

P†PќPŸPŸP PЈPљP!P†Pİ

**PrP»Cİ PjPµPrPëC‡PSPsPiPs P·P°CÍC,PsCÍCíPIP°PSPSCİ P»C-PeP°CĤCÍCHPePsPiPs
P·P°CÍPs±Cí**

PћPќP”PђPђP

(ONDAAR)

PŸPeP»P°Pr:

PrC-CHC‡P° CĤPµC‡PsPIPëPSP°: PsPSPrP°PSCÍPµC,CĤPsPS;

1 C,P°P±P»PµC,PeP°, C%Ps PrPëCÍPİPµCĤPiCíC”C,CHCÍCİ PI CĤPsC,PsPIC-PNë
PİPsCĤPsP¶PSPëPSC-, PjC-CÍC,PëC,CH PsPSPrP°PSCÍPµC,CĤPsPSCí 4 PjPi P°P±Ps 8 PjPi;

PrPsPiPsPjC-P¶PSC- CĤPµC‡PsPIPëPSPë:

C,P°P±P»PµC,PePë PİPs 4 PjPi: PjP°PSC-C, (P• 421), PeCĤPsCÍPİPsPIC-PrPsPS, PİPsPIC-PrPsPS,
C†PµP»CHP»PsP·P° PjC-PeCĤPsPeCĤPëCÍC,P°P»C-C‡PSP° CÍPëP»C-PePsPSC-P·PsPIP°PSP°,
PSP°C,CĤC-CH PeCĤPsC...PjP°P»CHPiP»C-PePsP»CİC, (C,PëPİ Pђ), P°CÍPİP°CĤC,P°Pj (P• 951),
P°CĤPsPjP°C,PëP·P°C,PsCĤ B«P»PëPjPsPSB», P°CĤPsPjP°C,PëP·P°C,PsCĤ B«PђBĤ™ CİC,P°B»,
C...C-PSPsP»C-PSPsPIPëPNë P¶PsPIC,PëPNë P»P°Pe (P• 104), PeCĤPµPjPSC-CH PrC-PsPeCÍPëPr
PePsP»PsC—PrPSPëPNë P±PµP·PIPsPrPSPëPNë, PSP°C,CĤC-CH CÍC,PµP°CĤPëP»C„CíPjP°CĤP°C,,
PjP°PiPSC-CH CÍC,PµP°CĤP°C,;

C,P°P±P»PµC,PePë PİPs 8 PjPi: PjP°PSC-C, (P• 421), PeCĤPsCÍPİPsPIC-PrPsPS, PİPsPIC-PrPsPS,
C†PµP»CHP»PsP·P° PjC-PeCĤPsPeCĤPëCÍC,P°P»C-C‡PSP° CÍPëP»C-PePsPSC-P·PsPIP°PSP°,
PSP°C,CĤC-CH PeCĤPsC...PjP°P»CHPiP»C-PePsP»CİC, (C,PëPİ Pђ), P°CÍPİP°CĤC,P°Pj (P• 951),
P°CĤPsPjP°C,PëP·P°C,PsCĤ B«P»PëPjPsPSB», P°CĤPsPjP°C,PëP·P°C,PsCĤ B«PђBĤ™ CİC,P°B»,
P¶PsPIC,PëPNë P·P°C...C-Pr FCF P»P°Pe (E 110), PeCĤPµPjPSC-CH PrC-PsPeCÍPëPr
PePsP»PsC—PrPSPëPNë P±PµP·PIPsPrPSPëPNë, PSP°C,CĤC-CH CÍC,PµP°CĤPëP»C„CíPjP°CĤP°C,,
PjP°PiPSC-CH CÍC,PµP°CĤP°C,.

P»C-PeP°CĤCÍCHPeP° C„PsCĤPjP°. PŸP°P±P»PµC,PePë, C%Ps
PrPëCÍPİPµCĤPiCíCHC,CHCÍCİ PI CĤPsC,PsPIC-PNë PİPsCĤPsP¶PSPëPSC-.

PћCÍPSPsPIPS- C„C-P·PëPePs-C...C-PjC-C‡PSC- PIP»P°CÍC,PëPIPsCÍC,C-:

C,P°P±P»PµC,PePë PİPs 4 PjPi: PeCĤCíPİP»C- PrPIPsPsPİCíPeP»C- C,P°P±P»PµC,PePë
P¶PsPIC,PsPiPs PePsP»CHPsCĤCí C-P· PIPeCĤP°PİP»PµPSPSCİPjPë, PİP»P°PrPµPSCHPeC- P·
PsP±PsC... P±PsPeC-PI;

C,P°P±P»PµC,PePë PİPs 8 PjPi: PeCĤCíPİP»C- PrPIPsPsPİCíPeP»C- C,P°P±P»PµC,PePë
CÍPIC-C,P»Ps-PsCĤP°PSP¶PµPIPsPiPs PePsP»CHPsCĤCí C-P· PIPeCĤP°PİP»PµPSPSCİPjPë,

PiP»P°PrPµPSCbPeC- P· PsP±PsC... P±PsPeC-PI.

PαP°CḡPjP°PePsC,PµCḡP°PīPµPIC,PëC‡PSP° PiCḡCíPīP°.

PµCḡPsC,PëP±P»CḡPIPsC,PSC- P·P°CíPsP±Pë C,P° PīCḡPµPīP°CḡP°C,Pë, C%Ps
CíCíCíPIP°CḡC,Cḡ PSCíPrPsC,Cí. PḡPSC,P°PiPsPSC-CíC,Pë CḡPµC†PµPīC,PsCḡC-PI
CíPµCḡPsC,PsPSC-PSCí (5PḡPḡ₃). PḡPsPr PḡPḡPí Pḡ04Pḡ Pḡ01.

PαP°CḡPjP°PePsP»PsPiC-C‡PSC- PIP»P°CíC,PëPIPsCíC,C-.

PαP°CḡPjP°PePsPrPëPSP°PjC-PeP°.

PḡPµC...P°PSC-P·Pj PrC-C—

PḡPSPPrP°PSCíPµC,CḡPsPS bḡ“ CíPëP»CḡPSPsPrC-CḡC‡PëPNḡ
PIPëCíPsPePsCíPµP»PµPeC,PëPIPsPëPNḡ P°PSC,P°PiPsPSC-CíC, 5PḡPḡ₃
(CíPµCḡPsC,PsPSC-PSPsPIPëC...) CḡPµC†PµPīC,PsCḡC-PI. PµCḡPµPīP°CḡP°C,
PīPsPīPµCḡPµPrP°CíC” P°P±Ps CíCíCíPIP°C” PSCíPrPsC,Cí C- P±P»CḡPIP°PSPSCí, C%Ps
CíPīCḡPëC‡PëPSCíCḡC,CḡCíCí C†PëC,PsC,PsPeCíPëC‡PSPsCḡ
C...C-PjC-PsC,PµCḡP°PīC-C”Cḡ C,P°/P°P±Ps PīCḡPsPjPµPSPµPIPsCḡ C,PµCḡP°PīC-C”Cḡ, P°
C,P°PePsP° PīC-CíP»CíPsPīPµCḡP°C†C-PNḡPSC- PSCíPrPsC,Cí C- P±P»CḡPIP°PSPSCí.
PḡPµC...P°PSC-P·Pj PrC-C— PsPSPPrP°PSCíPµC,CḡPsPSCí PrPs PeC-PSC†Cí PSPµ
P·bḡ™ CíCíCíPsPIP°PSPëPNḡ. PḡPsP°P»PëPIPs, PīCḡPµPīP°CḡP°C, P±P»PsPeCíC”
PIPëPSPëPePSPµPSPSCí P±P»CḡPIPsC,PSPsPiPs CḡPµC,,P»PµPeCíCí, PIPëCíPIP»CíCḡC‡Pë
P°PSC,P°PiPsPSC-CíC,PëC‡PSCí PrC-Cḡ C%PsPrPs 5PḡPḡ₃-CḡPµC†PµPīC,PsCḡC-PI, CíPeC-
P»PsPeP°P»C-P·CíCḡC,CḡCíCí Cí PSPµPNḡCḡPsPSP°C... CíPe PīPµCḡPëC,,PµCḡPëC‡PSPsC—,
C,P°Pe C- C†PµPSC,CḡP°P»CḡPSPsC— PSPµCḡPIPsPIPsC— CíPëCíC,PµPjPë. PµCḡPµPīP°CḡP°C,
PSPµ P·PjPµPSC€CíC” PīCíPëC...PsPjPsC,PsCḡPSPsC— P°PeC,PëPIPsPSCíC,C- PīP°C†C-C”PSC,P°
C- PSPµ PIPëCíPIP»CíC” CíPµPrP°C,PëPIPsPSPiPs PµC,,PµPeC,Cí.

PḡPsC‡PSPëPNḡ PjPµC...P°PSC-P·Pj PePsPSC,CḡPsP»Cḡ PSCíPrPsC,Pë C- P±P»CḡPIP°PSPSCí
PSPµPIC-PrPsPjPëPNḡ. PíC-PjC-PsC,PµCḡP°PīPµPIC,PëC‡PSC- P·P°CíPsP±Pë C-
PīCḡPsPjPµPSPµPIP° C,PµCḡP°PīC-Cí PjPsP°CíC,Cḡ PIPëPeP»PëPeP°C,Pë
PIPëPIC-P»CḡPSPµPSPSCí 5HT Cí C,PsPSPePsPjCí PePëC€PµC‡PSPëPeCí,
CíC,PëPjCíP»CḡCḡC‡Pë P±P»CḡPIPsC,PSPëPNḡ CḡPµC,,P»PµPeCíC €P»CíC...PsPj
P°PeC,PëPIP°C†C-C— PIP°PīP°P»CḡPSPëC... P°C,,PµCḡPµPSC,PSPëC... PSPµCḡPIC-PI
C‡PµCḡPµP· CḡPµC†PµPīC,PsCḡPë 5HT3. PḡPSPPrP°PSCíPµC,CḡPsPS P±P»PsPeCíC”
CíC,PëPjCíP»CḡPIP°PSPSCí C†CḡPsPiPs CḡPµC,,P»PµPeCíCí. PḡPeC,PëPIP°C†C-Cí
P±P»CíPeP°CḡC‡PëC... P°C,,PµCḡPµPSC,PSPëC... PSPµCḡPIC-PI PjPsP°Pµ C,P°PePsP°
PIPëPeP»PëPeP°C,Pë PIPëPIC-P»CḡPSPµPSPSCí 5HT Cí PrC-P»CíPSC†C-, C%Ps
CḡPsP·C,P°C€PsPIP°PSP° PSP° PrPSC- C†PµC,PIPµCḡC,PsPiPs C€P»CíPSPsC‡PeP° (area
postxema), C- C†Pµ C,P°PePsP° PjPsP°Pµ CíPīCḡPëC‡PëPSPëC,Pë P±P»CḡPIP°PSPSCí
C‡PµCḡPµP· C†PµPSC,CḡP°P»CḡPSPëPNḡ PjPµC...P°PSC-P·Pj. PḡP°PePëPj C‡PëPSPsPj, PIPīP»PëPI
PsPSPPrP°PSCíPµC,CḡPsPSCí PSP° PSCíPrPsC,Cí C,P° P±P»CḡPIP°PSPSCí,
PIPëPeP»PëPeP°PSC- C†PëC,PsC,PsPeCíPëC‡PSPsCḡ C...C-PjC-PsC,PµCḡP°PīC-C”Cḡ C,P°
PīCḡPsPjPµPSPµPIPsCḡ C,PµCḡP°PīC-C”Cḡ, PNḡPjPsPIC-CḡPSPs, PīPsCíCíPSCḡC”,CḡCíCí
P°PSC,P°PiPsPSC-P·PjPsPj 5PḡPḡ₃-CḡPµC†PµPīC,PsCḡC-PI PSP° PSPµPNḡCḡPsPSP°C...,
CḡPsP·C,P°C€PsPIP°PSPëC... CíPe Cí PīPµCḡPëC,,PµCḡPëC‡PSC-PNḡ, C,P°Pe C- PI

