- 2B<sub>7</sub>”8 B°C PiCH<sub>3</sub>PsC,CT<sub>r</sub>PiPsPjB 48 PiPsPrPëPS, P·P° PSP°CT<sub>r</sub>PIPSsCT<sub>r</sub>C,C- P·P°C...PëCT<sub>r</sub>C,C<sub>r</sub> PIC-Pr CT<sub>r</sub>PIC-C,P»P°.**

**P— PjC-PeCH<sub>3</sub>PsP±C-PsP»PsPiC-C<sub>t</sub>PSPsC— C,PsC<sub>t</sub>PePë P·PsCH<sub>3</sub>C<sub>r</sub> CH<sub>3</sub>PsP·C<sub>t</sub>PëPS PiCH<sub>3</sub>P<sub>μ</sub>PiP°CT<sub>r</sub>P°C,C<sub>r</sub> PiC-PrP»CT<sub>r</sub>PiP°C” PSP<sub>μ</sub>PiP°PN<sub>2</sub>PSPsPjC<sub>r</sub> PIPëPePsCH<sub>3</sub>PëCT<sub>r</sub>C,P°PSPSC<sub>t</sub>. PiPeC%<sub>0</sub>Ps CH<sub>3</sub>PsP·C<sub>t</sub>PëPS PSP<sub>μ</sub> PIPIP<sub>μ</sub>PrP<sub>μ</sub>PSPs PsPrCH<sub>3</sub>P°P·C<sub>r</sub> PiC-CT<sub>r</sub>P»CT<sub>r</sub> PiCH<sub>3</sub>PëPiPsC,C<sub>r</sub>PIP°PSPSCCT<sub>r</sub>, C,Ps PIC-PrPiPsPIC-PrP°P»CH<sub>3</sub>PSC-CT<sub>r</sub>C,CH<sub>3</sub> P·P° C<sub>r</sub>PjPsPIPë C,P° C,P<sub>μ</sub>CH<sub>3</sub>PjC-PS P·P±P<sub>μ</sub>CH<sub>3</sub>C-PiP°PSPSCCT<sub>r</sub> CH<sub>3</sub>PsP·C<sub>t</sub>PëPSC<sub>r</sub> PrPs PjPsPjP<sub>μ</sub>PSC,C<sub>r</sub> PN<sub>2</sub>PsPiPs PIPIP<sub>μ</sub>PrP<sub>μ</sub>PSPSCCT<sub>r</sub> PSP<sub>μ</sub>CT<sub>r</sub>P<sub>μ</sub> PePsCH<sub>3</sub>PëCT<sub>r</sub>C,C<sub>r</sub>PIP°C<sub>t</sub>. PiPeC%<sub>0</sub>Ps CH<sub>3</sub>PsP·C<sub>t</sub>PëPS PiPsC,C<sub>r</sub>PIP°P»Pë PSP<sub>μ</sub> PI PePsPSC,CH<sub>3</sub>PsP»CH<sub>3</sub>PsPIP°PSPëC... C,P° PIP°P»C-PrPsPIP°PSPëC... P°CT<sub>r</sub>P<sub>μ</sub>PiC,PëC<sub>t</sub>PSPëC... C<sub>r</sub>PjPsPIP°C..., C,Ps PN<sub>2</sub>PsPiPs CT<sub>r</sub>P»C-Pr P·P±P<sub>μ</sub>CH<sub>3</sub>C-PiP°C,Pë PiCH<sub>3</sub>Pë 2B<sub>7</sub>”8 B°C PiCH<sub>3</sub>PsC,CT<sub>r</sub>PiPsPj PSP<sub>μ</sub> PrPsPIC€P<sub>μ</sub> PSC-P¶ 24 PiPsPrPëPSPë.**

**PjPjPsPIPë P·P±P<sub>μ</sub>CH<sub>3</sub>C-PiP°PSPSCCT<sub>r</sub>.**

**P—P±P<sub>μ</sub>CH<sub>3</sub>C-PiP°C,Pë PI PsCH<sub>3</sub>PëPiC-PSP°P»CH<sub>3</sub>PSC-PN<sub>2</sub> C<sub>r</sub>PiP°PePsPIC<sub>t</sub>C- PrP»CT<sub>r</sub> P·P°C...PëCT<sub>r</sub>C,C<sub>r</sub> PIC-Pr CT<sub>r</sub>PIC-C,P»P° PI PSP<sub>μ</sub>PrPsCT<sub>r</sub>C,C<sub>r</sub>PiPSPsPjC<sub>r</sub> PrP»CT<sub>r</sub> PrC-C,P<sub>μ</sub>PN<sub>2</sub> PjC-CT<sub>r</sub>CT<sub>r</sub>C- PiCH<sub>3</sub>Pë C,P<sub>μ</sub>PjPiP<sub>μ</sub>CH<sub>3</sub>P°C,C<sub>r</sub>CH<sub>3</sub>C- PSP<sub>μ</sub> PIPëC%<sub>0</sub>P<sub>μ</sub> 25 B°P<sub>3</sub>. P<sub>3</sub>P<sub>μ</sub>**

P·P°PjPsCḡPsP¶CřPI P°C,Pë.

**PkPµCÍCžPjC-CÍPSC-CÍC,CH.**

P°P°PSPëPNë P»C-PeP°CḡCÍCHPePëPNë P·P°CÍC-P± PSPµ CÍP»C-Pr P·PjC-CëCřPI P°C,Pë P·C-PSCëPëPjPë P»C-PeP°CḡCÍCHPePëPjPë P·P°CÍPsP±P°PjPë, PsPeCḡC-Pj PIPeP°P·P°PSPëC... CřCḡPsP·PrC-P»C- B«PhCÍPsP±P»PëPIC- P·P°C...PsPrPë P±PµP·PïPµPePëB».

**PJPïP°PePsPIPeP°.**

PµPs 2 PjP», 5 PjP» P°P±Ps 15 PjP» Cř C„P»P°PePsPSC-; PïPs 1 C„P»P°PePsPSCř PI PeP°CḡC,PsPSPSC-PNë PePsCḡPsP±C†C-.

**PљP°C,PµPiPsCḡC-C¶ PIC-PrPïCřCÍPeCř.**

P—P° CḡPµC†PµPïC,PsPj.

**P°PëCḡPsP±PSPëPe.**

PḡPeP°C-PrP° P°PjP±P¶/AqVida GmbH.

**PњC-CÍC†PµP·PSP°C...PsPrP¶PµPSPSC¶ PIPëCḡPsP±PSPëPeP° C,P° P°PrCḡPµCÍP° PjC-CÍC†C¶ PïCḡPsPIP°PrP¶PµPSPSC¶ PNëPsPiPs PrC-C¶P»CHPSPsCÍC,C-.**

PљP°PNëP·PµCḡ-P°C-P»CHPiPµP»CHPj-PëC,Cḡ. 89, 20355 P°P°PjP±CřCḡPi, PќC-PjPµC†C†PëPSP°/Kaiser-Wilhelm-Str. 89, 20355 Hamburg, Germany.

**P—P°C¶PIPSPëPe.**

PḡPjP°PeCÍP° P>C,Pr/Amaxa Ltd.

**PњC-CÍC†PµP·PSP°C...PsPrP¶PµPSPSC¶ P·P°C¶PIPSPëPeP°.**

31 P°P¶PsPS P†CÍP»C-Pï PŸC,CḡC-C,, P>PsPSPrPsPS SW1P 4FE, P°PµP»PëPeP° P°CḡPëC,P°PSC-C¶/31 John Islip Street, London SW1P 4FE, United Kingdom.