C†PμPSC, CḡP°P»CHBPSC- PNē PSPμCḡPIPSPIC- PNē CḡPēCḡC, PμPjC-. PḡPμC...P°PSC-P·Pj PrC-C—
PīCḡPē PīC-CḡP»CḡPSPiPμCḡP°C†C- PNēPSC- PNē PSCḡPrPsC, C- C- P±P»CḡPIP°PSPSC-
PSPμPIC-PrPsPjPēPNē, PīCḡPsC, Pμ PjPμC...P°PSC-P·Pj PrC-C— PjPsPḡPμ P±CḡC, Pē
CḡC...PsPḡPēPj PSP° C, PsPNē, C%oPs CḡPīPsCḡC, PμCḡC-PiP°C”C, CHCḡCḡ PīCḡPē PSCḡPrPsC, C-
C, P° P±P»CḡPIP°PSPSC-, PIPēPeP»PēPeP°PSPēC... C†PēC, PsC, PsPeCḡPēC†PSPsCḡ
C, PμCḡP°PīC-C”Cḡ.

PḡPSPPrP°PSCḡPμC, CḡPsPS PSPμ P·PjC-PSCḡC” PePsPSC†PμPSC, CḡP°C†C-Cḡ
PīCḡPsP»P°PeC, PēPSCḡ Pī PīP»P°P·PjC- PeCḡPsPIC-.

P PsP»CH PsPSPPrP°PSCḡPμC, CḡPsPSCḡ PīCḡPē PSCḡPrPsC, C- C, P° P±P»CḡPIP°PSPSC-,
CḡPīCḡPēC†PēPSPμPSPēC... PrC-C”Cḡ PsPīC-P°C, C-PI, PrPsC, PμPīPμCḡ PSPμ
PICḡC, P°PSPsPIP»PμPSP°.

PḡP°CḡPjP°PePsPeC-PSPμC, PēPeP°.

PμC-CḡP»Cḡ PīPμCḡPsCḡP°P»CHBPSPsPiPs P·P°CḡC, PsCḡCḡPIP°PSPSCḡ
PsPSPPrP°PSCḡPμC, CḡPsPSCḡ PICḡPjPsPeC, CḡPIP°PSPSCḡ PIC-PrP±CḡPIP°C”C, CHCḡCḡ
CēPIPēPrPePs, PjC-PSC-PjP°P»CHBPSP° PīP»P°P·PjPsPIP° PePsPSC†PμPSC, CḡP°C†C-Cḡ Bḡ”
PīCḡPēP±P»PēP·PSPs 30 PSPi/PjP» Bḡ” PrPsCḡCḡPiP°C”C, CHCḡCḡ PīCḡPēP±P»PēP·PSPs
C†PμCḡPμP· 1,5 PiPsPrPēPSPē PīC-CḡP»Cḡ PIPiPμPrPμPSPSCḡ PrPsP·Pē 8 PjPi. PŸPēCḡPsPī C-
C, P°P±P»PμC, PePē P±C-PsPμPePIC-PIP°P»PμPSC, PSC- C, P° PjP°CḡC, CH P°P±CḡPsP»CḡC, PSCḡ
PīPμCḡPsCḡP°P»CHBPSCḡ P±C-PsPrPsCḡC, CḡPīPSC-CḡC, CH 60 %. P PsP·PīPsPrC-P»
PsPSPPrP°PSCḡPμC, CḡPsPSCḡ PīC-CḡP»Cḡ PīPμCḡPsCḡP°P»CHBPSPsPiPs,
PIPSCḡC, CḡC-CēPSCḡPsPIPμPSPSPsPiPs C- PIPSCḡC, CḡC-CēPSCḡPsPjBḡ™ CḡP·PsPIPSPiPs
P·P°CḡC, PsCḡCḡPIP°PSPSCḡ C” PsPrPSP°PePsPIPēPj, CḡPe C- PīPμCḡC-PsPr
PSP°PīC-PIPIPēPIPμPrPμPSPSCḡ, CḡPePēPNē CḡC, P°PSPsPIPēC, CH PīCḡPēP±P»PēP·PSPs 3
PiPsPrPēPSPē, CḡC, P°C†C-PsPSP°CḡPSPēPNē PsP±Bḡ™ C”Pj CḡPsP·PīPsPrC-P»Cḡ Bḡ”
PīCḡPēP±P»PēP·PSPs 140 P». PḡPSPPrP°PSCḡPμC, CḡPsPS PSPμ P·PjBḡ™ CḡP·CḡC”C, CHCḡCḡ P·
P±C-P»PeP°PjPē PīP»P°P·PjPē PeCḡPsPIC- (70Bḡ”76 %) C- PIPēPIPsPrPēC, CHCḡCḡ P·C-
CḡPēCḡC, PμPjPSPsPiPs PeCḡPsPIPSPsP±C-PiCḡ PīPμCḡPμPIP°PḡPSPs CēP»CḡC...PsPj
PīPμC†C-PSPePsPIPSPiPs PjPμC, P°P±PsP»C-P·PjCḡ P·P° CḡC†P°CḡC, Cḡ
C,, PμCḡPjPμPSC, P°C, PēPIC-PI. PḡPμPSCēPμ 5 % PIC-Pr PīPsPiP»PēPSPμPSPsC— PrPsP·Pē
PIPēPIPsPrPēC, CHCḡCḡ Cḡ PSPμP·PjC-PSPμPSPsPjCḡ PIPēPiP»CḡPrC- P·C- CḡPμC†PμCḡ.
PμCḡPē PIC-PrCḡCḡC, PSPsCḡC, C- C,, PμCḡPjPμPSC, Cḡ CYP2D6
(PrPμP±CḡPēP·PsC...C-PSPsPIPēPNē PīPsP»C-PjPsCḡC,, C-P·Pj) PSC-CḡPePēC... P·PjC-PS Cḡ
C,, P°CḡPjP°PePsPeC-PSPμC, PēC†C- PsPSPPrP°PSCḡPμC, CḡPsPSCḡ PSPμ
CḡPīPsCḡC, PμCḡC-PiP°C”C, CHCḡCḡ. PḡP°CḡPjP°PePsPeC-PSPμC, PēC†PSC-
PIP»P°CḡC, PēPIPsCḡC, C- PsPSPPrP°PSCḡPμC, CḡPsPSCḡ PSPμ P·PjC-PSCḡCḡC, CHCḡCḡ PīCḡPē
PīPsPIC, PsCḡPSPsPjCḡ P·P°CḡC, PsCḡCḡPIP°PSPSC-.

PḡCḡPsP±P»PēPIC- PīCḡCḡPīPē PīP°C†C-C”PSC, C-PI:

PŸC, P°C, CH

PḡPSPPrP°PSCḡPμC, CḡPsPS PīPs-CḡC-P·PSPsPjCḡ PIPiP»PēPIP°C” PSP° C†PsP»PsPIC-PeC-PI C, P°
PḡC-PSPsPe, PīCḡPēC†PsPjCḡ Cḡ PḡC-PSPsPe CḡPīPsCḡC, PμCḡC-PiP°C”C, CHCḡCḡ
P±C-P»CHCēP° CēPIPēPrPeC-CḡC, CH C- CḡC, CḡPīC-PSCḡ P°P±CḡPsCḡP±C†C-C—
PīC-CḡP»Cḡ PīPμCḡPsCḡP°P»CHBPSPsPiPs P·P°CḡC, PsCḡCḡPIP°PSPSCḡ, CḡPēCḡC, PμPjPSPēPNē
PeP»C-CḡPμPSCḡ C- PsP±CḡCḡPi CḡPsP·PīPsPrC-P»Cḡ P· CḡCḡP°C...CḡPIP°PSPSCḡPj PjP°CḡPē
C, C-P»P° P·PSPēPḡPμPSC-.

P''C-C,Pë C,P° PïC-PrP»C-C,PePë (PIC-PePsPj PIC-Pr 1 PjC-Cl'ClC†ClI PrPs 17 CËPsPeC-PI)

PJ PïPµPrC-P°C,CËPëC‡PSPëC... PïC-Cl'P»ClIpsPïPµCËP°C†C-PNëPSPëC... PïP°C†C-C''PSC,C-PI
PIC-PePsPj PIC-Pr 1 PrPs 4 PjC-Cl'ClC†C-PI (n=19) PeP»C-CËPµPSCÍ P±C†PI
PïCËPëP±P»PëP·PSPs PSP° 30 % PïPsPIC-P»CHbPSC-CëPëPNë, PSC-P¶ C† PïP°C†C-C''PSC,C-PI
PIC-PePsPj PIC-Pr 5 PrPs 24 PjC-Cl'ClC†C-PI (n=22), P°P»Pµ PrPsCËC-PIPSCHPIP°PI
PeP»C-CËPµPSCÍC† C† PïP°C†C-C''PSC,C-PI PIC-PePsPj PIC-Pr 3 PrPs 12 CËPsPeC-PI.
PµPµCËC-PsPr PSP°PïC-PIPIPëPIPµPrPµPSPSCÍ C† PïP°C†C-C''PSC,C-PI PIC-PePsPj PIC-Pr 1
PrPs 4 PjC-Cl'ClC†C-PI Cl'C,P°PSPsPIPëC,CH C† Cl'PµCËPµPrPSCbPsPjC† 6,7 PïPsPrPëPSPë
PïPsCËC-PIPSCHPIPSs P· 2,9 PïPsPrPëPSPë C† PïP°C†C-C''PSC,C-PI PIC-PePsPj PIC-Pr 5 PrPs 24
PjC-Cl'ClC†C-PI C- PIC-PePsPj PIC-Pr 3 PrPs 12 CËPsPeC-PI. P'C-PrPjC-PSPSPsCl'C,C- C†
C,,P°CËPjP°PePsPeC-PSPµC,PëC‡PSPëC... PïP°CËP°PjPµC,CËP°C... C† PïP°C†C-C''PSC,C-PI
PIC-PePsPj PIC-Pr 1 PrPs 4 PjC-Cl'ClC†C-PI C‡P°Cl'C,PePsPIPs PïPsClCÍPSCbCHC,CHCÍClI
PIPëC%PëPj PIC-PrCl'PsC,PePsPj P·P°PïP°P»CHbPSPsC— PeC-P»CHbPePsCl'C,C- PIPsPrPë C†
PSPsPIPsPSP°CËPsPrP¶PµPSPëC... C,P° PSPµPjPsPIP»ClI, C- P±C-P»CHCëPëPj
PsP±bË™ C''PjPsPj CËPsP·PïPsPrC-P»C† PIPsPrPsCËPsP·C‡PëPSPSPëC...
P»C-PeP°CËCl'CHbPePëC... P·P°Cl'PsP±C-PI, C,P°PePëC... ClIpe PsPSPrP°PSCÍPµC,CËPsPS. PJ
PïPµPrC-P°C,CËPëC‡PSPëC... PïP°C†C-C''PSC,C-PI PIC-PePsPj PIC-Pr 3 PrPs 12 CËPsPeC-PI,
ClIpeC- PïCËPsPNëCëP»Pë PïP»P°PSPsPIC† PsPïPµCËP°C†C-CH C-P· P·P°PïP°P»CHbPSPsCH
P°PSPµCl'C,PµP·C-C''CH, P°P±Cl'PsP»CHC,PSC- P·PSP°C‡PµPSPSCÍ ClIpe PeP»C-CËPµPSCÍC†,
C,P°Pe C- PsP±bË™ C''PjC† CËPsP·PïPsPrC-P»C† PsPSPrP°PSCÍPµC,CËPsPSC†
P·PjPµPSCëC†PIP°P»PëCl'ClI PïPsCËC-PIPSCHPIPSs P·C- P·PSP°C‡PµPSPSCÍPjPë C†
PrPsCËPsCl'P»PëC... PïP°C†C-C''PSC,C-PI. PhP±PëPrPIP° PïP°CËP°PjPµC,CËPë
P·CËPsCl'C,P°P»Pë P»C-PSC-PNëPSPs P·C- P·P±C-P»CHCëPµPSPSCÍPj PjP°Cl'Pë C,C-P»P° C-
PrPs 12 CËPsPeC-PI, P·PSP°C‡PµPSPSCÍ PSP°P±P»PëP¶P°P»PëCl'ClI PrPs P·PSP°C‡PµPSCb
PjPsP»PsPrPëC... PrPsCËPsCl'P»PëC.... PµPsP»Pë P·PSP°C‡PµPSPSCÍ PeP»C-CËPµPSCÍC† C-
PsP±bË™ C''PjC† CËPsP·PïPsPrC-P»C† PSPsCËPjP°P»C-P·C†PIP°P»PëCl'ClI P·P° PjP°Cl'PsCH
C,C-P»P°, P·PSP°C‡PµPSPSCÍ C†PëC... PïP°CËP°PjPµC,CËC-PI P±C†P»Pë PsPrPSP°PePsPIPëPjPë
C† CËC-P·PSPëC... PIC-PePsPIPëC... PïCËC†PïP°C.... P—P°Cl'C,PsCl'C†PIP°PSPSCÍ
PïCËPµPïP°CËP°C,C† PIC-PrPïPsPIC-PrPSPs PrPs PjP°Cl'Pë C,C-P»P° PePsPjPïPµPSCÍC†C''
PIC-PePsPIC- P·PjC-PSPë C- C'' PµC,,PµPeC,PëPIPSPëPj PïCËPë PSPsCËPjP°P»C-P·P°C†C-C—
Cl'PëCl'C,PµPjPSPsPiPs PIPïP»PëPIC† C† PrC-C,PµPNë. PµPsPïC†P»ClI†C-PNëPSPëPNë
C,,P°CËPjP°PePsPeC-PSPµC,PëC‡PSPëPNë P°PSP°P»C-P· PïCËPsPIPsPrPëP»Pë C†
PrPsP±CËPsPIPsP»CHC†C-PI (PsPSPePsP»PsPiC-C‡PSPëC... C...PIPsCËPëC...,
C...C-CËC†CËPiC-C‡PSPëC... PïP°C†C-C''PSC,C-PI C- P·PrPsCËPsPIPëC...
PrPsP±CËPsPIPsP»CHC†C-PI) PIC-PePsPj PIC-Pr 1 PjC-Cl'ClC†ClI PrPs 44 CËPsPeC-PI
PïC-Cl'P»ClI PIPSC†C,CËC-CëPSCbPsPIPµPSPSPsPiPs PIPIPµPrPµPSPSCÍ
PsPSPrP°PSCÍPµC,CËPsPSC†. P—P° CËPµP·C†P»CHC,P°C,P°PjPë P°PSP°P»C-P·C†,
Cl'PëCl'C,PµPjPSPëPNë PIPïP»PëPI (AUC) PsPSPrP°PSCÍPµC,CËPsPSC† PïC-Cl'P»ClI
PïPµCËPsCËP°P»CHbPSPsPiPs P°P±Ps PIPSC†C,CËC-CëPSCbPsPIPµPSPSPsPiPs
P·P°Cl'C,PsCl'C†PIP°PSPSCÍ C† PrC-C,PµPNë C,P° PïC-PrP»C-C,PeC-PI P±C†PI
PïPsCËC-PIPSCHPIPSPSPëPNë P· C,P°PePëPj C† PrPsCËPsCl'P»PëC..., P·P° PIPëPSCÍ,PePsPj
PrC-C,PµPNë PIC-PePsPj PIC-Pr 1 PrPs 4 PjC-Cl'ClC†C-PI. PhP±bË™ C''Pj CËPsP·PïPsPrC-P»C†
P·P°P»PµP¶P°PI PIC-Pr PIC-PeC† C- P±C†PI PSPëP¶C‡PëPj C† PrPsCËPsCl'P»PëC..., PSC-P¶ C†
PSPµPjPsPIP»ClI, C- PrC-C,PµPNë. P'PëPIPµPrPµPSPSCÍ P±C†P»Ps PïPsPIbË™ ClI·P°PSPs P·
PjP°Cl'PsCH C,C-P»P°, P° PSPµ P· PIC-PePsPj, P·P° PIPëPSCÍ,PePsPj PrC-C,PµPNë PIC-PePsPj
PIC-Pr 1 PrPs 4 PjC-Cl'ClC†C-PI. P'P°P¶PePs P·CËPsP±PëC,Pë PIPëCl'PSPsPIPsPe, C‡Pë
C-Cl'PSC†PIP°P»Ps PrPsPrP°C,PePsPIPµ P·PSPëP¶PµPSPSCÍ PeP»C-CËPµPSCÍC†,
PïPsPIbË™ ClI·P°PSPµ P· PIC-PePsPj C† PrC-C,PµPNë PIC-PePsPj PIC-Pr 1 PrPs 4
PjC-Cl'ClC†C-PI, C‡Pë C†Pµ P±C†P»Pë PïCËPëCËPsPrPSC- PIC-PrPjC-PSPSPsCl'C,C-
C‡PµCËPµP· PSPëP·CHbPeC† PeC-P»CHbPeC-Cl'C,CH PrPsCl'P»C-PrP¶C†PIP°PSPëC... C† C†C-PNë

PIC-PePsPIC-PN₆ PiC₇Cr₇PiC-. PhC₇PeC-P»CH₇PePë P₇P°C†C-C”PSC,Pë PIC-PePsPj PrPs 6
PjC-C†C₇Cl†C-PI PsC,C₇PëPjCr₇ChC,CH₇ C,C-P»CH₇PePë PsPrPSC₇ PrPsP·Cr₇ PiC₇Pë
PIPëPSPëPePSP₇PSPSC- PiC-C†P»C₇IPsPiP₇CH₇P°C†C-PN₆PSPëC... PSC₇PrPsC,Pë C,P°
P±P»C₇PIP°PSPSC₇, PN₆PjPsPIC-C₇PSPs, P·PSPëP₇PI₇PSPSC₇ PeP»C-C₇P₇PSC†C₇ PrP₇
P±C₇PrP₇ PjP°C,Pë PeP»C-PSC-C†PSPsPiPs P·PSP°C†P₇PSPSC₇.

P₇P°C†C-C”PSC,Pë P»C-C,PSCH₇PsPiPs PIC-PeC₇

P—P°PiP°P»PsPj PSP₇ P±C₇P»Ps PIPëC₇PIP»P₇PSPs PIC-PrPjC-PSPSPsC†C,P₇PN₆ C%₇PsPrPs
P±P₇P·PiP₇PePë C,P° P₇IC,,P₇PeC,PëPIPSPsC†C,C- P·P°C†C,PsC†C₇PIP°PSPSC₇
PsPSP₇P°PSC†P₇C,C₇PsPSC₇ PjPsP»PsPrPëPj PsPSPePsP»PsPiC-C†PSPëPj C...PIP₇C₇PëPj C-
PsPSPePsP»PsPiC-C†PSPëPj C...PIP₇C₇PëPj P»C-C,PSCH₇PsPiPs PIC-PeC₇, C,PsPjCr₇ PSP₇PjP°C”
PsC†PsP±P»PëPIPëC... C₇P₇PePsPjP₇PSP₇P°C†C-PN₆ C%₇PsPrPs PrPsP·Cr₇PIP°PSPSC₇ PrP»C₇
C...PIP₇C₇PëC... P»C-C,PSCH₇PsPiPs PIC-PeC₇.

Pj P₇P°C†C-C”PSC,C-PI PIC-PePsPj PIC-Pr 75 C₇PsPeC-PI PsC†C-PeC₇C”C,CH₇C†C₇
P±C-P»CH₇CëPëPN₆ PIP₇P»PëPI PsPSP₇P°PSC†P₇C,C₇PsPSC₇ PSP° C-PSC,P₇CH₇PIP°P» QTcF,
P₇PsC₇C-PIPSC₇IPSPs P· PjPsP»PsPrPëPjPë.

P₇PsC₇C₇CëP₇PSPSC₇ C,,C₇PSPeC†C-C— PSPëC₇PsPe

Pj P₇P°C†C-C”PSC,C-PI C-P· P₇PsC₇Cr₇CëP₇PSPSC₇IPjPë C,,C₇PSPeC†C-C— PSPëC₇PsPe
(PeP»C-C₇P₇PSC† PeC₇P₇P°C,PëPSC-PSC₇ 15b₇”60 PjP»/C...PI) C†PëC†C,P₇PjPSPëPN₆
PeP»C-C₇P₇PSC† C- PsP±b₇™ C”Pj C₇PsP·P₇PsPrC-P»C₇ P·PSPëP₇Cr₇ChC,CH₇C†C₇, C%₇Ps
C†PiC₇PëC†PëPSC₇C” P₇PsPjC-C₇PSP₇, P°P»P₇ PeP»C-PSC-C†PSPs PSP₇P·PSP°C†PSP₇,
P·P±C-P»CH₇CëP₇PSPSC₇ PiP₇CH₇C-PsPrC₇ PSP°PiC-PIPIPëPIP₇PrP₇PSPSC₇ (5,4 PiPsPrPëPSPë).
P”PsC†P»C-PrP₇PI₇PSPSC₇ Cr₇ P₇P°C†C-C”PSC,C-PI P· C,C₇IP₇PePsCh PSPëC₇PePsPIPsCh
PSP₇PrPsC†C,P°C,PSC-C†C,C₇, C₇PeC- PiPsC,C₇P₇P±C₇PIP°P»Pë C₇P₇PiC₇P»C₇CH₇PSPsPiPs
PiP₇PjPsPrC-P°P»C-P·C₇, P₇PsPeP°P·P°P»Ps, C%₇Ps C,,P°C₇PjP°PePsPeC-PSP₇C,PëPeP°
PsPSP₇P°PSC†P₇C,C₇PsPSC₇ PiC₇P°PeC,PëC†PSPs PSP₇ P·PjC-PSC₇C”C,CH₇C†C₇.

P₇PsC₇C₇CëP₇PSPSC₇ C,,C₇PSPeC†C-C— PiP₇C†C-PSPePë

Pj P₇P°C†C-C”PSC,C-PI P· C,C₇IP₇PePsCh PiP₇C†C-PSPePsPIPsCh
PSP₇PrPsC†C,P°C,PSC-C†C,C₇ C†PëC†C,P₇PjPSPëPN₆ PeP»C-C₇P₇PSC† PiPsPjC-C,PSPs
P·PSPëP₇Cr₇C”C,CH₇C†C₇ P· C,C₇PëPIP°P»PëPj PiP₇CH₇C-PsPrPsPj
PSP°PiC-PIPIPëPIP₇PrP₇PSPSC₇ (15b₇”32 PiPsPrPëPSPë), P° PiP₇CH₇PsC₇P°P»CH₇PSP°
P±C-PsPrPsC†C,C₇P₇PSC-C†C,C₇ PSP°P±P»PëP₇PIP°C”C,CH₇C†C₇ PrPs 100 % C†P₇CH₇P₇·
P·PjP₇PSCëP₇PSPSC₇ PiP₇CH₇P₇PrC†PëC†C,P₇PjPSPsPiPs PjP₇C,P°P±PsP»C-P·PjC₇.

P₇P»C-PSC-C†PSC- C...P°C₇P°PeC,P₇CH₇PëC†C,PëPePë.

P₇PsPeP°P·P°PSPSC₇.

P”PsC₇PsC†P»C-

PhPSP₇P°PSC†P₇C,C₇PsPS Cr₇ C,,PsC₇PjC- C,P°P±P»P₇C,PsPe, C%₇Ps
PrPëC†PiP₇CH₇PiC₇ChC,CH₇C†C₇ PI C₇PsC,PsPIC- PiPsC₇PsP₇PIPSPëPSC-,
PiC₇PëP·PSP°C†P°ChC,CH₇ PrP»C₇ P»C-PeC₇PIP°PSPSC₇ PSC₇PrPsC,Pë C,P°
P±P»C₇PIP°PSPSC₇, PIPëPeP»PëPeP°PSPëC... C†PëC,PsC,PsPeC†PëC†PSPsCh
C...C-PjC-PsC,P₇CH₇P°PiC-C”Ch C,P° PiC₇PsPjP₇PSP₇PIPsCh C,P₇CH₇P°PiC-C”Ch.

PhPSPPrP°PSCÍPµC,ChPsPS Cr C,,PsChPjC- C,P°P±P»PµC,PsPe, C%Ps
PrPëCÍPíPµChPiCrChC,ChCÍCÍ PI ChPsC,PsPIC-PNë PíPsChPsP¶PSPëPSC-,
PíChPëP·PSP°C±P°ChC,Ch PrP»CÍ PíChPsC,,C-P»P°PeC,PëPePë
PíC-CÍP»CÍPsPíPµChP°C†C-PNëPSPëC... PSCÍPrPsC,Pë C,P° P±P»ChPIP°PSPSCÍ (PµPhP´K´P´).

P°P»CÍ P»C-PeCÍPIP°PSPSCÍ PµPhP´K´P´ ChPµPePsPjPµPSPPrCÍC°C,ChCÍCÍ
PíChPëP·PSP°C±PµPSPSCÍ PsPSPPrP°PSCÍPµC,ChPsPSCÍ Cr PíPëPíP»CÍPrC-
C-PSB¶™ C°PeC†C-PNë.

P°C-C,Pë

PhPSPPrP°PSCÍPµC,ChPsPS Cr C,,PsChPjC- C,P°P±P»PµC,PsPe, C%Ps
PrPëCÍPíPµChPiCrChC,ChCÍCÍ PI ChPsC,PsPIC-PNë PíPsChPsP¶PSPëPSC-,
PíChPëP·PSP°C±P°ChC,Ch PrP»CÍ P»C-PeCÍPIP°PSPSCÍ PSCÍPrPsC,Pë C,P°
P±P»ChPIP°PSPSCÍ, PíPëPeP»PëPeP°PSPëC... C...C-PjC-PsC,PµChP°PíC-C°Ch, Cr PrC-C,PµPNë
PIC-PePsPj PIC-Pr 6 PjC-CÍCÍC†C-PI*.

P°P»CÍ PíChPsC,,C-P»P°PeC,PëPePë PµPhP´K´P´ Cr PrC-C,PµPNë PIC-PePsPj PIC-Pr 1
PjC-CÍCÍC†CÍ ChPµPePsPjPµPSPPrCÍC°C,ChCÍCÍ PíChPëP·PSP°C±P°C,Pë PíChPµPíP°ChP°C, Cr
PíPëPíP»CÍPrC- C-PSB¶™ C°PeC†C-C—.

* P—P°CÍC,PsCÍCÍPIP°PSPSCÍ PsPSPPrP°PSCÍPµC,ChPsPSCÍ PI ChC-P·PSPëC...
P»C-PeP°ChCÍChPePëC... C,,PsChPjP°C... PsPíPëCÍP°PSPs Cr ChPsP·PrC-P»C- B«PÿPíPsCÍC-P±
P·P°CÍC,PsCÍCÍPIP°PSPSCÍ C,P° PrPsP·PëB», PrPµ P·P°P·PSP°C±PµPSPs, C%Ps
P»C-PeCÍPIP°PSPSCÍ PrC-C,PµPNë C,P°P±P»PµC,PeP°PjPë ChPsP·PíPsC±PëPSP°C°C,ChCÍCÍ P·
PrPsCÍCÍPiPSPµPSPSCÍ PíP»PsC%C- PíPsPíPµChC...PSC- C,C-P»P° PrPëC,PëPSPë 0,6 Pj²,
C%Ps PíChPëP±P»PëP·PSPs PIC-PrPíPsPIC-PrP°C° 4-ChC-C±PSPsPjCr PIC-PeCÍ.

PµChPsC,PëPíPsPeP°P·P°PSPSCÍ.

P—P°CÍC,PsCÍCÍPIP°PSPSCÍ PsPSPPrP°PSCÍPµC,ChPsPSCÍ ChP°P·PsPj P·
P°PíPsPjPsChC,,C-PSCÍ PíC-PrChPsC...P»PsChPëPrPsPj PíChPsC,PëPíPsPeP°P·P°PSPµ.

PµC-PrPIPëC%PµPSP° C±CÍC,P»PëPIC-CÍC,Ch PrPs P±CÍPrChC-CÍPePsPíPs
PePsPjPíPsPSPµPSC,P° P»C-PeP°ChCÍChPePsPíPs P·P°CÍPsP±CÍ.

***P°P·P°C°PjPsPrC-CÍ P· C-PSC€PëPjPë P»C-PeP°ChCÍChPePëPjPë P·P°CÍPsP±P°PjPë C,P°
C-PSC€C- PíPëPrPë PíP·P°C°PjPsPrC-PNë.***

PhPSPPrP°PSCÍPµC,ChPsPS PSPµ PíChPëCÍPePsChChC° C- PSPµ PíP°P»ChPjCrC°
PjPµC,P°P±PsP»C-P·Pj C-PSC€PëC... PíChPµPíP°ChP°C,C-PI PíChPë PsPrPSPsC±P°CÍPSPsPjCr P·
PSPëPjPë P·P°CÍC,PsCÍCÍPIP°PSPSC-. PÿPíPµC†C-P°P»ChPSC- PrPsCÍP»C-PrP¶PµPSPSCÍ
PíPsPeP°P·P°P»Pë, C%Ps PsPSPPrP°PSCÍPµC,ChPsPS PSPµ PíP·P°C°PjPsPrC-C° P·
P°P»PePsPíPsP»PµPj, C,PµPjP°P·PµPíP°PjPsPj, C,,CÍChPsCÍPµPjC-PrPsPj,
P°P»C,,PµPSC,P°PSC-P»PsPj, C,ChP°PjP°PrPsP»PsPj, PjPsChC,,C-PSPsPj, P»C-PrPsPeP°C—PSPsPj,
C,C-PsPíPµPSC,P°P»PsPj P°P±Ps PíChPsPíPsC,,PsP»PsPj.

P—P°CÍC,PsCÍCíPIP°PSPSCII PsPSPPrP°PSCÍPμC,CĤPsPSCÍ CĤP°P·PsPj P·
P°PiPsPjPsCĤC,,C—PSCÍ PiC—PrCĤPsC...P»PsCĤPëPrPsPj PiCĤPsC,PëPiPsPeP°P·P°PSPμ,
PsCÍPeC—P»CHbPePë CÍPiPsCÍC,PμCĤC—PiP°P»PëCÍCII PIPëPiP°PrPePë CÍPëP»CHbPSPSc—
PiC—PiPsC,PμPSP·C—C— C,P° PIC,CĤP°C,Pë CÍPIC—PrPsPjPsCÍC,C— PiC—Pr C‡P°CÍ
CÍCíPjC—CÍPSPsPiPs P·P°CÍC,PsCÍCíPIP°PSPSCII.

PrPμPSC-C,PsC—PS, PeP°CḡP±P°PjP°P·PμPīC-PS C- CḡPēc,,P°PjPīC-C†PēPS

PJ PīP°C†C-C"PSC,C-PI, CḡPeC- P»C-PeCṛCḡC,CHCḡCḡ PīPsC,PμPSC†C-PNēPSPēPjPē
C-PSPrCṛPeC,PsCḡP°PjPē CYP3A4 (PSP°PīCḡPēPeP»P°Pr, C,,PμPSC-C,PsC—PSPsPj,
PeP°CḡP±P°PjP°P·PμPīC-PSPsPj C- CḡPēc,,P°PjPīC-C†PēPSPsPj), PeP»C-CḡPμPSCḡ
PsPSPrP°PSCḡPμC,CḡPsPSCṛ P·P±C-P»CHCēCṛC"C,CHCḡCḡ C- PNēPsPīPs
PePsPSC†PμPSC,CḡP°C†C-Cḡ Cṛ PeCḡPSPIC- P·PjPμPSCēCṛC"C,CHCḡCḡ.

PḡCḡP°PjP°PrPsP»

P—P° PrP°PSPēPjPē PrPμCḡPePēc... PeP»C-PSC-C†PSPēc... PrPsCḡP»C-PrPḡPμPSCḡ,
PsPSPrP°PSCḡPμC,CḡPsPS PjPsPḡPμ P·PjPμPSCēCṛPIP°C,Pē P°PSP°P»PīPμC,Pēc†PSPēPNē
PμC,,PμPeC, C,CḡP°PjP°PrPsP»Cṛ.

PhCḡPsP±P»PēPIPsCḡC,C- P·P°CḡC,PsCḡCḡPIP°PSPSCḡ.

PμCḡPē P»C-PeCṛPIP°PSPSC- PīP°C†C-C"PSC,C-PI C-P· PīCḡPsCḡPIP°PjPē
PīC-PīPμCḡC†CṛC,P»PēPIPsCḡC,C- PrPs C-PSCēPēc... CḡPμP»PμPeC,PēPIPsPēc...
P°PSC,P°PīPsPSC-CḡC,C-PI 5PḡPḡ3-CḡPμC†PμPīC,PsCḡC-PI CḡPīPsCḡC,PμCḡC-PīP°P»PēcCḡCḡ
CḡPμP°PeC†C-C— PīC-PīPμCḡC†CṛC,P»PēPIPsCḡC,C-.

P PμP°PeC†C-C—, PīPsPīBḡ™ CḡP·P°PSC- P· PrPēc...P°P»CHPSPsCḡ CḡPēcCḡC,PμPjPsCḡ,
P»C-PeCṛCḡC,CH CḡPēPjPīC,PsPjP°C,Pēc†PSPs. PhPμPrPēc†PSC- PīCḡP°C†C-PIPSPēPePē
PjP°CḡC,CH P·PIPμCḡC,P°C,Pē PSP° PSPēc... PsCḡPsP±P»PēPICṛ CṛPIP°PīCṛ,
PsCḡPeC-P»CHPePē PIPsPSPē C" PsP·PSP°PeP°PjPē CḡPμP°PeC†C-PNē PīC-PrPIPēc%PμPSPsC—
C†CṛC,P»PēPIPsCḡC,C- PSP° P»C-PeP°CḡCḡCHPePēPNē P·P°CḡC-P±.

PhPSPrP°PSCḡPμC,CḡPsPS Cṛ PrPsP·PsP·P°P»PμPḡPSC-PNē C,,PsCḡPjC- PīPsPrPsPIPḡCṛC"
C-PSC,PμCḡPIP°P» QT. P"PsPrP°C,PePsPIPs PīC-Pr C†P°Cḡ
PīC-CḡP»CḡPjP°CḡPePμC,PēPSPiPsPIPsPīPs CḡPīPsCḡC,PμCḡPμPḡPμPSPSCḡ P±CṛP»Pē
PīPsPIC-PrPsPjP»PμPSPSCḡ PīCḡPs PIPēPīP°PrPePē
C,CḡPμPjC,C-PSPSCḡ/PjPμCḡPμC...C,C-PSPSCḡ CēP»CṛPSPsC†PeC-PI (*torsade de pointes*)
PīCḡPē P·P°CḡC,PsCḡCṛPIP°PSPSC- PsPSPrP°PSCḡPμC,CḡPsPSCṛ. PḡP»C-Pr CṛPSPēPeP°C,Pē
P·P°CḡC,PsCḡCṛPIP°PSPSCḡ PsPSPrP°PSCḡPμC,CḡPsPSCṛ PīP°C†C-C"PSC,P°Pj C-P·
PICḡPsPrPḡPμPSPēPj CḡPēPSPrCḡPsPjPsPj PīPsPrPsPIPḡPμPSPSCḡ QT.
PhPSPrP°PSCḡPμC,CḡPsPS P· PsP±PμCḡPμPḡPSC-CḡC,Cḡ PīPsC,CḡC-P±PSPs
P·P°CḡC,PsCḡPsPICṛPIP°C,Pē PrP»Cḡ P»C-PeCṛPIP°PSPSCḡ PīP°C†C-C"PSC,C-PI, CḡPeC-
PjP°CḡC,CH P°P±Ps Cṛ CḡPePēc... PjPsPḡPμ CḡPsP·PIPēPSCṛC,PēcCḡCH PīPsPrPsPIPḡPμPSPSCḡ
C-PSC,PμCḡPIP°P»Cṛ QT P°P±Ps CḡPμCḡC†PμPIC- P°CḡPēc,PjC-C—, PīPeP»CḡC†P°CḡC†Pē
PīP°C†C-C"PSC,C-PI C-P· PīPsCḡCṛCēPμPSPSCḡPjPē PμP»PμPeC,CḡPsP»C-C,PSPsPīPs
P±P°P»P°PSCḡCṛ, P·P°CḡC,C-PNēPSPsCḡ CḡPμCḡC†PμPIPsCḡ PSPμPrPsCḡC,P°C,PSC-CḡC,Cḡ,
P±CḡP°PrC-P°CḡPēc,PjC-C"Cḡ, PīP°C†C-C"PSC,C-PI, CḡPeC- P»C-PeCṛCḡC,CHCḡCḡ
C-PSCēPēPjPē PīCḡPμPīP°CḡP°C,P°PjPē, C%Ps PjPsPḡCṛC,CH CḡPīCḡPēc†PēPSCḡC,Pē
PīPsPrPsPIPḡPμPSPSCḡ C-PSC,PμCḡPIP°P»Cṛ QT P°P±Ps PīPsCḡCṛCēPμPSPSCḡ
PμP»PμPeC,CḡPsP»C-C,PSPsPīPs P±P°P»P°PSCḡCṛ. PμPμCḡPμPr PīPsC†P°C,PePsPj
P·P°CḡC,PsCḡCṛPIP°PSPSCḡ PīCḡPμPīP°CḡP°C,Cṛ CḡP»C-Pr CḡPePsCḡPμPīCṛPIP°C,Pē
PīC-PīPsPeP°P»C-C"PjC-Cḡ C,P° PīC-PīPsPjP°PīPSC-C"PjC-Cḡ.

PμC-CḡP»Cḡ PsPrPSPsC†P°CḡPSPsPīPs P·P°CḡC,PsCḡCṛPIP°PSPSCḡ
PsPSPrP°PSCḡPμC,CḡPsPSCṛ C,P° C-PSCēPēc... CḡPμCḡPsC,PsPSC-PSPμCḡPīC-C†PSPēc...

РiСґРµРiР°СґР°С,С-Рi (РiРeР»СґС±Р°СґС±Рё РҰРґР—Р—РҰ Р,Р° РґР—Р—РҰРґ) Р±СґРi
РsРiРёСґР°Р°Р°Р°Р° СґРµСґРsС,РsРsС-РsРsРiРёР° СґРёРsРґСґРsРj (Сґ Р,РsРjСґ С±РёСґР»С-
Р·РjС-РsРё РiСґРёС...С-С±РsРsРiРs СґС,Р°РsСґ, РiРsСґСґСґРµРµРsРsС Р· Р±РsРёСґ
РiРµРiРµС,Р°С,РёРiРsРsС— РsРµСґРiРsРiРsС— СґРёСґС,РµРjРё Р,Р° РsРµСґРiРsРiРs-
РjРё™ СґР·РsРiС- РiРsСґСґСґРµРµРsРsС). РiРёС%Рs РsРґРsРsС±Р°СґРsРµ
Р»С-РёСґРiР°РsРsС РsРґРґР°РsСґРµС,СґРsРsРj Р,Р° С-РsСРёРёРjРё
СґРµСґРsС,РsРsС-РsРµСґРiС-С±РsРёРjРё РiСґРµРiР°СґР°С,Р°РjРё РeР»С-РsС-С±РsРs
РsР±Т'СґСґРsС,РsРiР°РsРs, СґРµРeРsРjРµРsРґСґС"С,СґСґСґ РiС-РґРiРsРiС-РґРsРµ
СґРiРsСґС,РµСґРµРµРµРsРsРsРsР° Р·Р° РiР°СґС-С"РsС,РsРj.

РґСґРeС-Р»СґРeРё РsРґРґР°РsСґРµС,СґРsРs РiРsСґР»Р°Р±»СґС
РiРµСґРёСґС,Р°Р»Сґ,РёРeСґ РeРёСґРµС±РsРёРeСґ, РiРsС,СґС-Р±РsРёР°
СґРµС,РµР»СґРsРёР° РsР°РiР»СґРґ Р·Р° РiР°СґС-С"РsС,Р°РjРё Р· РsР·РsР°РeР°РjРё
РiС-РґРiРsСґС,СґРsС— РsРµРiСґРsС...С-РґРsРsСґС,С- РeРёСґРµС±РsРёРeСґ РiС-Рґ С±Р°Сґ
Р·Р°СґС,РsСґСґРiР°РsРsС РiСґРµРiР°СґР°С,Сґ.

Рj РiР°СґС-С"РsС,С-Рi, СґРeРёРj РiСґРsРiРsРґРёС,СґСґСґ С...С-СґСґРiС-С±РsРµ
РiС,СґСґС±Р°РsРsС Рi Р°РґРµРsРsС,РsРsР·РёР»СґРsС-Р° РґС-Р»СґРsСґС-,
Р·Р°СґС,РsСґСґРiР°РsРsС РsРґРґР°РsСґРµС,СґРsРsС РґР»Сґ РiСґРsС,С-Р»Р°РeС,РёРeРё
РsСґРґРsС,Рё Р,Р° Р±Р»РiР°РsРsС РjРsРµРµ РjР°СґРeСґРiР°С,Рё РiРёРsРёРeРsРµРsРsС
РeСґРsРiРsС,РµС±С-. РҰРsРjСґ Р,Р°РeС- С...РiРsСґС- РiРsС,СґРµР±СґСґС,Сґ
СґРµС,РµР»СґРsРsРiРs РsР°РiР»СґРґ РiС-СґР»Сґ Р·Р°СґС,РsСґСґРiР°РsРsС
РsРґРґР°РsСґРµС,СґРsРsС.

Р»С-РeР°СґСґСґРeРёР° Р·Р°СґС-Р± РjС-СґС,РёС,Сґ Р°СґРiР°СґС,Р°Рj (Р· 951) Р,Р°
РjРsРµРµ РjР°С,Рё РsРµРiР°С,РёРiРsРёР° РiРiР»РёРi РsР° С...РiРsСґРёС... РsР°
С,,РµРsС-Р»РeРµС,РsРsСґСґС-Сґ.

РµРsРiС-РґРsРjР»СґР»РsСґСґ РiСґРs РiРёРiР°РґРeРё С-СґРµРjС-С— РjС-РsРeР°СґРґСґ Сґ
РiР°СґС-С"РsС,С-Рi, СґРeС- РsС,СґРёРjСґРiР°Р»Рё РsРґРґР°РsСґРµС Рj
РґРµСґРeС... РiР°СґС-С"РsС,С-Рi, РsСґРsР±Р»РiРs Сґ СґР°Р·С-
РiРsСґС,СґС-СґРsРsРiРµРsРiРs РiРiРµРґРµРsРsС, СґРёРjРiС,РsРjРё
Р·Рё™ СґРiРiРёР»РёСґС РsРґСґР°Р· РiС-СґР»Сґ РiРiРµРґРµРsРsС
РsРґРґР°РsСґРµС,СґРsРsС. РµР°СґС-С"РsС,С-Рi СґР»С-Рґ РiРsРiРµРµРiРµРiРeС,Рё РiСґРs
РsР·РsР°РeРё Р,Р° СґРёРjРiС,РsРjРё С-СґРµРjС-С— РjС-РsРeР°СґРґР°.

РҰР»С-Рґ РґРsС,СґРёРjСґРiР°С,РёСґС РsР±РµСґРµРµРsРsСґС,С- РiСґРё
Р·Р°СґС,РsСґСґРiР°РsРsС- РiРёСґРsРeРёС... РґРsР·, РsСґРsР±Р»РiРs Сґ РiР°СґС-С"РsС,С-Рi
Р· РiРµС±С-РsРeРsРiРsСґ Р,Р° РsРёСґРeРsРiРsС РsРґРґРsСґС,Р°С,РsС-СґС,Сґ,
РiРsР°СґР»С-РґРsРe РiС-РґРiРёС%РµРsРsС— СґРёР·РёРёРeСґ РeСґРjСґР»СґСґС— Р,Р°
СґРsР·РiРёС,РeСґ Р,РsРeСґРёС±РsРsСґС,С- (РjРµС,Р°Р±РsР»С-С±РsР»С-С±РsРёР° Р°СґРґРsР·).

Р"С-С,Рё

Рj РґС-С,РµР°, СґРeС- РsС,СґРёРjСґСґС,Сґ РsРґРґР°РsСґРµС,СґРsРs СґР°Р·РsРj С-Р·
РiРµРiР°С,РsС,РsРeСґРёС±РsРёРjРё С...С-РjС-РsС,РµСґР°РiРµРiС,РёС±РsРёРjРё
РiСґРµРiР°СґР°С,Р°РjРё, РiРsС,СґС-Р±РsРs СґРµС,РµР»СґРs СґС,РµРµРiРёС,Рё Р·Р°
РjРsРµРµР»РёРiРjРё РiРsСґСґСґРµРµРsРsС РjРё С,,СґРsРeСґС-С— РiРµС±С-РsРeРё.

РґСґРґРsС,Р° Р,Р° Р±Р»РiР°РsРsС, РiРёРeР»РёРeР°РsС- С...С-РjС-РsС,РµСґР°РiС-С"Сґ

РµСґРё СґРsР·СґР°С...СґРsРeСґ РґРsР·Рё Р·РiС-РґРsРs Р· РjР°СґРsСґ С,С-Р»Р°С-

P·P°CÍ'C,PsCÍ'CfPIP°PSPSC- C,CḡCHbPsC... PrPsP· C-P· 4-PiPsPrPëPSPSPëPj
C-PSC,PμCḡPIP°P»PsPj P·P°PiP°P»CHbPSP° PrPsP±PsPIP° PrPsP·P° P±CfPrPμ PIPëC%PsCḡ,
PSC-P¶ PīCḡPë P·P°CÍ'C,PsCÍ'CfPIP°PSPSC- PsPrPSC-C"C— PrPsP·Pë 5 PjPi/Pj² C- PsPrPSC-C"C—
PrPsP·Pë PīCḡPμPīP°CḡP°C,Cf PīPμCḡPsCḡP°P»CHbPSPs. PμPsCḡC-PIPSCIIP»CHbPSP°
PμC,,PμPeC,PëPIPSC-CÍ'C,CH C†PëC... PrPIPsC... CḡPμP¶PëPjC-PI PrPsP·CfPIP°PSPSCII PSPμ
P±CfP»P° PsC†C-PSPμPSP° Cf PeP»C-PSC-C†PSPëC... PrPsCÍ'P»C-PrP¶PμPSPSCII C....
PμPsCḡC-PIPSCIIPSPSCII CḡPμP·CfP»CHbC,P°C,C-PI CḡC-P·PSPëC... PrPsCÍ'P»C-PrP¶PμPSCḡ
CÍ'PIC-PrC†PëC,CH PīCḡPs PīPsPrC-P±PSCf PμC,,PμPeC,PëPIPSC-CÍ'C,CH PsP±PsC...
CḡPμP¶PëPjC-PI PrPsP·CfPIP°PSPSCII.

*P—P°CÍ'C,PsCÍ'CzPIP°PSPSCII Cz PīPμCḡC-PsPr PIP°PiC-C,PSPsCÍ'C,C- P°P±Ps
PiPsPrCzPIP°PSPSCII PiCḡCzPrPrCḡ.*

P-C-PSPePë PrC-C,PsCḡPsPrPSPsPiPs PIC-PeCz

Pj CḡP°P·C- P·P°CÍ'C,PsCÍ'CfPIP°PSPSCII PsPSPrP°PSCÍ'PμC,CḡPsPSCf P¶C-PSPeP°Pj
PrC-C,PsCḡPsPrPSPsPiPs PIC-PeCf CÍ'P»C-Pr CḡPsP·PiP»CIIIPSCfC,Pë PīPëC,P°PSPSCII PīCḡPs
PePsPSC,CḡP°C†PμPīC†C-Cḡ.

P'P°PiC-C,PSC-CÍ'C,CH

P—P° PrP°PSPëPjPë PīCḡPsPIPμPrPμPSPëC... PμPīC-PrPμPjC-PsP»PsPiC-C†PSPëC...
PrPsCÍ'P»C-PrP¶PμPSCḡ, PsPSPrP°PSCÍ'PμC,CḡPsPS PjPsP¶Pμ CÍ'PīCḡPëC†PëPSCIIC,Pë
PIP°PrPë C%PμP»PμPīPSPs-P»PëC†CHbPsPIPsC— PrC-P»CIIIPSPePë PīCḡPë
P·P°CÍ'C,PsCÍ'CfPIP°PSPSC- PīCḡPsC,CIIIPiPsPj P† C,CḡPëPjPμCÍ'C,CḡCf PIP°PiC-C,PSPsCÍ'C,C-.
P' PsPrPSPsPjCf P· PePsPiPsCḡC,PSPëC... PrPsCÍ'P»C-PrP¶PμPSCḡ, C%Ps PīPeP»CḡC†P°P»Ps
1,8 PjC-P»CHbPμPsPSP° PIP°PiC-C,PSPsCÍ'C,PμPμ, P·P°CÍ'C,PsCÍ'CfPIP°PSPSCII
PsPSPrP°PSCÍ'PμC,CḡPsPSCf Cf P† C,CḡPëPjPμCÍ'C,CḡC- P±CfP»Ps PīPsPībḡ™ CIIIP·P°PSPs P·
PīC-PrPIPëC%PμPSPëPj CḡPëP·PëPePsPj CḡPsP·C%PμPīP»PμPSPSCII PīC-PrPSPμP±C-PSPSCII
[3 PrPsPrP°C,PePsPIC- PIPëPīP°PrPePë PSP° 10000 P¶C-PSPsPe, CIIIPeC- PsC,CḡPëPjCfPIP°P»Pë
PsPSPrP°PSCÍ'PμC,CḡPsPS; CÍ'PePsCḡPëPiPsPIP°PSPëPμ PIC-PrPSPsCÍ'PSPëPμ CḡPëP·PëPe:
1,24 (95 % P"P† (PrPsPIC-CḡC†PëPμ C-PSC,PμCḡPIP°P») 1,03bḡ"1,48)].
P·PīC-PrPμPjC-PsP»PsPiC-C†PSC- PrPsCÍ'P»C-PrP¶PμPSPSCII CÍ'PμCḡC†PμPIPëC... PIP°Pr
PīPsPeP°P·CfCḡC,CH CÍ'CfPīPμCḡPμC†P»PëPIC- CḡPμP·CfP»CHbC,P°C,Pë.
P"PsCÍ'P»C-PrP¶PμPSPSCII PSP° C,PIP°CḡPëPSP°C... PSPμ PIPëCIIIPëP»Pë
CḡPμPīCḡPsPrCfPeC,PëPIPSPsC— C,PsPeCÍ'PëC†PSPsCÍ'C,C-. PhPSPrP°PSCÍ'PμC,CḡPsPS PSPμ
CÍ'P»C-Pr P·P°CÍ'C,PsCÍ'PsPICfPIP°C,Pë PīCḡPsC,CIIIPiPsPj P† C,CḡPëPjPμCÍ'C,CḡCf
PIP°PiC-C,PSPsCÍ'C,C-.

PμPμCḡC-PsPr PiPsPrCzPIP°PSPSCII PiCḡCzPrPrCḡ

P' PμPeCÍ'PīPμCḡPëPjPμPSC,P°P»CHbPSPëC... PrPsCÍ'P»C-PrP¶PμPSPSCII C... P±CfP»Ps
PīPsPeP°P·P°PSPs, C%Ps PsPSPrP°PSCÍ'PμC,CḡPsPS PīCḡPsPSPëPeP°C" Cf PīCḡCfPrPSPμ
PjPsP»PsPePs C,PIP°CḡPëPS. Pj CḡP°P·C- PSPμPsP±C...C-PrPSPsCÍ'C,C-
P·P°CÍ'C,PsCÍ'CfPIP°PSPSCII P»C-PeP°CḡCfCHbPePsPiPs P·P°CÍ'PsP±Cf CÍ'P»C-Pr
PīCḡPëPīPëPSPëC,Pë PīPsPrCfPIP°PSPSCII PīCḡCfPrPrCḡ.

PxPμCḡC,PëP»CHbPSC-CÍ'C,CH

PkPμPjP°C" C-PSC,,PsCḡPjP°C†C-C— C%PsPrPs PIPīP»PëPICf PsPSPrP°PSCÍ'PμC,CḡPsPSCf PSP°

C,,PμCḡC,PëP»CHPSC-ĆĆC,CH.

*P—PrP°C,PSC-ĆĆC,CH PIPiP»PëPIP°C,Pë PSP° C€PIPëPrPeC-ĆĆC,CH CḡPμP°PeC†C-C— PïCḡPë
PePμCḡC¿PIP°PSPSC- P°PIC,PsC,CḡP°PSCĴPïPsCḡC,PsPj P°P±Ps C-PSC€PëPjPë
PjPμC...P°PSC-P·PjP°PjPë.*

PμĆĴPëC...PsPjPsC,PsCḡPSC- C,PμĆĴC,Pë PïPsPeP°P·P°P»Pë, C%Ps PsPSPPrP°PSCĴPμC,CḡPsPS
PSPμ PIPiP»PëPIP°C” PSP° P·PrP°C,PSC-ĆĆC,CH PePμCḡCĴPIP°C,Pë PjPμC...P°PSC-P·PjP°PjPë C-
PSPμ C†PëPSPëC,CH ĴĴPμPrP°C,PëPIPSPsC— PrC-C—.

PŸPïPsĆĴC-P± P·P°ĆĴC,PsĆĴC¿PIP°PSPSCĴ C,P° PrPsP·Pë.

PŸP°P±P»PμC,PePë ĴĴP»C-Pr P·P°ĆĴC,PsĴĴPsPICĴPIP°C,Pë PsPrCḡP°P·CĴ PïC-ĴĴP»CĴ
PIPëP»ĆĴC†PμPSPSCĴ P· ĴĴPïP°PePsPIPePë.

PμPsPjC-ĆĴC,PëC,Pë C,P°P±P»PμC,PeCĴ PSP° CĴP·PëPe PrPs PïPsPIPSPsPiPs
CḡPsP·PïP°PrP°PSPSCĴ. PŸP°P±P»PμC,PeCĴ ĴĴP»C-Pr P±CḡP°C,Pë ĴĴCĴC...PëPjPë
CḡCĴPeP°PjPë.

*PĴC¿PrPsC,P° C- P±P»CḡPIP°PSPSCĴ, ĴĴPïCḡPëC†PëPSPμPSC- C...C-PjC-PsC,PμCḡP°PïC-C”Cḡ
C,P° PïCḡPsPjPμPSPμPIPsCḡ C,PμCḡP°PïC-C”Cḡ*

P”PsCḡPsĴĴP»C-

P·PjPμC,PsPiPμPSPSPëPNë PïPsC,PμPSC†C-P°P» C,PμCḡP°PïC-C— CḡP°PeCĴ PIP°CḡC-CḡC”
P·P°P»PμP¶PSPs PIC-Pr PrPsP·Pë C- PePsPjP±C-PSP°C†C-C— CḡPμP¶PëPjC-PI
C...C-PjC-PsC,PμCḡP°PïC-C— C,P° PïCḡPsPjPμPSPμPIPsC— C,PμCḡP°PïC-C—. P’PëP±C-Cḡ
CḡPμP¶PëPjCĴ PrPsP·CĴPIP°PSPSCĴ P·P°P»PμP¶PëC,CH PIC-Pr C,CĴP¶PePsĴĴC,C-
PμPjPμC,PsPiPμPSPSPsPiPs PIPiP»PëPICĴ.

P·PjPμC,PsPiPμPSPSP° C...C-PjC-PsC,PμCḡP°PïC-CĴ C,P° PïCḡPsPjPμPSPμPIP° C,PμCḡP°PïC-CĴ

P”PsP·CĴ 8 PjPi PïCḡPëPNëPjP°CḡC,CH P·P° 1Бḡ”2 PïPsPrPëPSPë PrPs
C...C-PjC-PsC,PμCḡP°PïC-C— P°P±Ps PïCḡPsPjPμPSPμPIPsC— C,PμCḡP°PïC-C—, PïPsC,C-Pj
PrPsP·CĴ 8 PjPi PïCḡPëPNëPjP°CḡC,CH PePsP¶PSC- 12 PïPsPrPëPS PïCḡPsC,CĴPiPsPj
PjP°PeCĴPëPjCĴPj 5 PrPSC-PI PrP»CĴ PïCḡPsC,,C-P»P°PeC,PëPePë PIC-PrĴĴC,CḡPsC†PμPSPsPiPs
P°P±Ps C,CḡPëPIP°P»PsPiPs P±P»CḡPIP°PSPSCĴ.

*P’PëĴĴPsPePsPμPjPμC,PsPiPμPSPSP° C...C-PjC-PsC,PμCḡP°PïC-CĴ (PSP°PïCḡPëPeP»P°Pr,
PIPëĴĴPsPeC- PrPsP·Pë C†PëĴĴPïP»P°C,PëPSC¿): ĴĴP»C-Pr P·P°ĆĴC,PsĴĴPsPICĴPIP°C,Pë
PïCḡPμPïP°CḡP°C, ĴĴ PIPëPiP»CĴPrC- PsPrPSPsCḡP°P·PsPIPsC— PrPsP·Pë PrPs 24 PjPi
PsPSPPrP°PSCĴPμC,CḡPsPSCĴ P· 12 PjPi PrPμPeCĴP°PjPμC,P°P·PsPSCĴ PSP°C,CḡC-Cḡ
C,,PsĴĴC,,P°C,Ĵ PïPμCḡPsCḡP°P»CHPSPs, P·P° 1Бḡ”2 PïPsPrPëPSPë PrPs
C...C-PjC-PsC,PμCḡP°PïC-C—.*

P”P»CĴ PïCḡPsC,,C-P»P°PeC,PëPePë PIC-PrĴĴC,CḡPsC†PμPSPsPiPs P°P±Ps C,CḡPëPIP°P»PsPiPs
P±P»CḡPIP°PSPSCĴ PïC-ĴĴP»CĴ PïPμCḡC€PëC... 24 PïPsPrPëPS
CḡPμPePsPjPμPSPPrCĴ”C,CHĴĴCĴ PïPμCḡPsCḡP°P»CHPSPμ P·P°ĆĴC,PsĴĴCĴPIP°PSPSCĴ
PïCḡPμPïP°CḡP°C,Ĵ PïCḡPsC,CĴPiPsPj PjP°PeCĴPëPjCĴPj 5 PrPSC-PI PïC-ĴĴP»CĴ PeCĴCḡCĴCĴ

$P \gg C - PeCfPIP^{\circ}PSPSCfI$.

$P \cdot P_{\mu}PePsPjP_{\mu}PSPPrPsPIP^{\circ}PSP^{\circ} PrPsP \cdot P^{\circ} PrP \gg CfI \Pi P_{\mu}CfPsCfP^{\circ}P \gg CHbPSPsPiPs$
 $P \cdot P^{\circ}CfC, PsCfCfPIP^{\circ}PSPSCfI CfC, P^{\circ}PSPsPIP^{\circ}C, CHb 8 PjPi 2 CfP^{\circ}P \cdot P^{\circ}PSP^{\circ} PrPsP \pm Cf.$

$P''C - C, P^{\circ}$

$P PsP \cdot CfP^{\circ}C \dots C^{\circ}PSPsPe PrPsP \cdot P^{\circ} PrP \gg CfI PrC - C, P_{\mu}PN_{\circ} PIC - PePsPj PIC - Pr 6 PjC - CfCfCfC - PI$
 $C, P^{\circ} PiC - PrP \gg C - C, PeC - PI PIC - PePsPj PrPs 17 CfPsPeC - PI$

$P''PsP \cdot Cf \Pi CfP_{\mu}PiP^{\circ}CfP^{\circ}C, Cf PjPsP \Pi PSP^{\circ} CfPsP \cdot CfP^{\circ}C \dots CfPIP^{\circ}C, P^{\circ} P \cdot P^{\circ} PiP \gg PsC^{\circ}P_{\mu}Cf$
 $PiPsPIP_{\mu}CfC \dots PSC - C, C - P \gg P^{\circ} P^{\circ} P \pm Ps P \cdot P^{\circ} PjP^{\circ}CfPsCf C, C - P \gg P^{\circ} PrP^{\circ}C, P^{\circ}PSP^{\circ}. P \Pi PeC^{\circ}Ps$
 $PrPsP \cdot Cf CfPsP \cdot CfP^{\circ}C \dots PsPICfCfC, CHb P \cdot P^{\circ} PjP^{\circ}CfPsCf C, C - P \gg P^{\circ}, P \cdot P^{\circ}PiP^{\circ}P \gg CHbPSP^{\circ}$
 $PrPsP \pm PsPIP^{\circ} PrPsP \cdot P^{\circ} PIP^{\circ}C^{\circ}P^{\circ} PiPsCfC - PIPSCfIPSPs P \cdot PrPsP \cdot CfPIP^{\circ}PSPSCfI Pj P \cdot P^{\circ}$
 $PiP \gg PsC^{\circ}P_{\mu}Cf PiPsPIP_{\mu}CfC \dots PSC - C, C - P \gg P^{\circ}.$

$P PsP \cdot CfP^{\circ}C \dots C^{\circ}PSPsPe PrPsP \cdot P^{\circ} P \cdot PiC - PrPSPs P \cdot PiP \gg PsC^{\circ}P_{\mu}Cf PiPsPIP_{\mu}CfC \dots PSC - C, C - P \gg P^{\circ}$
 $PrP^{\circ}C, P^{\circ}PSP^{\circ}$

$PhPSPPrP^{\circ}PSCfP_{\mu}C, CfPsPs CfP \gg C - Pr PIPiPsPrP^{\circ}C, P^{\circ} P \pm P_{\mu}P \cdot PiPsCfP_{\mu}CfP_{\mu}PrPSCfPs$
 $PiP_{\mu}CfP_{\mu}Pr C \dots C - PjC - PsC, P_{\mu}CfP^{\circ}PiC - C''Cf C \notin P \gg CfI C \dots PsPj PsPrPSPsCfP^{\circ}P \cdot PsPiPsC -$
 $PIPSCfC, CfC - C \notin PSCHbPsPiP_{\mu}PSPSPsC - C - PSb_{\text{TM}} C''PeCfC - C - Cf PrPsP \cdot C - 5 PjPi/Pj^2,$
 $PIPSCfC, CfC - C \notin PSCHbPsPiP_{\mu}PSPSP^{\circ} PrPsP \cdot P^{\circ} PSP_{\mu} PjP^{\circ}C'' PiP_{\mu}CfP_{\mu}PiP^{\circ}C^{\circ}CfPIP^{\circ}C, P^{\circ} 8 PjPi.$
 $PSP_{\mu}CfP_{\mu}P \cdot 12 PiPsPrP^{\circ}PS PjPsP \Pi PSP^{\circ} CfPsP \cdot PiPsC \pm P^{\circ}PSP^{\circ}C, P^{\circ} PiP_{\mu}CfPsCfP^{\circ}P \gg CHbPSP_{\mu}$
 $P \cdot P^{\circ}CfC, PsCfCfPIP^{\circ}PSPSCfI PiCfP_{\mu}PiP^{\circ}CfP^{\circ}C, Cf, CfPeP_{\mu} PjPsP \Pi P_{\mu} C, CfP^{\circ}PiP^{\circ}C, P^{\circ} C^{\circ}P_{\mu} 5$
 $PrPSC - PI (PrP^{\circ}PI. C, P^{\circ}P \pm P \gg P^{\circ}CfCf 1). P - P^{\circ}PiP^{\circ}P \gg CHbPSP^{\circ} PrPsP \pm PsPIP^{\circ} PrPsP \cdot P^{\circ}$
 $(CfPsP \cdot PiPsPrC - P \gg P_{\mu}PSP^{\circ} PSP^{\circ} PiCfP^{\circ}PN_{\circ}PsPjP^{\circ}) PSP_{\mu} PiPsPiP^{\circ}PSPSP^{\circ}$
 $PiP_{\mu}CfP_{\mu}PiP^{\circ}C^{\circ}CfPIP^{\circ}C, P^{\circ} PrPsP \cdot Cf PrP \gg CfI PrPsCfPsCfP \gg P^{\circ}C \dots 32 PjPi.$

$P^{\circ}P \pm P \gg P^{\circ}CfCf 1$

$P PsP \cdot CfP^{\circ}C \dots CfPSPsPe PrPsP \cdot P^{\circ} P \cdot PiC - PrPSPs P \cdot PiP \gg PsC^{\circ}P_{\mu}Cf PiPsPIP_{\mu}CfC \dots PSC - C, C - P \gg P^{\circ}$
 $PrP \gg CfI PrC - C, P_{\mu}PN_{\circ} PIC - PePsPj PIC - Pr 6 PjC - CfCfCfC - PI C, P^{\circ} PiC - PrP \gg C - C, PeC - PI$

$P_{\mu}P \gg PsC^{\circ}P^{\circ} C, C - P \gg P^{\circ}$ $PrP^{\circ}C, P^{\circ}PSP^{\circ}$	$P''P_{\mu}PSCf 1^{(P^{\circ}, P^{\pm})}$	$P''P_{\mu}PSCf 2b_{\text{TM}} 6^{(P^{\pm})}$
$< 0,6 Pj^2$	$0,5 PjPi/Pj^2$ $PIPSCfC, CfC - C \notin PSCHbPsPiP_{\mu}PSPSPs$ $CfP^{\circ}CfPsPi^* Cf PrPsP \cdot C - 2 PjPi$ $C \pm P_{\mu}CfP_{\mu}P \cdot 12 PiPsPrP^{\circ}PS$	$P^{\circ}P^{\circ}CfPsPi^* Cf PrPsP \cdot C - 2$ $PjPi PePsP \Pi PSC - 12$ $PiPsPrP^{\circ}PS$
$\geq 0,6 Pj^2 PrPs \leq 1,2 Pj^2$	$5 PjPi/Pj^2$ $PIPSCfC, CfC - C \notin PSCHbPsPiP_{\mu}PSPSPs$ $C, P^{\circ}P \pm P \gg P_{\mu}C, PeP^{\circ} Cf PrPsP \cdot C - 4 PjPi$ $C \pm P_{\mu}CfP_{\mu}P \cdot 12 PiPsPrP^{\circ}PS$	$C, P^{\circ}P \pm P \gg P_{\mu}C, PeP^{\circ} Cf$ $PrPsP \cdot C - 4 PjPi PePsP \Pi PSC -$ $12 PiPsPrP^{\circ}PS$
$> 1,2 Pj^2$	$5 PjPi/Pj^2 P^{\circ}P \pm Ps 8 PjPi$ $PIPSCfC, CfC - C \notin PSCHbPsPiP_{\mu}PSPSPs$ $C, P^{\circ}P \pm P \gg P_{\mu}C, PeP^{\circ} Cf PrPsP \cdot C - 8 PjPi$ $C \pm P_{\mu}CfP_{\mu}P \cdot 12 PiPsPrP^{\circ}PS$	$C, P^{\circ}P \pm P \gg P_{\mu}C, PeP^{\circ} Cf$ $PrPsP \cdot C - 8 PjPi PePsP \Pi PSC -$ $12 PiPsPrP^{\circ}PS$

* $P - P^{\circ}CfC, PsCfPsPICfC''C, CHbCfCf C - PSC \notin P^{\circ}PN_{\circ} P \gg C - PeP^{\circ}CfCfCHbPeP^{\circ}PN_{\circ} P \cdot P^{\circ}CfC - P \pm,$
 $C^{\circ}Ps PjC - CfC, P^{\circ}C, CHb PsPSPPrP^{\circ}PSCfP_{\mu}C, CfPsPs Cf PIP^{\circ}PiP \gg CfI PrC - CfP^{\circ}CfPsPiCf.$

P±. P—P°PiP°P»CHbPSP° PrPsP±PsPIP° PrPsP·P° PSPµ PîPsPIPëPSPSP°
PîPuCHPuPIPëC%CrPIP°C,Pë PrPsP·Cr PrP»CII PrPsCHPsCÍP»PëC... 32 PjPi.

$$PuP^{\circ}C\uparrow C-C''PSC,PeP\cdot PSP\ddot{e}C\uparrow PePsPIPsC\uparrow PSP\mu PrPsC\uparrow C,P^{\circ}C,PSC-C\uparrow C,C\uparrow$$

PhPSPPrP°PSCÍPµC,ChPsPS PíPsPrPsPIP¶CíC” C-PSC,PµChPIP°P» QT P·P°P»PµP¶PSPs PIC-Pr
PrPsP·Pë. PJ ChP°P·C- PíPµChPµPrPsP·CíPIP°PSPSCÍ ChPµPePsPjPµPSPPrCíC”C,ChCÍCÍ
PíChPsPIPµPrPµPSPSCÍ P·PµP”-PjPsPSC-C,PScHjPëSPiCí.

P”C-C,Pë

PµPsPIC-PrPsPjP»CÍP»PScÍCÍ PíChPs PIPëPíP°PrPePë CÍPµChPsC,PSPSC-PSPsPIPsPiPs
CÍPëPSPPrChPsPjCí Cí PrC-C,PµPNë PíC-CÍP»CÍ PSPµPSP°PIPjPëCÍPSPsPiPs
PíPµChPµPrPsP·CíPIP°PSPSCÍ PsPSPPrP°PSCÍPµC,ChPsPSCí PíPµChPsChP°P»ChPSPs
(PíPµChPµPIPëC%PëP»P° ChPsP·ChP°C...CíPSPePsPICí PrPsP·Cí 4 PjPi/PePi) Cí
PSPµPjPsPIP»CÍC, C,P° PrC-C,PµPNë PIC-PePsPj PIC-Pr 12 PjC-CÍCÍC†C-PI PrPs 2 ChPsPeC-PI.

P>C-PeCíPIP°PSPSCÍ

PŸPíPµC†PëC,,C-C†PSPsPiPs P°PSC,PëPrPsC,Cí PSPµ C-CÍPSCíC”, C,PSPjCí Cí
PIPëPíP°PrPeP°C... PíPµChPµPrPsP·CíPIP°PSPSCÍ PSPµPsP±C...C-PrPSPs
P·P°CÍC,PScÍPsPICíPIP°C,Pë CÍPëPjPíC,PSPjP°C,PëC†PSCí C,P°
PíC-PrC,ChPëPjCíPIP°P»ChPSCí C,PµChP°PíC-Ch.

P—P°CÍC,PScÍCíPIP°PSPSCÍ C-PíPµPeP°PeCíP°PSPë PrP»CÍ P>C-PeCíPIP°PSPSCÍ
PíPµChPµPrPsP·CíPIP°PSPSCÍ PsPSPPrP°PSCÍPµC,ChPsPSCí PSPµ
ChPµPePsPjPµPSPPrCíC”C,ChCÍCÍ, PsCÍPeC-P»ChPePë C—C— PrC-CÍ PSPµ PjPsP¶Pµ
PIPëCÍPIPëC,PëCÍCÍ C†PµChPµP· P°PSC,PëPµPjPµC,PëC†PSPëPNë PIPíP»PëPI
PsPSPPrP°PSCÍPµC,ChPsPSCí.

PµPsP±C-C†PSC- ChPµP°PeC†C-C—.

PµPsP±C-C†PSC- ChPµP°PeC†C-C—, PSP°PIPµPrPµPSC- PSPëP¶C†Pµ,
PeP»P°CÍPëC,,C-PePsPIP°PSC- P·P° PsChPiP°PSP°PjPë C- CÍPëCÍC,PµPjP°PjPë C,P° P·P°
C†P°CÍC,PSc,PScH PIPëPSPëPePSPµPSPSCÍ. P—P° C†P°CÍC,PSc,PScH PIPëPSPëPePSPµPSPSCÍ
PíPsP±C-C†PSC- ChPµP°PeC†C-C— ChPsP·PíPsPrC-P»PµPSPs PSP° C,P°PeC-
PeP°C,PµPiPsChC-C—: PrCíP¶Pµ C†P°CÍC,Ps (≥1/10), C†P°CÍC,Ps (≥1/100 C,P° <1/10),
PSPµC†P°CÍC,Ps (≥1/1000 C,P° <1/100), ChC-PrPePs (≥1/10000 C,P° <1/1000), PrCíP¶Pµ
ChC-PrPePs (<1/10000). P”CíP¶Pµ C†P°CÍC,C-, C†P°CÍC,C- C,P° PSPµC†P°CÍC,C-
PíPsP±C-C†PSC- ChPµP°PeC†C-C— P±CíP»Pë P·P°PíP°P»PsPj PIPëCÍPIP»PµPSC- Cí
PeP»C-PSC-C†PSPëC... PrPsCÍP»C-PrP¶PµPSPSCÍC.... P C-PrPeC- C,P° PrCíP¶Pµ ChC-PrPeC-
PíPsP±C-C†PSC- ChPµP°PeC†C-C— PI PsCÍPSPsPIPsPjCí P±CíP»Pë PIPëCÍPIP»PµPSC- Cí
PíC-CÍP»CÍChPµC”CÍC,ChP°C†C-PNëPSPëPNë PíPµChC-PsPr.

PµChPsC,,C-P»Ch PíPsP±C-C†PSPëC... ChPµP°PeC†C-PNë Cí PrC-C,PµPNë C,P°
PíC-PrP»C-C,PeC-PI P±CíPI C,P°PePëPj P¶Pµ, CÍPe C- Cí PrPsChPsCÍP»PëC....

P— P±PsPeCé C-PjCéPSPSPsC— CÍPëCÍC,PµPjPë: ChC-PrPePs bH” ChPµP°PeC†C-C—
PíC-PrPIPëC%PµPSPsC— C†CíC,P»PëPIPsCÍC,C- PSPµPiP°PNëPSPsPiPs C,PëPíCí, C-PSPePsP»Pë
C,CÍP¶PeC-, P°P¶ PrPs P°PSP°C,,C-P»P°PeCÍC-C—.

P— P±PsPeCé PSPµChPIPsPIPsC— CÍPëCÍC,PµPjPë: PrCíP¶Pµ C†P°CÍC,Ps bH”
PíPsP»PsPIPsPëPNë P±C-P»Ch; PSPµC†P°CÍC,Ps bH” CÍCíPrPsPjPë, ChCíC...PsPIC-
PíPsChCíC¶PµPSPSCÍ (PIPeP»ChC†P°ChC†Pë PµPeCÍC,ChP°PíC-ChP°PjC-PrPSC-

PJPiPsPIPë P·P±PμCḦC-PiP°PSPSCı.

P—P±PμCḡC–PiP°C,Pë PïCḡPë C,PμPjPïPμCḡP°C,ĆCḡC– PSPμ PIPëC‰Pμ 30 B°PŸ PI
PsCḡPëPiC–PSP°P»CḤPSC–PN̄ ĆPïP°PePsPIC†C–.

P—P±PμCḡC–PiP°C,Pë Ć PSPμPrPsĆC,ĆPïPSPsPjĆ PrP»Cḡ PrC–C,PμPN̄ PjC–ĆC†C–.

PJPïP°PePsPIPëP°.

PμPs 10 C,P°P±P»PμC,PsPe Ć P±P»C–ĆC,PμCḡC–, PïPs 1 P±P»C–ĆC,PμCḡĆ PI
PeP°CḡC,PsPSPSC–PN̄ ĆPïP°PePsPIC†C–.

PḡP°C,PμPiPsCḡC–Cḡ PIC–PrPïĆĆPeĆ.

P—P° CḡPμC†PμPïC,PsPj.

P’PëCḡPsP±PSPëPe.

PḡP°PSPëP°PN̄PSP† PᄋP°CḡPjP° P>C–PjC–C,PμPr, P®PSC–C,-II.

**PḡC–ĆC†PμP•PSP°C...PsPrP¶PμPSPSCḡ PIPëCḡPsP±PSPëPeP° C,P° P°PrCḡPμĆP°
PjC–ĆC†Cḡ PïCḡPsPIP°PrP¶PμPSPSCḡ PN̄PsPiPs PrC–CḡP»CḤPSPsĆC,C–.**

P’C–P»PμPrP¶ PḡC–C€P°PSPïĆCḡP°, Pμ.Pḡ. P”P¶P°PjPSC–PIP°P»P°, PŸPμC...ĆC–P»
PμP°PsPSC,P° PŸP°C...C–P±, P”C–ĆC,CḡC–PeC, PŸC–CḡPjPsĆCḡ 173025, PḡC–PjP°C‡P°P»
PμCḡP°PrPμC€, P†PSP†C–Cḡ.

P—P°CḡPIIPSPëPe.

PḡPḡP PᄋPḡP PḡPḡ PᄋP—P>P>PŸ

AAR PHARMA FZ-LLC

PḡC–ĆC†PμP•PSP°C...PsPrP¶PμPSPSCḡ P•P°CḡPIIPSPëPeP°.

PμCḡPëPjC–C‰PμPSPSCḡ 702, 7-PN̄ PïPsPIPμCḡC..., P’ĆPrC–PIP»Cḡ: P”C–P•ĆPŸC–
PŸP°ĆPμCḡ, Pï/Ć вḡ“ 478837, P”ĆP±P°PN̄, PḡP±вḡ™C”PrPSP°PSC– PḡCḡP°P±ĆCḤPeC–
P•PjC–CḡP°C,Pë.

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